



RESEARCH AND SCIENCE TODAY

~ Scientific Review ~

~Spring~

**No. 1(19)/2020
March 2020**

**ISSN-p: 2247 – 4455
ISSN-e: 2285 – 9632
ISSN-L: 2247 – 4455**

Târgu-Jiu 2020

Cover: Batcu Alexandru

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CONSIDERATIONS REGARDING THE SECURITY EQUATION DETERMINED BY THE PROBLEMATICS OF REFUGEES IN THE MIDDLE EAST

Cătălin PEPTAN¹

ABSTRACT:

THE AUTHOR ADDRESSES A TOPICAL ISSUE AT EUROPEAN LEVEL, NAMELY THE EVOLUTION OF THE SECURITY EQUATION AT THE CONTINENTAL LEVEL DETERMINED BY THE NEW WAVE OF REFUGEES FROM THE MIDDLE EAST. IN ORDER TO UNDERSTAND THE PHENOMENA ASSOCIATED WITH THE PROBLEM, WE REVIEW THE SECURITY CLIMATE IN THE MIDDLE EAST AT THE END OF THE TWENTIETH CENTURY AND THE BEGINNING OF THE TWENTY-FIRST CENTURY, MAINLY DETERMINED BY THE MANIFESTATION OF AN INCREASING HOSTILITY OF NATIONALISM AND THAT CONECTED WITH ARABIA, AGAINST THE SERIOUS PROBLEMS, WITH DIFFERENT CAUSALITY, WHICH ARE FOUND IN MOST COUNTRIES IN THE REGION, WHICH HAVE POTENTIATED THE TERRORIST PHENOMENON, AFFECTING THE ECONOMIC AND SECURITY OF MANY STATES IN THE REGION AND GENERATING A NEW SECURITY THREAT, RESPECTIVELY THE PHENOMENON OF ILLEGAL MIGRATION OF IMPORTANT GROUPS PEOPLE OF ISLAMIC RELIGION TO THE WESTERN COUNTRIES OF THE OLD EUROPEAN CONTINENT.

THE AUTHOR ADDRESSES THE ISSUES WICH ARISES FROM THE RECENT DECISIONS OF THE AUTHORITIES IN ANKARA TO OPEN NATIONAL BORDERS TO ALLOW REFUGEES ON THE TERRITORY OF TURKEY TO TRAVEL TO DESTINATIONS IN THE EUROPEAN UNION, DOING A GEOPOLITICAL ANALYSIS OF THE CAUSES THAT HAVE GENERATED THE STATE OF AFFAIRS, OF THE MEASURES THAT ARE REQUIRED IN ORDER TO MANAGE THE SITUATION AND THE POSSIBLE CONSEQUENCES IN SECURITY AT EUROPEAN LEVEL.

KEY WORDS: TERRORISM, GLOBALIZATION, CRIME, MIGRATION, REFUGEE, THREAT, SECURITY.

GENERAL CONSIDERATIONS REGARDING THE MIDDLE EAST

The Middle East, historically speaking, has always been characterized by instability and unpredictability - a fact that has led specialists to often consider it a „volcano in activity of geopolitics (...) whose uninterrupted eruptions (...) destabilizes the region (...) and makes it the most virulent outbreak of religious, civil and/or interstate and terrorist wars ”², and viewed from a cultural, economic and political perspective, it is a geographical area of geopolitical interference with an exceptional strategic significance, which represents the

¹ Lecturer, „Constantin Brâncuși” University Târgu Jiu

²Pascal, Lamy, Nicole, Gnesotto, Jean-Michel Baer, Where is the world going ?, (Bucharest: Niculescu Publishing House, 2018), 105.

intersection of the political interests of the current world powers.³

The end of the twentieth century and the beginning of the 21st century⁴ was marked by the deterioration of the security climate in the Middle East, the main cause being what we generically call the end of the bipolar international order and the transition to the „new multipolar international order”, although much the clamored creation, with the support and direct involvement of the great global powers, of the "New Middle East" fails to solve the historical problems that the region continues to face⁵.

Therefore, we are witnessing an increasing hostility of nationalism and pan-Arabism, which has caused many Muslims to return to the original Islam, to radical instrumentalized militantism, often from political Islam⁶ characterized by an exceptional social mobilization potential, explainable by the toxic mix between politics and religion, but also by not accepting the stakes of modernization and the values of Western democracy, Islamism is still the foundation of civilization of the same name, expanding on the same multisecular principles. These realities were determined by multiple causes, such as: the policies of authoritarian-totalitarian regimes that violated citizens' rights and freedoms; non-performing governance marked by corruption; the slow pace of economic development, with direct consequences on rising unemployment and inflation; widening the gap between the poor and the rich; population growth, lack of education and lack of young people's perspective of a normal life.⁷ The reactions of the government authorities, in many countries of the Middle East, to the unresolved social problems, generated extreme protest movements, which affected the socio-economic life and the security of the region. At the same time, they have generated the favorable context of the reappearance and manifestation of terrorism, with a new proteiform morphology, enhanced, more than ever, by the rigor and incisiveness of ideologies with great non-cultural capacity, even if they are not characterized by an ideological or normative corpus that will explain to the followers the reality and/or the social rules, well known being the fact that terrorism is nourished by a real „hate incubator”, which has contextualizing elements of social, economic, political and cultural nature.⁸

Terrorism in the Middle East has gained, over the last decade⁹, the valence of a phenomenon, with "diffusion" tendencies to other geographical areas in nearby Africa, old Europe or far America, transforming some regions of the world into a true modern jungle, in which the criminals have no rule knowing only to kill, although, at the end of 2017, the Iraqi authorities announced the „end of the war against the Islamic State” and the destruction of the group and¹⁰, in March 2019, the Syrian authorities announced that "Syrian democratic forces

³Cătălin, Peptan, *Terrorism. Events and developments in the hot areas of the world. Middle East. Asia. Africa*, (Târgu Jiu: Academica Brâncuși Publishing House, 2019), 53.

⁴ Flavius Cristian Marceau, Mihaela Andreea Ciorei, „The vision about international security at the beginning of the XXI century”, in *European Scientific Journal*, april 2013 edition vol.9, no.11, 301-311

⁵ Flavius Cristian Mărcău, Mihaela Andreea Ciorei, „The role of intelligence in the fight against terror,” in *European Scientific Journal*, IX (2013), no. 2, p. 1-11

⁶ Anoushiravan, Ehteshami, *Globalization and Geopolitics in the Middle East Old Games, New Rules*, (London, Routledge, 2007), 90.

⁷ Cătălin, Peptan, *Terrorism. Events and developments in the hot areas of the world....*, 55-56

⁸ Serkan, Tasgin, Taner, Cam, „Reasons for Terrorism in the Middle East”, în Alexander R. Dawoody (editor), *Eradicating Terrorism from the Middle East Policy and Administrative Approaches*, Springer, 2016, pg. 86.

⁹ Flavius Cristian Mărcău, Mihaela Andreea Ciorei, *The role of intelligence in the fight against terror....*, 1-11

¹⁰<https://www.ziare.com/international/status-islamic/2017-anul-prabusirii-califat-statul-islamic-1495057/> accessed 18.09.2019.

declare total elimination of the so-called caliphate and 100% territorial defeat of ISIS ”¹¹. In this context, the arab world has become a real „theater of military operations” that has deeply affected the economic and security situation of many states in the region, generating a new security threat, respectively the phenomenon of illegal migration of important groups of people of Islamic religion, to the Western countries of a old European continent.

THREATENING OF ILLEGAL MIGRATION - THE "WEAPON" IN THE MIDDLE EAST

The wave of migrants from the countries of the Middle East, followers of the Islamic religion, which overturned Western Europe in the second half of the past decade, represents the climax of a broader process that has been steadily unfolding since the end of the second world conflagration, currently constituting , one of the potential sources of conflict between the Christian and the Muslim civilization, respectively between the two societies, Christian and Muslim, which are in a relationship „continuously deep in conflict (...), intense rivalry and hectic war of different degrees”.¹²

Serious economic, social and political problems in countries such as Syria, Iran, Iraq or Afghanistan are at the origin of waves of migrants leaving their country of origin and leaving for the unknown, looking for a job and a new home. for the young and their large family, where religious life heats, towards an aging Europe, preoccupied to renounce its origins, to detach from Christianity and to appear as a secular one. A first temporary destination is Turkey, since there are no alternative options for the migrant groups in the countries mentioned, taking into account the political and economic particularities of the countries of the Middle East or the official positions of the authorities of the western countries and of the civil society which, through various mechanisms, resort to practices of deterring and harassing migrants.¹³ Although Turkey is considered „an island of peace in the region in which it is located, because it is a shelter and conscience of humanity”¹⁴ and praises its role as the „core state” of Islamic civilization¹⁵, the recent military incursions of the Turkish army since October 2019, from northern Syria, known under the generic name of "Peace Spring", with the stated purpose of eliminating terrorist elements in the border area¹⁶, worsened the security situation in the region, with more and more important voices saying that any plan to appease the social and political system and to keep peace in the Middle East must be designed in accordance with the geo-security profile of the region.¹⁷

The increase of the Turkish-Syrian conflict, with support from Turkish authorities¹⁸ of Islamist rebels in northern Syria's Idlib region, in the fight against Syrian President Bashar al-Assad's armed forces, followed by their retaliatory measures in February 2020, reinforces

¹¹https://www.adevarul.ro/international/in-lume/statului-islamic-ras-fata-pamantului-siria-1_5c95ec51445219c57e9038d4/index.html; accessed 15.11.2019.

¹²Samuel, Huntington, *Clash of Civilizations and the Restoration of the World Order*, (Bucharest: Litera Publishing House, 2019), 383.

¹³<https://www.trt.net.tr/romana/programs/2019/07/30/turcia-si-migratia-ieri-astazi-maine-1245110/> accessed 07.03.2020., point of view expressed by prof.dr . Kudret BÜLBÜL, Dean of the Faculty of Political Science at Yildirim Beyazid University in Ankara.

¹⁴<https://www.trt.net.tr/romana/programs/2019/07/30/turcia-si-migratia-ieri-astazi-maine-1245110/> accessed 07.03.2020

¹⁵ Samuel, Huntington, *Clash of Civilizations and the Restoration of the World Order*, 327-328.

¹⁶ Kurdish militias and ISIS cells, motivated by the need to "restore peace and peace in Syria".

¹⁷ Ece Temelcura, *Turkey, between madness and melancholy*, Corint Books, Bucharest, 2017, pp. 259-261.

¹⁸ According to authorities, Turkey wants to create a buffer zone in which to surround the approximately 3.5 million Syrian refugees currently in its territory.

the security equation in the East it creates and creates the premises for a large military confrontation, if we analyze in depth the nature of this conflict, the causes of its escalation and the risks it generates at the regional level. In fact, Sunni Turkey re-Islamized under President Erdoğan's „hidden Islamist agenda, concealed under pro-European discourse”¹⁹, backs Sunni Islamist forces in the region, while Syrian authorities, backed by Shiite allies in Iran and Russia, appear to be victorious in the civil war in Syria.

In context, despite international agreements, which regulate the issue of refugees on the territory of Turkey, to which it is a part, the authorities in Ankara declared, during February 2020, that the conflict in the Idlib region would not be resolved and that the Syrian army's attacks on military Turkish capabilities would cease. Turkish military will determine to open the borders of Syrian refugees in Turkey so that they can move to destinations in western Europe, the ruling party in Ankara declaring that "our refugee policy is the same, but here we have a serious situation. we can keep them in place".²⁰ Also worth mentioning are Turkey's intentions, expressed at the end of 2019, for the repatriation of ISIS fighters detained in Turkish prisons, on the grounds that „Turkey is not a tourist hotel”²¹. This creates the premises for a new wave of migrants to destinations in the western part of the European continent, including elements that belong to or embrace ideologies and conceptions specific to terrorist groups, if we consider that, according to the authorities in Ankara on Turkish territory over 3.6 million Syrian refugees and other nationalities are cantoned, who refuse to return to their native country, their supreme goal being the joy of freedom in a western country where they enjoy the respect of citizens' rights and have real chances to a prosperous, free and respectable life.

ROAD TO EUROPE - A RISK TAKEN BY THE ACTORS INVOLVED

The first day of the calendar spring of 2020 was marked by an avalanche of news from news agencies in Europe and the Middle East, which were announcing the statements of Turkish Minister of Internal Affairs, Suleyman Soyly, according to which Turkey would open in Edirne the crossing points, of the border to Greece and Bulgaria, allowing 76,385 Syrian refugees to move to European Union countries, at the same time, threatening to allow a new influx of Syrian refugees to pass if they do not get concrete support from international bodies in the conflict in northern Syria²². It is worth noting that Turkey has motivated these decisions by the inability to cope with a new wave of Syrian refugees from the Idleb region, following the offensive launched by the Damascus authorities.

¹⁹ Carmen Gavriluță, *Revolt of the Orient*, (Iași: Polirom Publishing House, 2013), 257.

²⁰ <https://www.dw.com/en/extraordinare-nato-după-escaladarea-sitiei-din-siria/a-52572751/> accessed 08.03.2020.

²¹ <https://www.dw.com/en/commentary-game-of-puters-in-the-supporters-isis-repatriators/a-51213795/> accessed 19.11.2019.

²² <https://www.digi24.ro/stiri/actualitate/turcia-sustine-ca-a-lasat-75-000-de-migranti-sa-treaca-frontiera-cu-ue-harta-cu-traseul-refugiatilor-passing-through-the-middle-of-Romania-1268534/> / accessed 08.03.2020.



Figure 1. Syrian refugee travel routes

In the context, Turkish news agencies²³ have published the map of possible Syrian refugee travel routes (figure 1) from the Syrian province of Idlib, estimated at around one million, to Western Europe, listing Greece, Bulgaria, Romania and Hungary as transit countries to the final destination.

So far, an alarming situation, regarding the refugee crisis, has been found in the Greek island of Lesbos, the geographical area considered the traditional host of refugees since the 1990s, when they came mainly from the former Yugoslavia, the scene of an abominable civil war. Today, the large number of refugees, encamped in specially equipped camps, have led human rights activists to report that the situation on the islands of Lesbos, Chios and Samos has become unbearable for both locals and immigrants, and that coherent measures should be taken to managing the situation.²⁴ Considered to be just transit locations, within a time horizon that cannot be estimated with certainty, the Greek islands will be left by refugees who, in their quest to reach Western Europe, have as an alternative variant the Italian peninsula, the geographical area marked by the COVID -19 epidemic, which caused the Italian authorities to take the army out into the street in order to „hermetize” the entire national territory. Against this background it is almost certain that the Italian authorities will not allow the penetration of waves of migrants on the national territory that could further affect the social problems that characterize the peninsula, as they have to look for other possibilities to reach the final destination.

Another variant of displaced refugees currently on the territory of Turkey, upheld by the media from Ankara, also includes the territory of Romania, which requires the adoption by the national authorities of pragmatic response strategies, able to reduce the threats to our country and to generate, internationally, the image of a security exporting state and not a generator of security risks. This scenario reconfirms the idea conveyed during the migration crisis of 2014-2016, according to which Romania, although not traditionally confronting with

²³<https://www.english.alarabiya.net/en/media/television-and-radio/2020/02/29/Turkish-state-owned-TRT-Arabic-posts-map-showing-refugees-path-to-France.html?Fbclid=IwAR3uEyzE4WhiN4teDjglTlgg0HYCcXbhfPDB0WAjmYPmowbRzE36jjMR5M> / accessed 08.03.2020.

²⁴<https://www.dw.com/en/criza-refugiaatii-in-grecia-situatiea-se-agravata-pelesbos/a-52605453> accessed 08.03.2020.

a significant number of illegal migration cases, is a transit area preferred by organized crime groups specialized in illegal migration. In this way, risk factors and vulnerabilities for the security of Romania can be generated, such as: non-compliance with the specific legislation of border crossing and difficulty in identification of migrants; infiltration of terrorist elements or organized crime into migrant groups; dissemination on the national territory of biological risk factors that can affect the health of the population and last but not least affect the national budget by allocating additional human and material capacities necessary for the optimal management of migrants (accommodation and feeding costs of migrants, expenses with medical assistance, providing translators in refugee camps, costs related to community integration, etc.). On this issue, the former president of Romania, Traian Basescu, recently stated that Romania is not prepared to face a migratory flow and that the possible consequences in the security plan of entering their national territory can be disastrous.

Regardless of the travel route targeted by the refugees, in their efforts to move to western Europe, the reactions of the affected European states have been strong, especially in the context in which Turkey has signed with the European Union an agreement²⁵ that undertakes to control the flows of illegal migrants, in exchange for receiving funds and accelerating the process of joining the Union.

If, in the middle of the last decade, Germany, aged and with a large labor deficit, has opened its gates and received about one million migrants, today Chancellor Angela Merkel considers unacceptable the „pressure put by Turkey on the European Union” by opening border points on the border with Greece and is opposed to receiving a new wave of refugees on the territory of Germany, which would fuel the revival of the extreme right and would worsen the internal security equation.²⁶ The solution proposed by the German Chancellor refers to the observance of the agreement concluded in 2016 between the European Union and Turkey aimed at obstructing the movement of migrants to western Europe.

On the other hand, the President of France, Emanuel Macron for avoiding a humanitarian crisis caused by the problems of migrants in Turkey, urging joint European efforts to help quickly and to protect the borders of Greece and Bulgaria. A similar view was also expressed by the President of the European Commission, Ursula von der Leyen, who announced that the European Union will support Greece and Bulgaria through Frontex at land borders²⁷, intending to determine the management of the problem at the level of state entities in the vicinity of the area, cantoning them. The position of the Austrian Chancellor Sebastian Kurz recommends solidarity with regard to convergent actions to strengthen the protection of the external borders of the European Union, in order to prevent the recurrence of a migrant crisis on the European continent similar to the one of the previous decade.

A realistic approach to the issues under discussion belongs to MEP Traian Băsescu, who proposes to the international community three essential elements for managing the phenomenon of illegal migration, namely: the signing by the European Union of readmission agreements with the countries of origin of migrants, the establishment by the European Union Collaboration agreements with the authorities of the countries of transit to counter the networks of organized cross-border crime involved in the trafficking of illegal migrants and the surveillance of the traffic on the North Coast of Africa or the East Mediterranean towards

²⁵Through the agreement concluded in 2016, the European Union has committed to grant Turkey 6 billion euros, of which 3.2 billion have been paid so far.

²⁶<https://24-ore.ro/2020/03/02/angela-merkel-declara-ca-este-inacceptabil-ca-turcia-sa-faca-presiuni-asupra-ue-pe-spatele-refugiatilor/> accessed 08.03.2020.

²⁷<https://www.news.ro/externe/franta-deplin-solidara-cu-grecia-si-bulgaria-afirma-macron-care-vrea-sa-se-evite-o-criza-umanitara-si-a-migratiei-in-urma-unui-aflux-de-migranti-din-turcia-1922401302002020031319286947>.

Greece, by the military fleets deployed in the Mediterranean and in the return to the territorial waters of countries of origin of vessels having migrants on board.²⁸

The key to resolving the created crisis lies in the negotiations between Vladimir Putin and Recep Tayyip Erdogan, the leaders of the anti-democratic and anti-Western regimes in Moscow and Ankara, „conjuncture allies” who often claim good relations²⁹ despite Turkey's status as a NATO member state. Important is position of the US Department of State for Turkey's support and the imperative call for the immediate cessation of the offensive launched by Syria, Russia and the combat groups supported by Iran, or the solidarity expressed by NATO, through the voice of the alliance's secretary general, Jens. Stoltenberg.³⁰

A possible solution to the refugee crisis in the Middle East countries, currently located in the territory of Turkey, is their integration into the Turkish society itself, given the labor shortage³¹ and the problems of the national economy where the purchasing power is affected by the high level of inflation and foreign investments collapsed by 30% in 2019. The possibility of absorbing a significant part of the refugees from the rich countries of the Arabian peninsula is also not to be neglected, a possible destination being Saudi Arabia, the country having the status of "financial superpower"³² involved in various mutual assistance programs worldwide, on the territory where there are about five million foreigners, many of them being Western citizens engaged in activities subsequent to oil extraction and refining, with possibilities of absorption of the labor force in the field. Therefore, the conditions for maintaining large groups of refugees in geographical areas belonging to the same civilization would be created, which would ensure optimal conditions for reintegration into the refugee society.

CONCLUSIONS. POSSIBLE SECURITY CONSEQUENCES FOR THE EUROPEAN CONTINENT CAUSED BY MIGRATION

The realities of the contemporary world show us the spectrum of Islamization of Western Europe, under the pressure of the Islamic society that is pulsating with religious life and is constantly expanding, is more current than ever, in the context of the voluntary secularization established with the acceptance of the social contract between man and the secular authority, proposed by the French philosopher Jean Jaques Rousseau, when society became preoccupied mainly with respect for human rights, the Christian religion being held in its private sphere and being in a continuous regress.

Western Europe is currently facing serious demographic problems, is aging and has a substantial labor shortage, and „the European Union needs migrants due to negative births”, provided, however, that migration „is a legal one, good” quality, numerically controlled and capable of integrating into the cultural and social values of Europe³³. The level of economic

²⁸https://www.europarl.europa.eu/doceo/document/CRE-9-2020-02-12-INT-3-564-0000_RO/ / accessed 09.03.2020.

²⁹ <https://www.dw.com/en/in-drum-spre-un-nou-război-ruso-turc/a-52574097> The head of Turkish diplomacy, Mevlut Cavusoglu, argued that "bilateral strategic relations with Russia" would be "unshakable" / accessed 08.03.2020.

³⁰<https://www.dw.com/ro/reuniune-extraordinară-nato-după-escaladarea-situației-din-siria/a-52572751> / accessed 08.03.2020.

³¹ <https://www.business24.ro/articles/forta+munca+turcia/accesse> 09.03.2020/see the Manpower Group 2018 study.

³² Peter Mansfield, A History of the Middle East, (Bucharest: Humanitas Publishing House, 2015), 303.

³³ See <https://www.epochtimes-romania.com/news/basescu-o-noua-interventie-in-parliament-european-ce-zice-de-migratia-ilegala-care-continua-in-ue---297146/> / accessed 09.03.2020 / point of view expressed by the former President of Romania, Traian Basescu, in the work of the European Parliament.

development and the concern for ensuring and respecting the fundamental human rights and freedoms, make this geographical area a favorite destination for migrants from the Arab area. Because they value different notions such as money, work, freedom, value, social coexistence, migrants are often regarded as social heretics, unintelligible in the Euro-Atlantic world, and the standards of Western life seem to be in permanent contradiction with the Koranic precepts, almost impossible. to be abandoned by their great mass. In this context, Western Europe is subject to the danger of changing its demographic and religious weight as a result of mass migration of groups of Islamic populations, with irreversible effects on everything that characterizes Western civilization.

Potential waves of Islamist migrants are perceived as a real threat to what is considered „modus vivendi occidentalis”, because „Islam has been a sword religion from the beginning”³⁴ According to Westerners, they will create bloody breaches in the civilization order in the European space, both distressing and unacceptable to Muslims, with the clear purpose of instilling fear and disrupting the „bonoma” of Western daily life. In support of this view, one starts from the finding that „Muslims are involved in more violence between groups than those belonging to other civilizations?”³⁵, which fuels the dilemma of the European world regarding the compatibility of the values to which the Islamic world relates to the Christian values, for which freedom represents the supreme wealth of the human being.

The realities of the last years show us a Western Europe in which the phenomenon of crime has experienced alarming quotas, at the origin of many of the antisocial activities being migrants, some even to the third generation, not integrated in the family or in the society, with a confused religious identity determined by leaving the places to which they are linked with their identity, with serious behavioral problems related to self-control and anger, with problematic personality that irreparably marks their feelings, inner experiences or evolution and which determines that their personal opinions be imposed by threat or violence of the members of the communities to which they belong, assuming consciously the illegal character of the actions taken.³⁶

The reactions of public opinion and extremist political forces, to the unprecedented manifestation of the phenomena associated with crime in which migrants from the Middle East are involved, are prompt and seem to concern the national authorities of Western European states themselves. Extreme right-wing groups are gaining increasing popularity in the context of claiming an anti-immigration public position, the main themes being the „Islamization” of European society and the loss of national identity, and the common denominator of the approaches is radicalization, the hatred against Islamists, holding the absolute truth” in terms of solving the refugee problem and the desire to "restore order" including extreme measures. Against this background, far-right and nationalist parties such as the Alternative for Germany, Germany, the National Front/National Assembly from France, VOX in Spain, Sweden Democrats, Golden Dawn in Greece, Law and Justice in Poland, The Freedom Party in the Netherlands and the Danish People's Party have recorded a decline in popularity and electoral success.³⁷

We can therefore conclude that a new wave of refugees from the Middle East to western Europe will affect the continent's security, on multiple levels, the consequences being unforeseeable. In the field of knowledge, prevention and countering the threats

³⁴ Samuel, Huntington, *Clash of Civilizations and the Restoration of the World Order*, 392

³⁵ Samuel, Huntington, *Clash of Civilizations and the Restoration of the World Order*, 391

³⁶ Cătălin, Peptan, *Terrorism. Events and developments in the hot areas of the world...*, 37.

³⁷<https://monitorulapararii.ro/extrema-dreapta-europeana-dominata-de-lone-wolfs-si-radicalizarea-online-1-25424/> accessed 09.03.2020

potentiated by the phenomenon of migration, a special role belongs to the intelligence structures of the affected European states, which must develop their capabilities for capturing and processing information and diversify their forms of international cooperation, within NATO or the European Union, based on the needs to value the experience, expertise and capabilities of the partners³⁸, by providing relevant information on the dynamics of the evolution of risk factors and threats to regional security in the fields related to the phenomenon of migration. The European leadership will have to integrate into the values of a secular, Euro-Atlantic society, indoctrinated religious populations, with little chance of success if we refer only to the specificities of the Islamic world.

³⁸Cătălin, Peptan, *Information and intelligence in security equation*, Annals of the „Constantin Brâncuși” of Târgu Jiu, Letter ans Social Science, Series2/2019, 39-45.

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ECONOMIC INTEGRATION STRUGGLES IN THE POST-SOVIET SPACE: THE ORGANIZATION FOR DEMOCRACY AND ECONOMIC DEVELOPMENT (GUAM)

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ABSTRACT:

THE COLLAPSE OF THE SOVIET UNION BROUGHT FORWARD A NEW FRAMEWORK FOR MULTILATERAL COOPERATION INSPIRED BY THE MODELS OF THE WESTERN WORLD SUCH AS EUROPEAN UNION'S SINGLE MARKET OR NAFTA. THIS NEW LANDSCAPE STARTED TO EMERGE FROM THE PREVIOUS EXISTING BILATERAL AGREEMENTS WHICH PAVED THE ROAD AHEAD FOR A REGIONAL ECONOMIC INTEGRATION PROCESS, COMMONLY KNOWN AS A FREE TRADE AREA, BUT THE DIFFICULT NEGOTIATING POSITIONS OF THE MEMBER STATES GAVE LITTLE SUPPORT FOR THE CREATION OF A PROPER COMMON MARKET AMONG THEM. THE PRESENCE OF THE RUSSIAN FEDERATION IN THE REGION REMAINED DOMINANT, SINCE ALMOST ALL FORMS OF TRADE PARTNERSHIPS AND FORMAL AGREEMENTS NEEDED ITS SUPPORT OR GUIDANCE. OF ALL THE FORMS OF ECONOMIC INTEGRATION, OUR ARTICLE FOCUSES ON THE ORGANIZATION FOR DEMOCRACY AND ECONOMIC DEVELOPMENT (GUAM), THE ONLY REGIONAL DEVELOPMENT ARCHITECTURE OF WHICH RUSSIA IS NOT PART OF. USING ANALYTICAL GRAPHS, WE ARGUE THAT ALBEIT DIFFERENT FORMS OF ECONOMIC INTEGRATION, THE TRADE FLOWS FOLLOW THE INTERNATIONAL TRENDS AND THUS THE GUAM COMMERCIAL TIES ARE BASED MOSTLY ON PROXIMITY AND HISTORICAL LINKAGES RATHER THAN FREE TRADE AREA AGREEMENTS.

KEY WORDS: GUAM, FREE TRADE AREA, TRADE FLOWS, MULTILATERAL TRADE AGREEMENTS

INTRODUCTION

After 1992, trade liberalization created strong incentives for developing trade relations in the post-Soviet space. In fact, significant imbalances in commodity prices between Russia and the newly independent states have stimulated foreign trade, which has become the most dynamic developing sector and the only source of foreign currency in the first years of reform.

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Between 1993 and 2003 post-Soviet regional cooperation in the economic field was manifested in three formats: the Economic Union of the Commonwealth of Independent States, the Eurasian Economic Union and the Single Economic Space.

On September 24, 1993, Armenia, Azerbaijan, Belarus, Kazakhstan, the Republic of Kyrgyzstan, the Republic of Moldova, the Russian Federation, Tajikistan and Uzbekistan signed the Agreement establishing the Economic Union of the Commonwealth of Independent States (CIS), which aimed at creating an economic union through the future formation of a multilateral free trade area, a customs union, a common market and a monetary union.

Georgia and Turkmenistan signed the new Agreement by the end of the same year. Ukraine remained the only state of the Commonwealth of Independent States that did not sign this agreement, although it acceded as an associate member in 1994. However, the Economic Union Treaty was only a framework agreement, which was to be implemented by a specific number of other agreements to be established at a later date.

One of them, the Agreement of the Community of Independent States on the creation of the Free Trade Area, aimed at reducing trade barriers and encouraging economic integration, was signed on April 15, 1994, by Armenia, Azerbaijan, Belarus, Georgia, Republic of Moldova, Kazakhstan, Kyrgyzstan, Russia, Tajikistan, Ukraine and Uzbekistan.

This Agreement concerned in particular with trade in goods, paved the way for the liberalization of service markets (Article 17)³ and provided for the elimination of customs duties, of charges with equivalent effects and of quantitative restrictions on trade in goods within the Community of Independent States. The preamble defines the establishment of the free trade area as an act of successive implementation of the provisions of the 1993 Agreement on the creation of the Economic Union. Specifically, Article 21⁴ stated that the free trade area would be considered a transitional step towards the formation of a customs union. However, achieving a free trade area as a first step in creating an Economic Union faces three main obstacles.

First, the signatories were unable to draw up a single list of goods exempt from the customs regime and therefore agreed to identify the exceptions to free trade in bilateral documents (to be phased out). Secondly, the stipulations with regards of the transition to a customs union, an essential step towards economic and monetary union, were removed from the text as a result of the amendments introduced by the Protocol of 2 April 1999⁵. Third, and most importantly, all the signatories parties have ratified the Free Trade Agreement and Protocol except the Russian Duma, due to the Russian Federation's insistence on establishing a unilateral list of exclusions from the Free Trade Agreement, - in particular oil and gas - and the introduction of restrictive quotas for sensitive exports, such as metallurgy, chemicals and agricultural products⁶.

In accordance with Article 23 the Free Trade Agreement entered into force in 1994 for the parties that ratified it, from the date of deposit of the instrument of ratification. However, since Russia prevented the ratification of a multilateral agreement that includes all members, the trade flow between the states of the Commonwealth of Independent States was in practice regulated through a network of bilateral preferential trade agreements.

³ Brzezinski and Sullivan, *Russia and the Commonwealth of Independent States*, 86.

⁴ Brzezinski and Sullivan, *Russia and the Commonwealth of Independent States*, 87.

⁵ Zhukov and Reznikova, *Economic Integration in the Post-Soviet Space*, 31.

⁶ Vinokurov, *The Customs Union and the Single Economic Space: Towards the Eurasian Economic Union*, 58.

Therefore, the multilateral agreement practically coexisted with the bilateral ones, providing a legal framework for trade between countries that do not have a bilateral agreement. Both the multilateral and bilateral agreements had numerous provisions with a similar substance and scope; in case of conflict, the multilateral one prevailed.

The multilateral free trade agreement allows parties to participate in external trade policy agreements (an agreement involving third parties) and extends the rights and privileges of the parties to participate in economic associations, border trade, preferential treatment for developing countries and other free trade areas agreements⁷.

In addition, the provisions of the multilateral agreement did not contravene the World Trade Organization's (WTO) rules. Indeed, even though most CIS countries did not accede to the WTO at that time, the parties agreed to rely on GATT / WTO agreements for the purpose of interpreting the agreement.

Bilateral agreements within the Commonwealth of Independent States have indeed introduced some free trade mechanisms, such as the cancellation of import tariffs and quota restrictions between states, while allowing the parties to take protective measures (for example, countervailing measures to protect domestic markets from subsidized imports), if necessary, in accordance with the rules and principles of the World Trade Organization. However, this network of bilateral treaties did not lead to true integration in terms of regional trade.

All bilateral agreements within the Commonwealth of Independent States have common features, as:

- These included, in a separate protocol, a wide range of asymmetric exceptions. Such exemptions were expected to be phased out in accordance with an agreed timetable (there were no penalties if the deadlines were not met).
- Bilateral agreements were not considered permanent as they could be substantially revised and modified in line with the political evolution of the area.
- The agreements were lax, leaving room for interpretation to impose various trade remedies, anti-dumping and countervailing duties or quantitative restrictions using almost any pretext. This led to a series of trade wars in the area of the Commonwealth of Independent States in the years that followed.

Therefore, the idea of creating a customs union of the Commonwealth of Independent States, as initially provided for in the Economic Union Treaty, did not materialize as a result of the long lists of exceptions to free trade, the lack of progress in terms of external harmonization of trade policies. There were also significant differences regarding the prospects for mutual cooperation of the states from this area.

Regional economic cooperation in the post-Soviet space then continued with the "different speeds" integration. This was not something new, because even the European Union experienced the scenarios of "two-speed Europe" or "multispeed Europe" in the mid 1990s. Each successive stage of integration would involve only those countries that were best prepared to accept it. The notion of "different speed" eventually led to different integration trends in the region, largely driven by the three countries that were most engaged in the (re) integration process: Russia, Belarus and Kazakhstan⁸.

In January 1995, Belarus, Kazakhstan and the Russian Federation signed an agreement - the Trilateral Agreement on Customs Union. The Republic of Kyrgyzstan and Tajikistan acceded to the Agreement in 1996 and 1999. On February 26, 1999, the five

⁷ For example, the Republic of Moldova became a member of the CEFTA Free Trade Area.

⁸ Vinukov, *Introduction to the Eurasian Economic Union*, 165.

countries concluded the Treaty on Customs Union and the Single Economic Area, which provided for the establishment of a single tariff area and the establishment of a common market for goods, services, capital and labor, as the two consecutive stages of integration process.

2. The first attempts of Economic Integration:

2.1 The Eurasian Economic Community

On October 10th, 2000, the presidents of Belarus, Kazakhstan, Kyrgyzstan, Russia and Tajikistan met in Astana to sign the Treaty establishing the Eurasian Economic Community, which entered into force on May 30, 2001. Uzbekistan acceded in 2006, but withdrew its participation in 2008.

The Eurasian Economic Community had all the attributes of an international organization (international personality based on treaties, members - sovereign states, organizational structure and decision-making system) and produced hundreds of agreements constituting most of the "law of the Eurasian Economic Community". Its most important characteristics were: creating a large-scale regime of free trade with goods without exceptions and restrictions, the granting of a treatment more favorable to a third country than that granted to other members of the Eurasian Economic Community was not allowed and the harmonization of indirect taxes.

Despite its nominal ambitions, the Eurasian Economic Community remained largely an incomplete free trade regime that could not develop into a customs union and failed to eliminate trade and discrimination issues between Member States.

2.2 The Single Economic Space (SEA)

Two years after the launch of the Eurasian Economic Community, the presidents of Belarus, Kazakhstan, the Russian Federation and Ukraine signed an Agreement on the Formation of a Single Economic Space at the Yalta Summit of Independent States on September 19, 2003. The concept of a single economic space introduced in the document was very similar to the one that was the basis of the Eurasian Economic Community; it seemed that the new project had been launched mainly to capture Ukraine in a more intense form of integration with the other three countries.

Although the draft agreements were initially agreed between Belarus, Kazakhstan and the Russian Federation, Ukraine eventually approved them by introducing a clause stating that the Single Economic Area must be compatible with the Ukrainian constitution and the strategic objective of Kiev - that of European integration. According to Ukraine, integration into the post-Soviet space was possible only if it was compatible with the European Union's integration space⁹.

Ukraine and the Russian Federation had different approaches ever since the development stage regarding the purpose of the Single Economic Area. Russian leaders stated that the ultimate goal of the SEA would have been to create a monetary union based on a common currency, but Ukraine rejected this idea. As no country can adhere to two customs or monetary systems at the same time, Ukraine has faced strong internal opposition to joining a customs union that could impede accession to the European Union. In fact, after Ukrainian President Leonid Kuchma and Prime Minister Viktor Yanukovich agreed to sign the Single Economic Area agreement in Yalta, the leader of the People's Movement of Ukraine (Rukh), Boris Tarasuk, demanded Kuchma's removal. Moreover, there were public protests against

⁹ Tandon, *Trade is War. The West's War Against the World*, 77.

this agreement in the largest cities in western Ukraine in September and October 2003. Following the December 2004 presidential elections and the "Orange Revolution" that brought Viktor Yushchenko to power, Ukraine had radically changed the position towards the Single Economic Area: the Verkhovna Rada ratified the agreement with the reservation that this, and later other agreements, will not affect the Ukrainian constitution.

In August 2005, at the Summit of Heads of State within the Single Economic Area, President Yushchenko said that his country wanted to sign only the 15 documents related to the free trade regime and that, according to the Constitution of Ukraine, he did not intend to approve agreements related to the creation of supranational bodies and a customs union. Thus, the Single Economic Area could not be implemented mainly due to Ukraine's attitude towards integration outside the free trade area.

2.3 The Commonwealth of Independent States (CIS)

After the collapse of the Soviet Union, the new independent states participated in various processes of integration and reintegration. Based on historical links and the similarity of their socio-economic models, all these states - apart from the Baltic republics - have aimed to maintain and develop their economic and trade links through new regional arrangements.

On December 8, 1991 the Heads of State of Belarus, Russia and Ukraine signed the Agreement on the Formation of the Commonwealth of Independent States (CIS), an agreement by which the Soviet Union was dissolved and a new *commonwealth* was established to coordinate regulations in the legislative field, trade policy and security, as well as to provide a transnational formula for multilateral cooperation between sovereign states. On December 21, 1991, 8 other states from the former USSR - Armenia, Azerbaijan, Kazakhstan, Kyrgyzstan, Republic of Moldova, Tajikistan, Turkmenistan and Uzbekistan joined the CIS. These states acceded by signing the Alma-Ata Protocol¹⁰.

The agreement initially signed between the three states constituted the main document of the Community of Independent States until January 22, 1993 when in Minsk the Charter of the Community of Independent States was signed and adopted, document signed by all 11 states¹¹. Once it entered into force, the Charter defined and formalized several aspects such as: the purpose and principles of the Community of Independent States, the sphere of joint activities, regulated the cooperation and coordination, the rules of accession, the institutional framework (which was strictly intergovernmental), the decision-making process (based on consensus) and the financing rules.

Georgia joined the Community of Independent States in December 1993, but withdrew in 2008 as a result of the war with Russia. Turkmenistan has never ratified the CIS Charter, although it continued to attend the summits until August 26, 2005 in a non-formal capacity through its president Saparmyrat Nyýazow. After August 26, 2005, Saparmyrat Nyýazow changed the status of his country into an associate member of the CIS in order to be in line with the neutral status recognized by the United Nations.

Ukraine, although one of the founding members of the Commonwealth of Independent States, has not ratified the Charter since 1993. Ukrainian leaders have maintained an ambiguous status regarding the CIS, taking part in the summits, without formalizing their country's official status.

¹⁰ "Alma-Ata Protocol"

¹¹ "Charter Establishing the Commonwealth of Independent States (CIS)"

3. The regional free trade agreement between Georgia, Ukraine, Azerbaijan and Moldova - GUAM

The Organization for Democracy and Economic Development (GUAM) started functioning as a consultative body in 1997 and was launched as a full regional organization on May 23, 2006. The objective of this organization is - in addition to the issues related to security and conflict resolution - to promote favorable conditions for economic growth and mutually beneficial trade relations and to implement multilateral programs and projects in the fields of production, trade, transport, energy, international lending services, customs and fiscal services, communications, science, technology, education and culture. The most important areas of cooperation include the development of transport corridors and the implementation of the GUAM free trade regime.

Despite these priorities, the organization places less emphasis on the integration profile. GUAM members are also working on a draft protocol on the implementation of the project to facilitate trade and transport, which aims, *inter alia*, to reduce the time spent on border control and increase customs efficiency¹².

Regarding the *institutional structure*, GUAM consists of the Council and the Secretariat.

The Council is the supreme organ of the Organization and works at the level of Heads of State, Foreign Ministers, National Coordinators and Permanent Representatives. However, permanent or provisional working bodies and subsidiaries may be set up. In addition, meetings of the representatives of the ministries and / or of the departments concerned may be organized based on the decision of the Council.

The Secretariat provides organizational and technical support for the operations of GUAM and works under the authority of the Secretary General. The GUAM Secretariat is located in Kiev.

3.1 GUAM's Free Trade Area Agreement

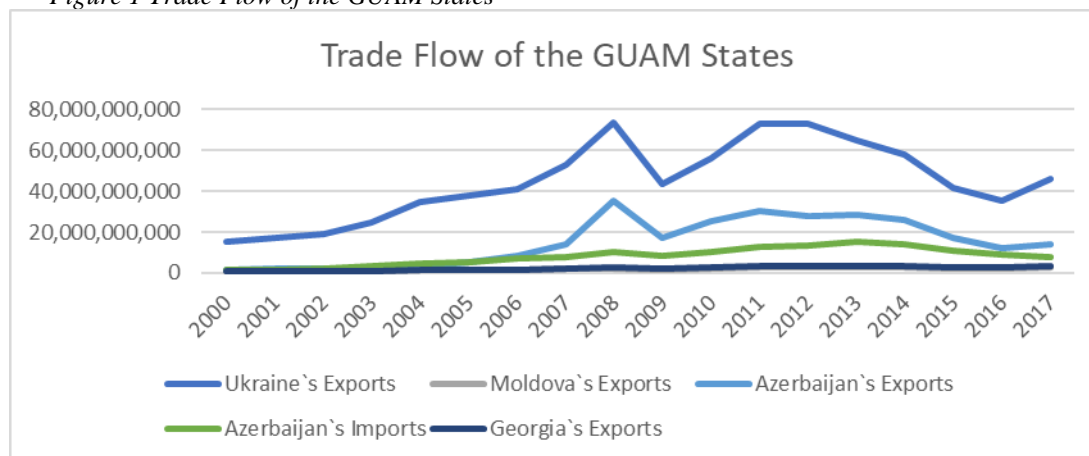
The agreement establishing the free trade area between the States participating in GUAM was signed on July 20, 2002 and entered into force on December 10, 2003. The signatories - while reaffirming their commitments under the rules and provisions of the GATT / WTO agreements - have aimed, among other things, the creation of optimal conditions for the free movement of goods and services. In this regard, upon the entry into force of the free trade agreement (or having 12 months after ratification), they eliminated customs duties and equivalent duties and quantitative restrictions (in terms of imports and exports) in the trading of goods¹³.

The graph below illustrates the main trade tendencies of the GUAM states, before and after the development of the Free Trade Area.

¹² Tino, *Non-Governmental Interests in International Regional Organizations*, 75.

¹³ Hierman, *Russia and Eurasia*, 166.

Figure 1 Trade Flow of the GUAM States



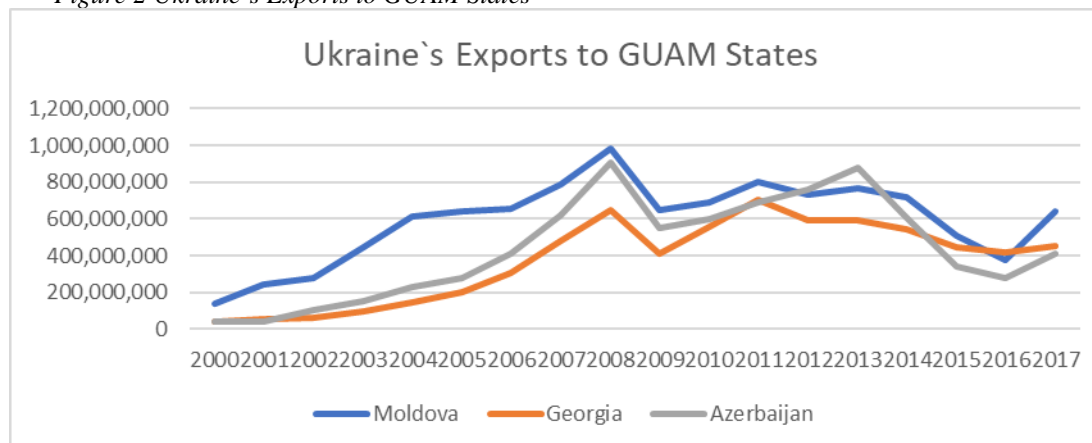
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

We can observe a tendency towards a growth in the international trade up to the year 2008, an abrupt decrease for 2009 and then the struggling to surpass the effects of recession. Although it can be argued that the GUAM's FTA and other trade agreements as well as the involvement of the World Bank and the International Monetary Fund had also an impact in the recovery of the trade flows, the data show that in terms of trade these states had followed the international market trends.

As far as tariffs are concerned, GUAM's FTA is more ambitious than the one signed by the Community of Independent States, as it does not include exceptions to free trade. On the contrary, it emphasizes that other obstacles to the free movement of goods and services should also be removed. Interestingly, the contracting parties stated that they would establish the harmonization of their legislation so that they could ensure the proper and efficient functioning of free trade. In practice, the parties to the Free Trade Agreement within the GUAM have agreed that EU law should be used as a model in the harmonization process.

As showed in the graphs below, the trade flows between and within the GUAM states started to intensify slightly. Mostly, the trade relations followed the model established by the former Soviet Union and the proximity criterion.

Figure 2 Ukraine's Exports to GUAM States



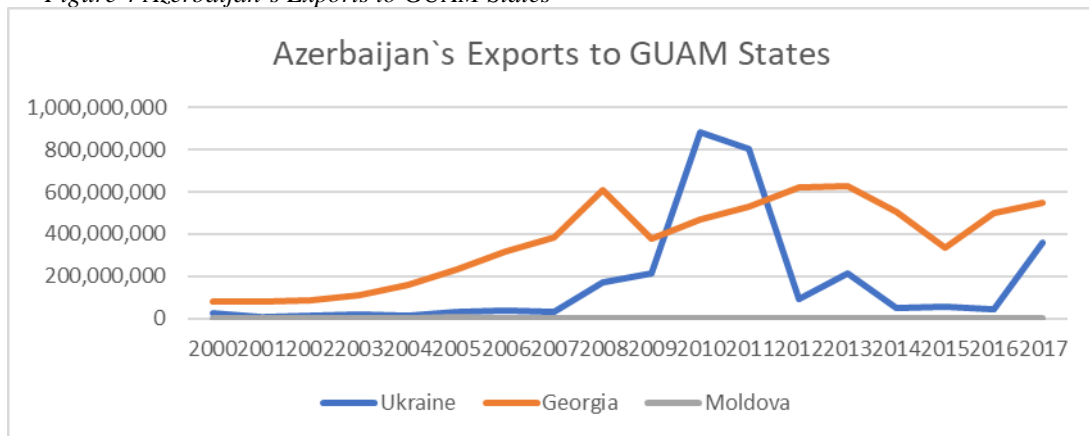
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 3 Moldova`s Exports to GUAM States



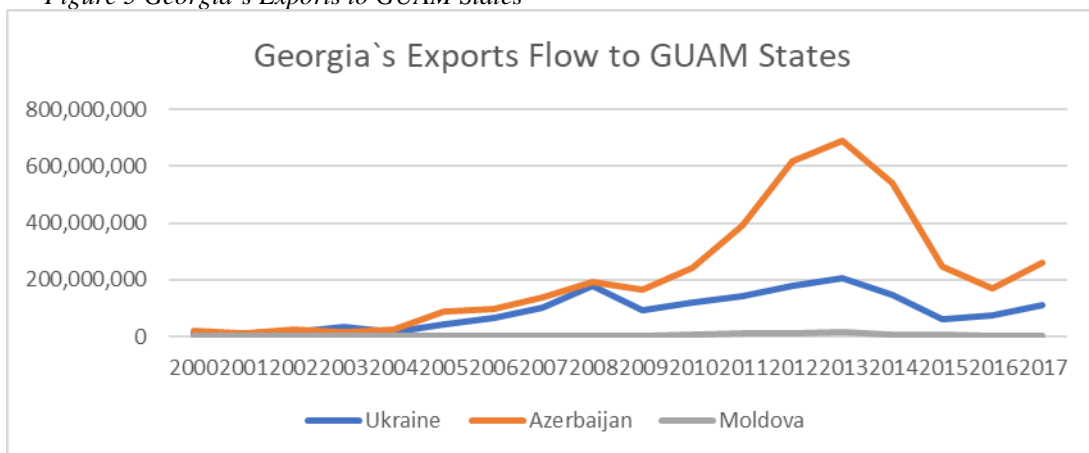
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 4 Azerbaijan`s Exports to GUAM States



Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 5 Georgia`s Exports to GUAM States

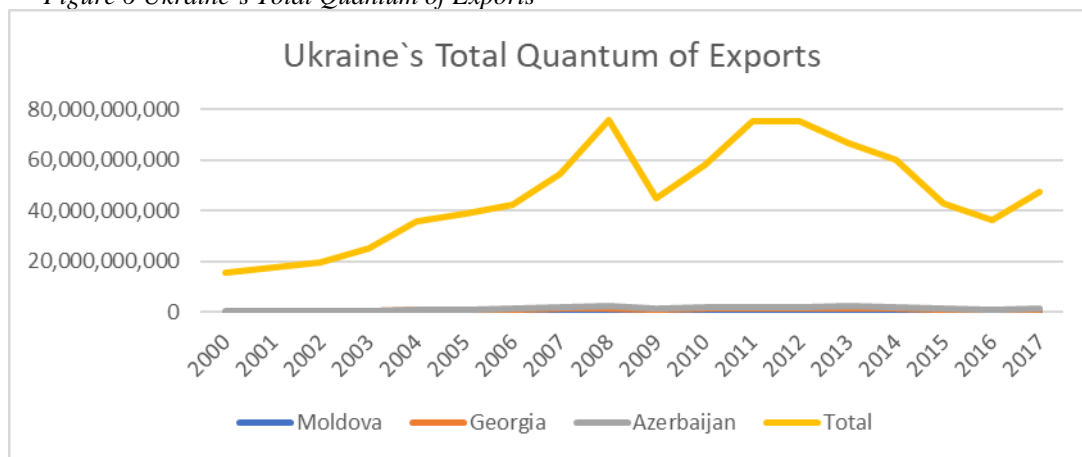


Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

As shown above, Ukraine's main export partner within GUAM is Moldova, Moldova's most important partner is Ukraine, and the same situation can be observed in the case of Georgia and Azerbaijan.

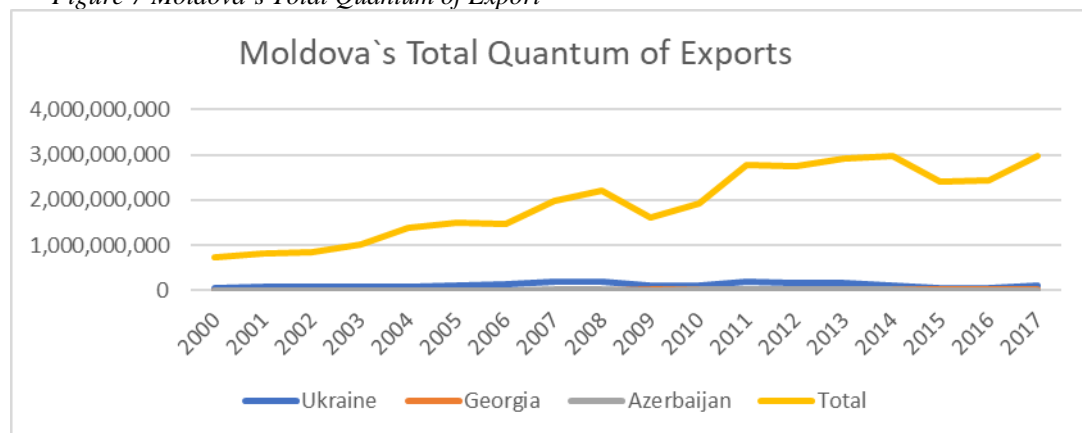
By comparison, Moldova slightly counts as an export partner if we take a look at the graph below which shows the quantum of each partner in the global exports.

Figure 6 Ukraine's Total Quantum of Exports



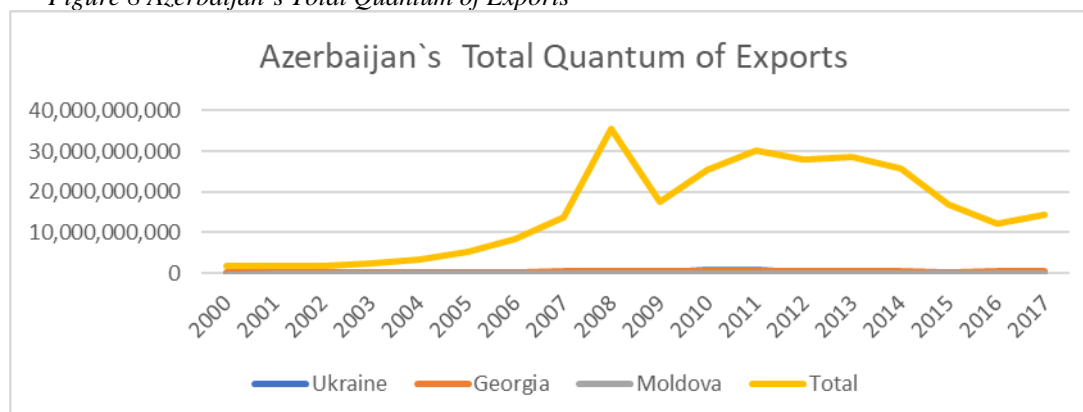
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 7 Moldova's Total Quantum of Export



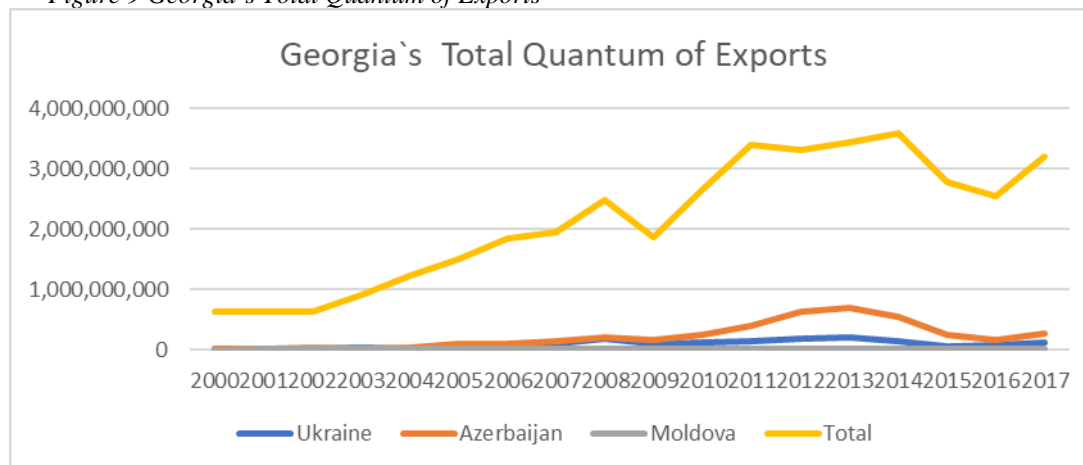
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 8 Azerbaijan's Total Quantum of Exports



Source: Authors, based on the data gathered from: *The Observatory for Economic Complexity*, <https://oec.world/en/>

Figure 9 Georgia's Total Quantum of Exports



Source: Authors, based on the data gathered from: *The Observatory for Economic Complexity*, <https://oec.world/en/>

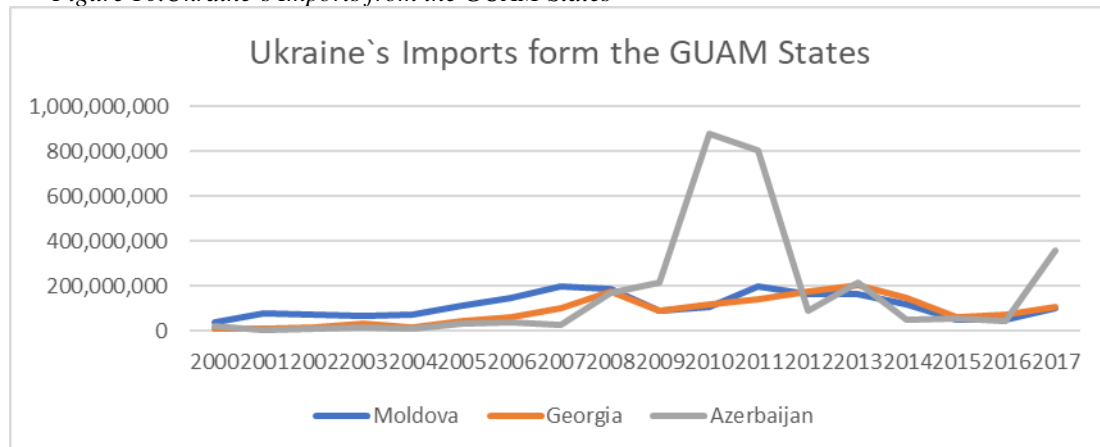
Regarding other provisions related to trade, the free trade agreement within GUAM includes the following aspects: technical barriers to trade (with emphasis on non-discrimination and cooperation in the area of standardization, metrology and certification), harmonization of customs procedures - internal taxes and other taxes with fiscal character, subsidies (respecting fair competition and transparency in granting subsidies), freedom of transit, development of industrial and scientific cooperation.

General exceptions and exceptions for security reasons (if trade protection measures are required), anti-dumping and countervailing measures as well as the elaboration of the Protocol on the rules of origin are also comprised among the main points of the GUAM's FTA Agreement.

Services, bilateral and international cooperation, competition - agreements between companies, abuse of a dominant position, public procurement, intellectual property rights, expert consultations and settlement of disputes completed the provisions of the FTA.

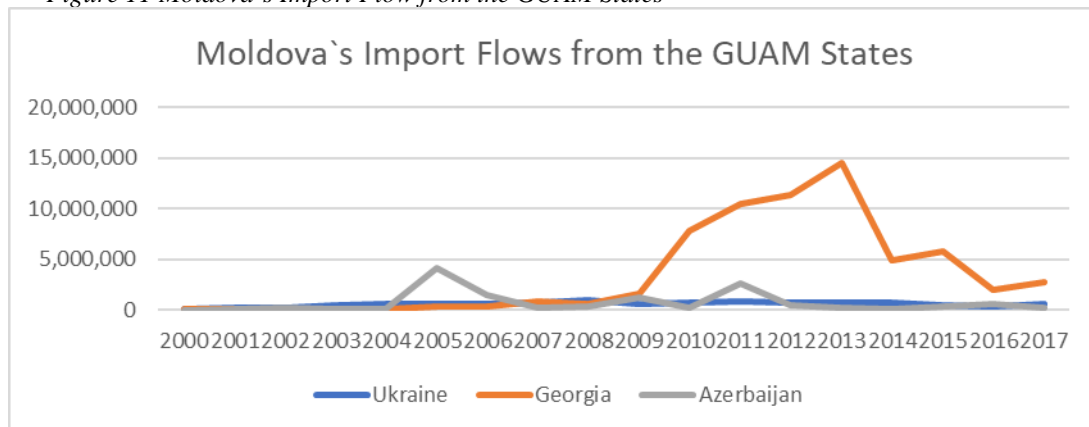
The patterns shown above in case of exports are also followed in regards with the imports. Thus, the main tendencies when choosing the import partner remain the same-proximity criterion and historical links, with a few exceptions as shown in the graphs below.

Figure 10. Ukraine`s Imports from the GUAM States



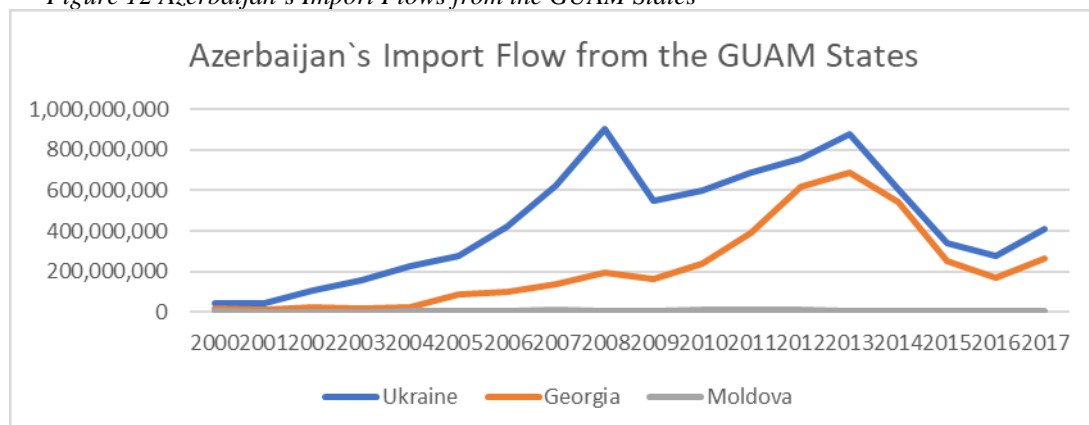
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 11 Moldova`s Import Flow from the GUAM States



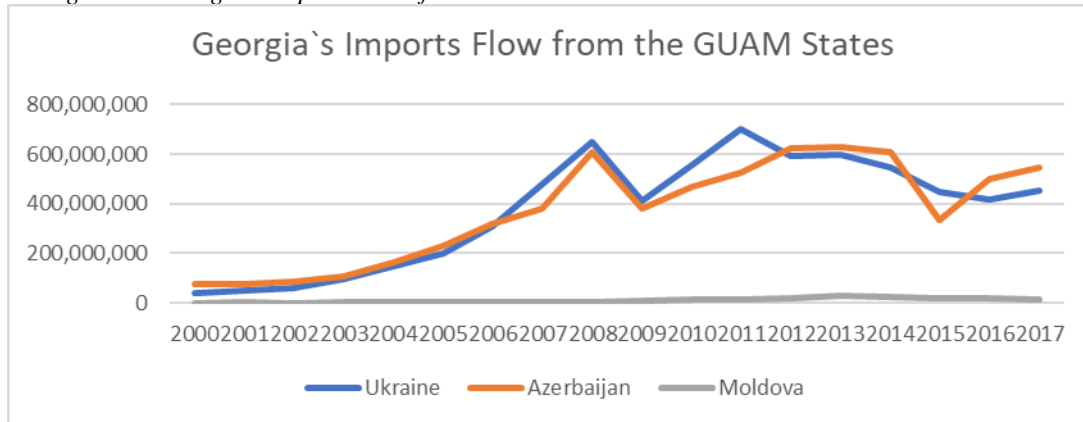
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 12 Azerbaijan`s Import Flows from the GUAM States



Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

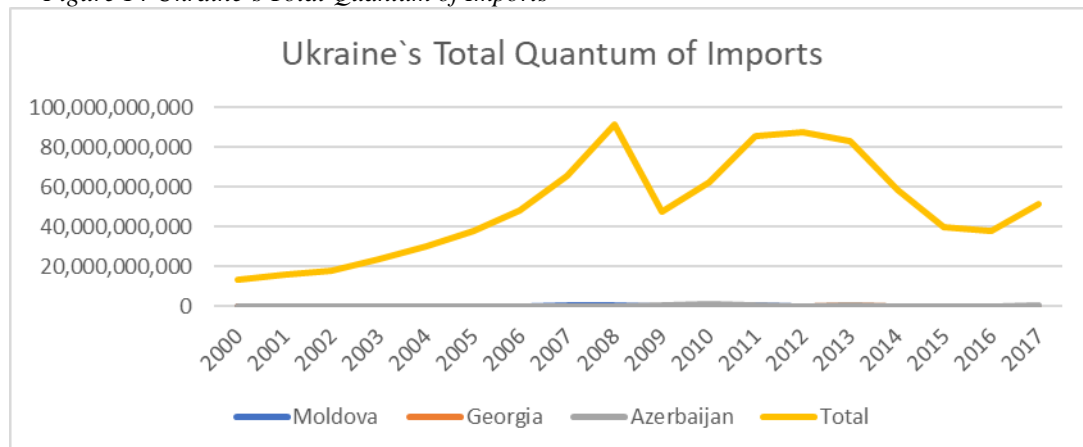
Figure 13 Georgia's Imports Flow from the GUAM States



Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

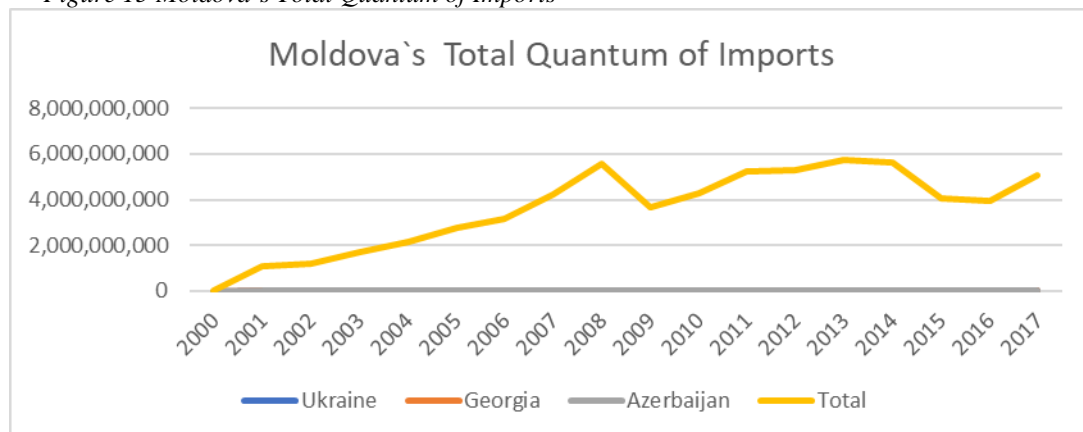
Similarly, the second series of graphs illustrate the small quota of the GUAM states regarding the imports overall.

Figure 14 Ukraine's Total Quantum of Imports



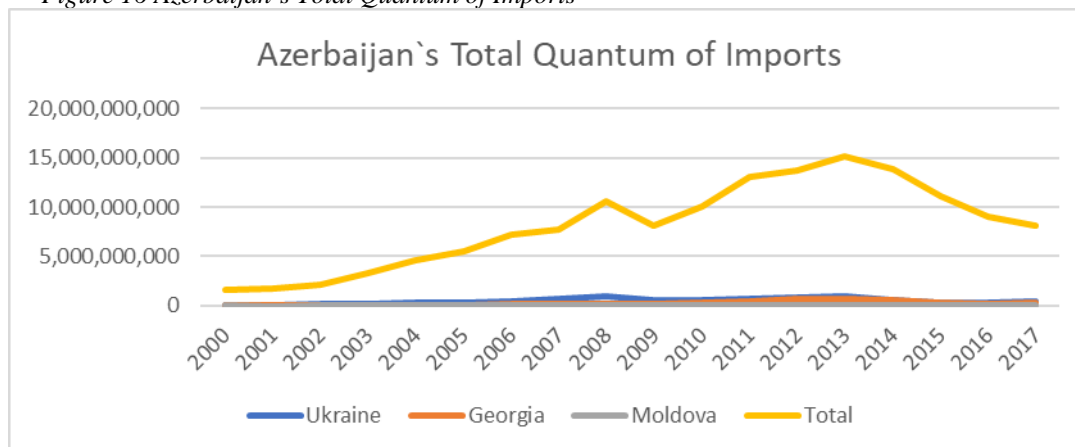
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 15 Moldova's Total Quantum of Imports



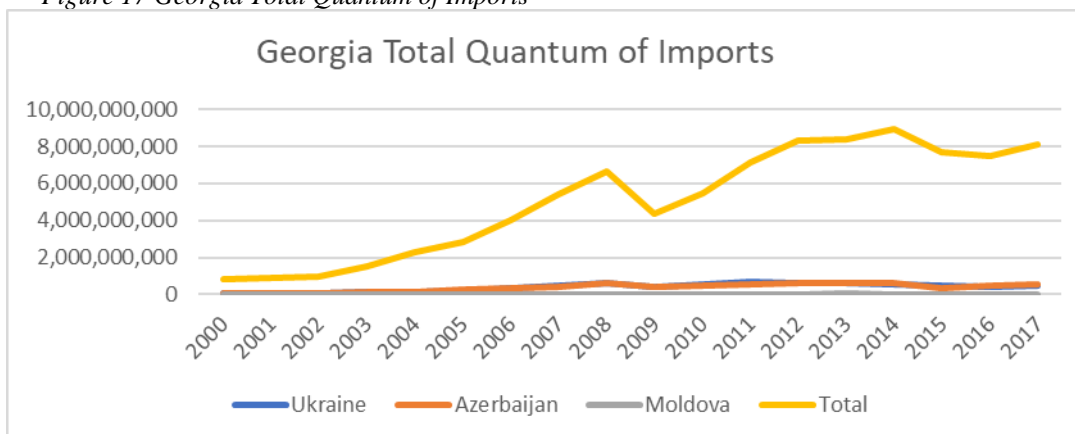
Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 16 Azerbaijan's Total Quantum of Imports



Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

Figure 17 Georgia Total Quantum of Imports



Source: Authors, based on the data gathered from: The Observatory for Economic Complexity, <https://oec.world/en/>

The GUAM FTA is open to other partners as well, and includes provisions on its correlation with other obligations of the parties arising from other international agreements. Thus, the main features of the Free Trade Agreement within GUAM are as follows: the Parties (Georgia, Ukraine, Azerbaijan and the Republic of Moldova) reaffirmed their commitments under the GATT / WTO agreements in order to create conditions for the free movement of goods and services. Other features include market access, import tariffs and equivalent taxes, as well as quantitative restrictions on trade in goods were eliminated on the day of the entry into force of the GUAM Free Trade Agreement or within one year (without exceptions).

The Agreement also refers to a correlation with other obligations of the parties arising from international agreements and includes dispute settlement. The GUAM FTA does not provide for a specific institutional structure, but the parties ensure the harmonization of legislation for the proper and efficient functioning of free trade. The main commitments of the GUAM Free Trade Agreement regarding trade are: establishing the protocol regarding the

rules of origin, harmonization of customs procedures, freedom of transit, creating conditions for the mutual liberalization of services and public procurement (based on non-discrimination), cooperation in the field of eradicating technical barriers to trade, intellectual property rights, fair competition and transparency in the granting of subsidies, sanitary and phytosanitary standards have not been explicitly mentioned in the agreement, but it can be assumed that the parties are guided by the principles of the World Trade Organization Agreement on sanitary and phytosanitary measures.

On March 27, 2017, two documents were signed by the government officials of the GUAM countries:

1) approval of the establishment of the working body for the coordination of the actions of the signatory parties to the Agreement, regarding the establishment of the free trade area as it was foreseen on July 20, 2002, and the elaboration of the terms of reference for the coordination body;

2) Agreement between the customs administrations of the GUAM Member States on the mutual recognition of the individual results of the customs control on the movement of goods and cross-border transport throughout the GUAM.

Both these documents were complimented by numerous meetings focused on the: coordination of combating crime, terrorism, drug trafficking, cyber security or illegal migration. One of the most challenging goals for the current agenda is the launching of a Digital Trade Hub, made in December 2019, with a clear emphasis on providing e-services, as well as enforcing better commitments in the FTA and the Transport Corridor of the GUAM Member States.

CONCLUSIONS

The Organization for Democracy and Economic Development was established with the aim of developing transport corridors and implement a new form of Free Trade Area based on the model provided by the European Union's Single Market. The first regional organization that formed without Russia's initiative and interference, this was supposed to be a new framework of cooperation, closer to the "western world". Although in theory, at least the Agreements that formed GUAM and later its Free Trade Area were more liberal and with fewer restrictions than the former economic integration projects, it quickly became obvious that albeit having a permissive framework, the signatory states were not able to transpose this into their trade relations. Being part of the other Agreements that were signed with Russia, mostly under CIS, the GUAM states could not capitalize the benefits that the FTA could have brought them. The Import and Export flows followed the international trade tendencies (with hiccups in the first year after the economic crisis) and remained dominated by the proximity criterion.

Today, the economic network is supplemented by an increasing number of political-economic structures that incorporate even the countries of the post soviet space. Thus, while the poles of economic development in Europe and the Asia-Pacific region have been clearly delimited from a geographical point of view, the presence of Central and Northern Eurasia makes the border between them less tangible.

Eventhough GUAM has mostly failed in its aim at creating new transit corridors, the states that are part of this organization can easily adhere to other structures and adapt, while finding new ways of economic integration and further development.

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AERODYNAMIC ANALYSIS OF SIKORSKY UH-60 ROTARY WINGS

Andrei GOGA¹

ABSTRACT:

MODERN HELICOPTERS HAVE SEEN A SUBSTANTIAL IMPROVEMENT OVER THE YEARS. MISSIONS OF ALL TYPES WERE ASSIGNED AND THE NECESSITY OF HELICOPTERS RAISED, SO THOSE NEED TO BE AS PERFORMANT AS IT CAN. THE SIKORSKY UH-60 BLACK HAWK IS A VERY GOOD EXAMPLE OF MULTIROLE HELICOPTER USED BY A LOT OF COUNTRIES ALL OVER THE WORLD. THIS PAPER ILLUSTRATES 3D SIMULATIONS OF SEVERAL VARIANTS FOR THE MAIN ROTOR BLADES BY EXPOSING PERFORMANCE ANALYSIS USING A SOFTWARE TOOL ON AN EQUIVALENT MODEL.

KEY WORDS: BLACK HAWK, UH-60, QBLADE, HELICOPTER, PERFORMANCE

Symbols and acronyms

V	Speed (m/s)	h	Air column above the blade (m)
AFB	Air Force Base	NACA	The National Advisory Committee for Aeronautics
AEFA	Aviation Engineering Flight Activity	TSR	Tip speed ratio
BIMt	Blade inspection method		

1. INTRODUCTION

Wind tunnel testing has been extensively used in the development and improvement of rotorcraft designs in addition to providing databases for refinement of theoretical models. The Sikorsky UH-60 helicopter is one of the more thoroughly tested rotorcraft systems, having undergone extensive flight and model-scale wind tunnel testing. One of those testing has included hover and forward flight performance tests conducted by the U.S. Army Aviation Engineering Flight Activity (AEFA) at Edwards AFB and tests of a highly-instrumented rotor ² at the U.S. Army Aeroflightdynamics Directorate and NASA Ames Research Center.

To expand the existing UH-60 database and to investigate rotor performance and loads in the low speed flight regime, a full-scale UH-60 rotor test has been conducted in the 80 x 120m wind tunnel. In this paper is shown a theoretical analysis of model blades,

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²Technical manual UH-60; DEPARTMENT OF THE ARMY 31 OCTOBER 1996 available at <http://www.dtic.mil/dtic/tr/fulltext/u2/a409934.pdf>

designed using 2D and 3D software, to extent the database of UH-60 and give some information about the influence of the design and its limitations.



Sikorsky UH-60 helicopter

2.GENERAL CONSIDERATIONS REGARDING SIKORSKY UH-60 MAIN ROTOR

The UH-60 main rotor system consists of four subsystems: main rotor blades, hub, flight controls and the vibration absorber. Four titanium-spar main rotor blades attach to spindles which are retained by elastomeric bearings contained in one-piece titanium hub. The elastomeric bearing permits the blade to flap, lead and lag. Lag motion is controlled by hydraulic dampers and blade pitch is controlled through adjustable control rods which are moved by the swash plate.

When the rotor is not turning, the blades and spindles rest on hub mounted droop stops. Upper restraints called anti-flapping stops retain flapping motion caused by the wind. Both stops engage as the rotor slows down during engine shutdown. Blade retaining pins can be pulled from the blade spindle joint and the blades folded along the rear of the fuselage³.

The vibration absorber reduces rotor vibration at the rotor. The absorber is mounted on top of the hub and consists of a four arm plate with attached weights. Main rotor dampers are installed between each of the main rotor spindles modules and the hub to restrain hunting (lead and lag motions) of the main rotor blades during rotation and to absorb rotor head starting loads.

2.1 UH-60 main rotor blades

The structure aft of the spar consists of fiberglass skin, Nomex honeycomb filler and a graphite/fiberglass trailing edge. The leading edge of each blade has a titanium abrasion strip, the outboard portion of which is protected by a replaceable nickel strip. Electro-thermal blankets are bonded into the blades leading edge for deicing. A Blade Inspection Method (BIMt) indicator is installed on each blade at the root end trailing edge to visually indicate when blade spar structural integrity is degraded. If a spar crack occurs, or a seal leaks, nitrogen will escape from the spar. When the pressure drops below minimum the indicator will show red bands. A manual test lever is installed on each BIM indicator to provide a maintenance check.

³ Thomas R. Norman "Full-Scale Wind Tunnel Test of the UH-60A Airloads Rotor" available at https://rotorcraft.arc.nasa.gov/Publications/files/AHS11_TestSummary_Norman.pdf

The blades are attached to the rotor head by two quick-release expandable pins⁴, that require no tools to either remove or install. To conserve space, all blades can be folded to the rear and downward along the tail cone.

Table 1. Main rotor specifications

Rotor diameter	16.36m	Max. RPM	258
Disc area	210m ²	Airfoils	SC1095 / SC1095R8

3. SOFTWARE ANALYSIS

3.1 Software description

QBlade is an open source wind turbine simulation and calculation software hosted by sourceforge.net. The integration of the XFOIL/XFLR5 functionality allows the user to design airfoils and analyze them in 2D and 3D (lifting surface)^{5,6}. The software is adequate for teaching, as it provides an easy way to simulate a model wind turbine.

QBlade also provides processing functionality for the rotor and turbine. In addition to that, the software is a very flexible and user-friendly platform for wind turbine blade design that can be used to simulate rotary wings for educational purposes.

XLFR5 is an airfoil design and analysis program, the most "user-friendly" of its type. This software uses the vortex panel method and integral boundary layer equations to calculate airfoil pitching moment at different angles of attack, drag and lift. Direct comparisons of up to three airfoils at a time may be performed. Changes to the performance characteristics of an airfoil may be made in seconds. The airfoil can be defined using NACA feature or introducing the specific coordinates. Results show an excellent comparison to published wind tunnel data⁷.

3.2 Airfoils analysis

The SC1095 airfoil and the SC1095 R8 airfoil, modified from the SC1095 by adding droop at the leading edge, are illustrated in figure 1. The effect of the nose droop was to extend the SC1095 chord from 20.76 in. to 20.965 in., thereby reducing the airfoil thickness from 9.5 percent to 9.4 percent. The addition of nose droop also rotated the mean chordline by -1° , as shown in figure 1.

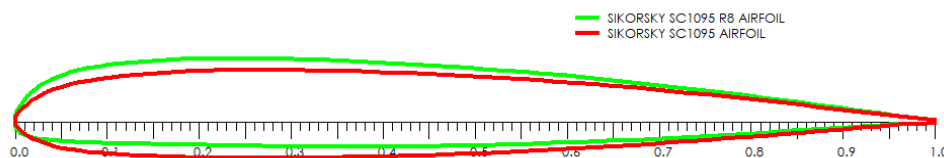


Figure 1. SC1095(red) and SC1095R8(green)

Table 2 Simulation parameters

Air density	1.225 (kg/m ³)	Reynolds number	8,250,000
Relax factor	0.35	Velocity	221m/s (tip speed)
Viscosity	1.465(mPa.s)		

⁴ Helicopter Flying Handbook Version 1/2009

https://www.faa.gov/regulations_policies/handbooks_manuals/aviation/helicopter_flying_handbook/media/hfh_ch11.pdf

⁵ Vasile Prisacariu THE AERODYNAMIC ANALYSIS OF HIGH LIFT DEVICES

⁶ QBlade open-source software hosted by <https://q-blade.org>

⁷ XFLR5 Guidelines hosted by <http://www.xflr5.tech/xflr5.htm>

The lift coefficient of a fixed-wing aircraft varies with angle of attack. Increasing angle of attack is associated with increasing lift coefficient up to the maximum lift coefficient, after which lift coefficient decreases. A symmetrical wing has zero lift at 0 degrees angle of attack. The lift curve is also influenced by the wing shape, including its airfoil section and wing plan form. A swept wing has a lower, flatter curve with a higher critical angle. For SC1095 the highest value of lift coefficient (1.86) corresponds with an angle of 18.6 and for SC1095R8 the lower value of lift coefficient (1.55) corresponds with an angle of 13.5° (see fig.2).



Fig. 2 Lift coefficient values between -20° and 30° for SC1095(green) and SC1095R8 (blue)

In aviation, induced drag tends to be greater at lower speeds because a high angle of attack is required to maintain lift, creating more drag (see fig.3) ⁸. However, as speed increases the angle of attack can be reduced and the induced drag decreases. Parasitic drag, however, increases because the fluid is flowing more quickly around protruding objects increasing friction or drag. For SC1095 airfoil, the smallest value of drag coefficient is 5.7×10^{-3} at an angle of attack of 3.2° and for SC1095R8, the value of minimum is 5.55 at an angle of attack of 3.3°.

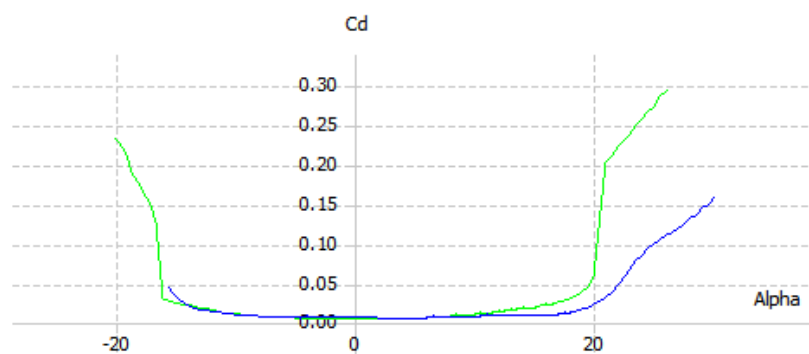


Fig. 3 Drag coefficient between -20° and 30° for SC1095(green) and SC1095R8 (blue)

Line missing - the airfoil could not be converged.

The glide ratio (see fig.4) is numerically equal to the lift-to-drag ratio, but is not necessarily equal during maneuvers, especially if speed is not constant. A glider's glide ratio varies with airspeed, but there is a maximum value which is frequently quoted. Glide ratio

⁸ John D Anderson Jr.(2007) Fundamentals of aerodynamics, Fourth Edition ISBN 007-1254-08-0

usually varies little with vehicle loading ⁹; a heavier vehicle glides faster, but nearly maintains its glide ratio.

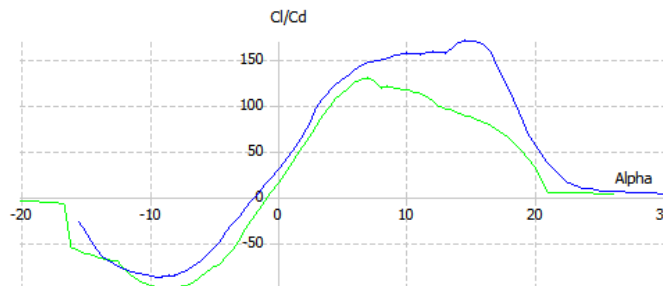


Fig. 4 Glide ratio for SC1095 and SC1095R8 airfoils for SC1095(green) and SC1095R8 (blue)

In fluid dynamics, a stall is a reduction in the lift coefficient generated by a foil as angle of attack increases. This occurs when the critical angle of attack of the foil is exceeded ¹⁰. The critical angle of attack is typically about 15 degrees, but it may vary significantly depending on the fluid, foil, and Reynolds number.

The graph shows that the greatest amount of lift is produced as the critical angle of attack is reached. This angle is 18.6 degrees in SC1095 airfoil case, but it varies from airfoil to airfoil. In particular, for aerodynamically thick airfoils, the critical angle is higher than with a thin airfoil of the same camber. Symmetric airfoils have lower critical angles. The graph shows that, as the angle of attack exceeds the critical angle, the lift produced by the airfoil decreases (see fig 5).

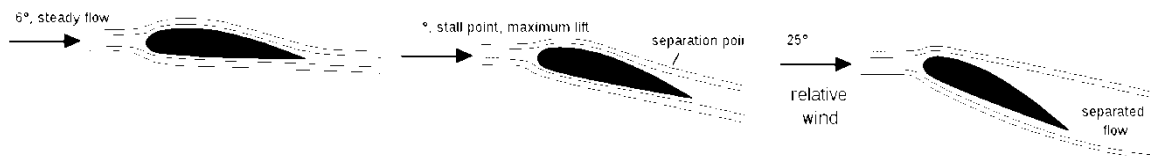


Fig. 5 Stall point illustration

3.3 Blades 3D analysis

A propeller creates a thrust force out of the supplied power ¹¹. The magnitude of this force is not constant for a given propeller, but depends on the velocity of the incoming air and the rotational velocity of the propeller itself. Thus tests of propellers usually cover a wide regime of operating conditions.

Table 3 Simulation parameters

Air rho	1.225 kg/m ³	Tip Speed Ratio	1...20
Relax factor	0.35	Velocity	221m/s
Viscosity	1.465 mPa·s		

⁹ John D Anderson Jr.(2007) Fundamentals of aerodynamics, Fourth Edition ISBN 007-1254-08-0

¹⁰ Principles of Flight, 2-18 and 3-1, Nordian Aviation Training Systems, 2017, ISBN 828107148

¹¹ Design and Analysis of Black Hawk UH-60 Rotor Blade Using Composite Materials;Dr. M Satyanarayana Gupta,Mr Badugu Uday Kumar ;September 2016
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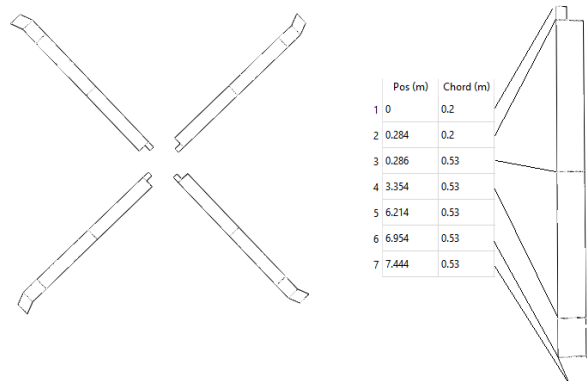


Fig 6 UH-60 Rotor blades with positions and chord lengths

The area under the graph illustrates the efficiency of the propeller(see fig. 7)

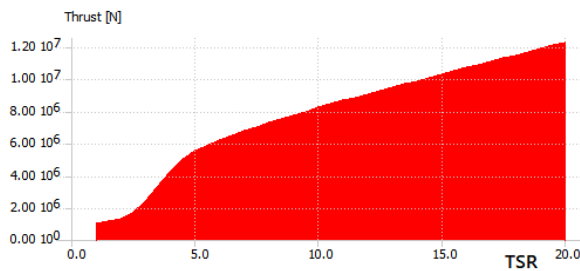


Fig. 7 Rotor efficiency

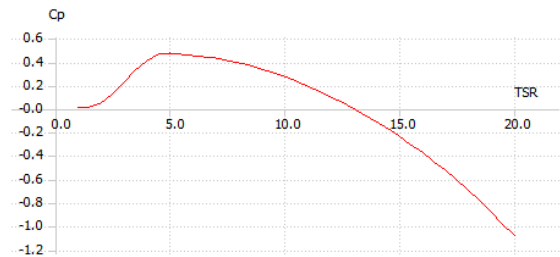


Fig. 8 The curve of power for UH-60 rotor

The relationship between the wind speed and the rate of rotation of the rotor is characterized by a non-dimensional factor known as Tip speed ratio TSR¹². Power coefficient as a function of the TSR for a four bladed rotor determines the curve of power(see fig.8). Maximum power occurs at the optimal TSR.

Maximum airflow through the main rotor:

$$\text{Volume} = h \cdot (\pi R^2 - \pi r^2), \text{ for one blade, one rotation}$$

$$h = \sin(18.6) \cdot C$$

$$h = 0.3189 \cdot 0.53 = 0.169\text{m} = 16.9\text{cm}$$

$$V = 0.169(\pi \cdot 8.18^2 - \pi \cdot 0.736^2) = 395.2$$

$$\text{AirFlow} = V \cdot bl \cdot n \cdot RPM$$

$$\text{AirFlow} = 395.2 \cdot 4 \cdot 258$$

$$\text{AirFlow} = 407846\text{m}^3 / \text{min}$$

¹² David Marten, Juliane Wendler, Qblade Guidelines, 2013, 76 , available at http://q-blade.org/project_images/files/guidelines_v06.pdf

3.4 Modified blades analysis

3.4.1. Longer blades (+0.5m)

Helicopter longer blades solution is a highly reliable one for improving the lifting force. However, the lateral and longitudinal stability may be affected by the modifications, because of the higher centrifugal and centripetal forces acting on the blades in flight.

Simulation parameters are the same one as the first analysis.

Consequences of longer blades:

Airflow: from 407846m³/min to 435194m³/min

- *higher Maximum Takeoff Weight apx 25000lbs*
- *higher Maximum Speed apx 170Kts*
- *higher Service Ceiling apx 20250ft*
- *higher fuel consumption*

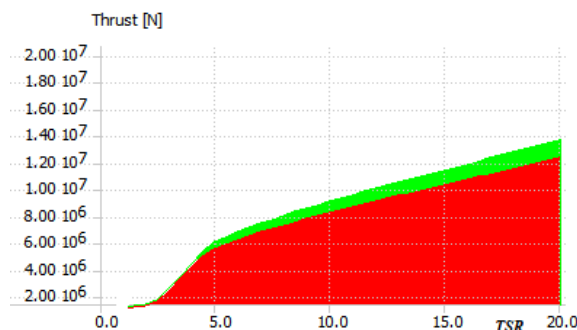


Fig. 9 Original rotor vs longer blades rotor efficiency

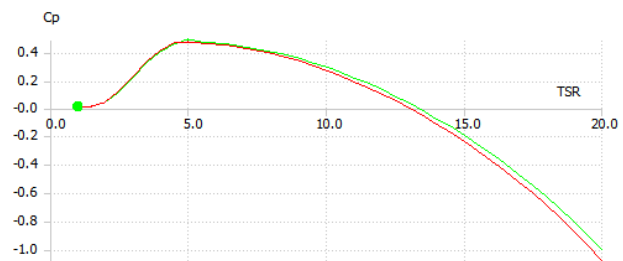


Fig 10 Power curves-original (red) vs. longer blades rotors (green)

The efficiency of the main rotor is characterized by the relation between the thrust and the tip speed ratio of that blades¹³. Yet, the efficiency of the main rotor is the area under the graph; red for the original rotor and green for the rotor with longer blades, which you can see it has a 8-9 % improvement.

The power curve in figure 10 illustrates that the highest point is about the same for the configurations, but also it can be seen that the longer blades rotor requires a little bit more power to work.

3.4.2 Wider blades (+0.1m)

Simulation parameters are the same one as the first analysis.

Consequences of wider blades

Airflow: from 407846m³/min to 517651m³/min

- *higher Maximum Takeoff Weight apx 30000lbs*
- *higher Maximum Speed apx 200Kts*
- *higher Service Ceiling apx 24000ft*
- *higher fuel consumption*

¹³ Prisacariu V., *CFD Analysis of UAV Flying Wing*, INCAS Bulletin, vol. 8, 3/2016, ISSN 2066 – 8201, DOI: 10.13111/2066-8201.2016.8.3.6, p 65-72

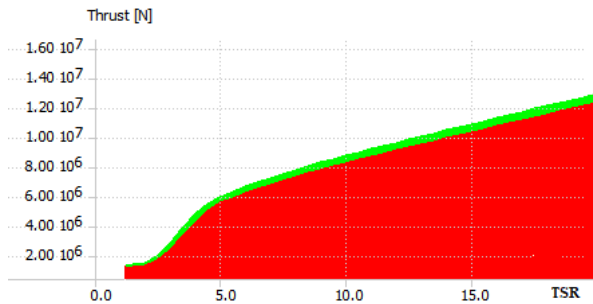


Fig. 11 Original rotor vs wider blades rotor efficiency

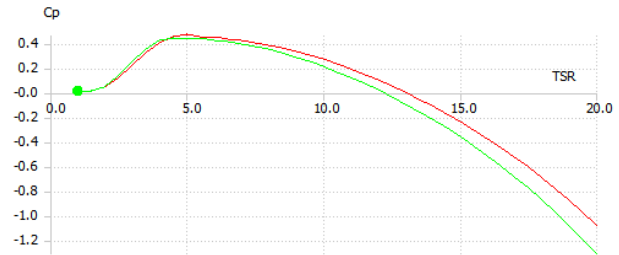


Fig 12. Power curves-original (red) vs longer blades rotors(green)

The efficiency of the main rotor is characterized by the relation between the thrust and the tip speed ratio of that blades. Yet, the efficiency of the main rotor is the area under the graph; red for the original rotor and green for the rotor with wider blades, which you can see it has a 3-4 % improvement¹⁴.

The power curve in figure 12 illustrates that the highest point¹⁵ is about the same for the configurations, but also it can be seen that the wider blades rotor requires a little bit more power to work.

Author conclusions regarding the theme

1. The effect of the dimensions for blades; wider and longer blades mean higher lift and efficiency, but for this to happen there must be considered a more powerful engine or a higher fuel consumption
2. The airfoil must preferably be wider to delay the separation of the limit layer.

Author contributions regarding the theme

1. Determining the influence of blades dimensions for a modern helicopter
2. Analyse and illustrate SC1095 and 1095R8 airfoils properties and limitations
3. Execute a 1:1 model of the rotors using the same airfoils as the manufacturer did.

¹⁴ The aerodynamic analysis of the profiles for flying wings, JOURNAL OF DEFENSE RESOURCES MANAGEMENT, vol.4 issue 1(6)/2013, ISSN:2068-9403, eISSN:2247-6466, ISSN-L: 2247-6466, p211-218

¹⁵ Prisacariu V., Boşcoianu C., Luchian A., Considerations of the bird strike on aircraft wing, RECENT Journal, Vol. 18, no. 2(52), July, 2017, Transilvania University of Brasov, Romania, ISSN 1582-0246, p 109-115

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AERODYNAMIC ANALYSIS OF ALOUETTE III ROTARY WINGS

Mircea CORPODEAN¹

ABSTRACT:

EVER SINCE THE FIRST MODELS APPEARED, THE HELICOPTER HAS REPRESENTED AND WILL BE A SOLID SUBJECT OF STUDY, ALWAYS BEING A PLACE OF IMPROVEMENT IN ITS TECHNOLOGY WITH THE EVOLUTION OF SCIENCE. IN THIS PAPER I WILL PRESENT SOME IDEAS REGARDING THE AERODYNAMIC PERFORMANCES OF THE BEARING ROTORS, USING NUMERICAL SOFTWARE SIMULATIONS BASED ON A SCALE MODEL OF THE SA 316B HELICOPTER.

KEY WORDS: ROTOR, XFLR5, QBLADE, HELICOPTER, ROTARY WINGS, ALOUETTE III

LIST OF ACRONIMS AND ABBREVIATIONS

Cl	Lift coefficient	Cp	Power coefficient
Rot	Rotational speed	RPM	Rotations per minute
Rho-ρ	Density	R	Rotor radius
r	Rotor hub radius	V	volume
TSR	Tip Speed Ratio	ISA	Internat. Standard Atmosphere
E	Glide Ratio	AoA	Angle of attack

1. INTRODUCTION

The Alouette III ²has its origins with an earlier helicopter design by French aircraft manufacturer Sud-Est, the SE 3120 Alouette, which, while breaking several helicopter speed and distance records in July 1953, was deemed to have been too complex to be realistic commercial product. Having received financial backing from the French government, which had taken an official interest in the venture, the earlier design was used as a starting point for a new rotorcraft that would harness the newly developed turboshaft engine; only a few years prior, Joseph Szydlowski, the founder of Turbomeca, had successfully managed to develop the Artouste, a 260 hp (190 kW) single shaft turbine engine derived from his Orédon turbine engine. This engine was combined with the revised design to quickly produce a new helicopter, initially known as the SE 3130 Alouette II.

¹ Student, "Henri Coandă" Air Force Academy, Braşov

² "The French Navy Is Finally Retiring These Antique Helicopters After 55 Years of Service."

During April 1956, the first production Alouette II was completed, becoming the first production turbine-powered helicopter in the world. The innovative light helicopter, soon broke several world records and became a commercial success. As a result of the huge demand for the Alouette II, manufacturer Aérospatiale took a great interest in the development of derivatives, as well as the more general ambition of embarking on further advancement in the field of rotorcraft.

In accordance with these goals, the company decided to commit itself to a new development programme with the aim of developing a more powerful helicopter that would be capable of accommodating up to 7 seats or a pair of stretchers. The design team was managed by French aerospace engineer René Mouille. The design produced, which was initially designated as the SE 3160, featured several improvements over the Alouette II; efforts were made to provide for a higher level of external visibility for the pilot as well as for greater aerodynamic efficiency via the adoption of a highly streamlined exterior.



Fig.1 Alouette III

2. GENERAL CONSIDERATIONS

The helicopter is an aircraft which uses rotary wings to produce lifting forces for propulsion and command. The rotor blades³ are rotating around a vertical axis, describing a disc in horizontal or nearly horizontal plan. The helicopter can generate aerodynamic forces even when the aircraft speed is zero, which a fixed wings aircraft don't because it needs translational speed to generate lifting forces.

2.1. The helicopter rotor

The conventional consists of two or more blades identically equidistant, attached to a central hub. The blades are maintained in a uniform rotational speed usually by a torque moment applied to the main rotor⁴. Lifting and dragging forces which action on these blades produce lift, drag, and other forces and momenta of the rotor.

The mechanical aspect of the rotor hub is built that way to permit flapping and lagging of the blade. This thing permits a fundamental classification⁵ of the rotor types, as shown below:

- fully-articulated rotor

³ Cottez, Henri. Dictionnaire des structures du vocabulaire savant. Paris: Les Usuels du Robert. 1980. ISBN 0-85177-827-5.

⁴ Munson, Kenneth. Helicopters and other Rotorcraft since 1907. London: Blandford Publishing, 1968. ISBN 978-0-7137-0493-8. 85-92

⁵ Rotorcraft Flying Handbook: FAA Manual H-8083-21.. Washington, D.C.: Federal Aviation Administration (Flight Standards Division) , 2001. ISBN 1-56027-404-2. 115-143

- semi-rigid rotor
- rigid rotor

2.2. The configuration with a single main rotor

This is the most common configuration nowadays, generalized in the past 30 years but without remaining the single one. It consists, basically, of an aerodynamic fuselage, a main rotor and a tail rotor. The last one is a tiny auxiliary rotor, vertically placed, used to counteract the momentum produced by the main rotor and to command the steering. It is placed on the top of the helicopter tail and it has the thrust orientated in the same way as the main rotor blades are rotating.

3. SOFTWARE ANALISYS

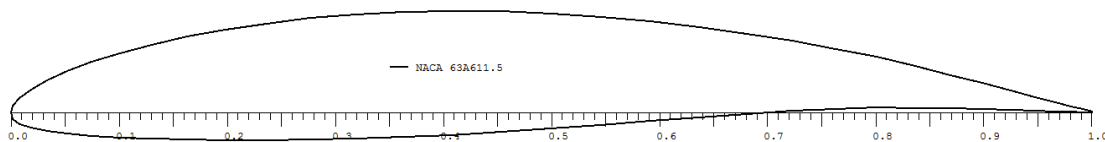


Fig.2 NACA 63A611.5

3.1. Software description

QBlade⁶ is an open source wind turbine simulation and calculation software

The integration of the XFOIL/XFLR5 functionality allows the user to design airfoils and analyze them in 2D and 3D.

The software is adequate for teaching, as it provides an easy way to simulate a model wind turbine and see it's efficiency.

QBlade also provides processing functionality for the rotor and turbine. In addition to that, the software is a very flexible and user-friendly platform for wind turbine blade design.

XFLR5⁷ is an airfoil design and analysis program XFOIL, the most "user-friendly" of its type.

XFOIL is an interactive program for the design and analysis of subsonic isolated airfoils. Given the coordinates specifying the shape of a 2D airfoil, Reynolds and Mach numbers, XFOIL can calculate the pressure distribution on the airfoil and hence lift and drag characteristics. The program also allows inverse design - it will vary an airfoil shape to achieve the desired parameters. It is released under the GNU GPL.

XFLR5 uses the vortex panel method and integral boundary layer equations to calculate airfoil pitching moment at different angles of attack, drag and lift. Direct comparisons of up to three airfoils at a time may be performed. Changes to the performance characteristics of an airfoil may be made in seconds. The airfoil can be defined using NACA feature or introducing the specific coordinates. Results show an excellent comparison to published wind tunnel data.

⁶ David Marten, Qblade short manual, available at https://www.researchgate.net/publication/281279669_Qblade_Short_Manual_v08

⁷ *** Guidelines for XFLR5 v6.03, 2011, 72

3.2. NACA 63A611.5 airfoil analysis

Simulation parameters:

Rho	1.225 kg/m ³	Viscosity	1.465 pa·s
Relax factor	0.35	Max ε	0.0001
Reynolds nr.[6]	1'650'000	Velocity	70m/s

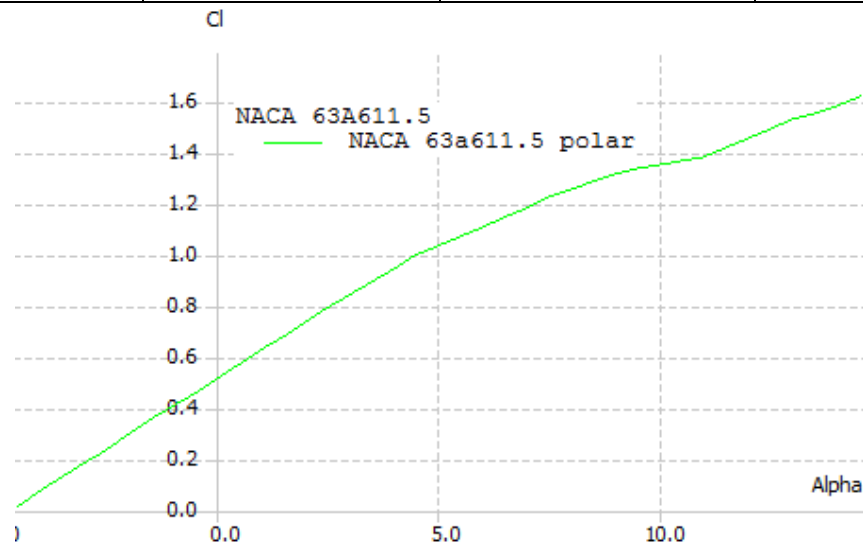


Fig.3 Lift coefficient at different AoA

The lift coefficient of a fixed-wing aircraft varies with angle of attack. Increasing angle of attack is associated with increasing lift coefficient up to the maximum lift coefficient, after which lift coefficient decreases. A symmetrical wing has zero lift at 0 degrees angle of attack. The lift curve is also influenced by the wing shape, including its airfoil section and wing plan form.⁸ A swept wing has a lower, flatter curve with a higher critical angle. For NACA 63A611.5 the highest value of lift coefficient (**1.615**) corresponds with an angle of **14.5°** (see fig.3).

The glide ratio⁹ (see fig.4) (E) is numerically equal to the lift-to-drag ratio, but is not necessarily equal during manoeuvres, especially if speed is not constant. A glider's glide ratio varies with airspeed, but there is a maximum value which is frequently quoted. Glide ratio usually varies little with vehicle loading; a heavier vehicle glides faster, but nearly maintains its glide ratio.

⁸ Principles of Flight, Nordian Aviation Training Systems, 2017, ISBN 8281071486, 43-44

⁹ Principles of Flight, Nordian Aviation Training Systems, 2017, ISBN 8281071486, 46-48

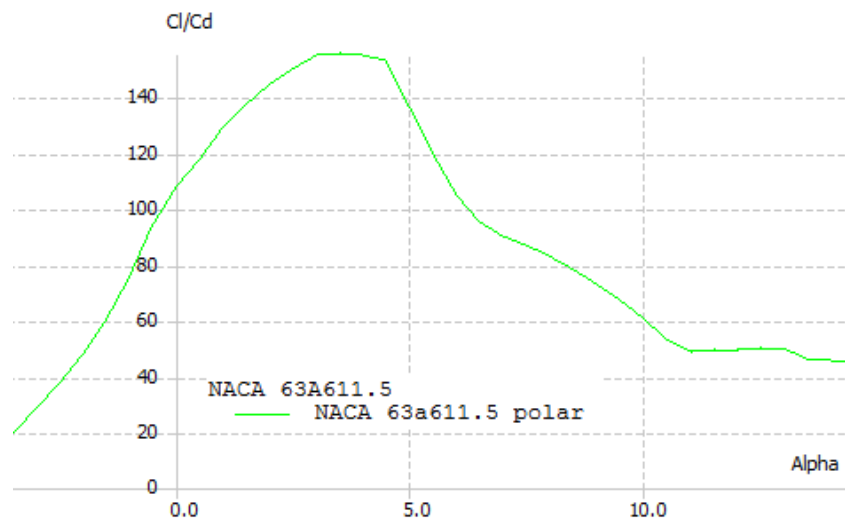


Fig.4 Glide ratio of NACA 63A611.5

In aviation, induced drag¹⁰ tends to be greater at lower speeds because a high angle of attack is required to maintain lift, creating more drag (*see fig.4*). However, as speed increases the angle of attack can be reduced and the induced drag decreases. Parasitic drag, however, increases because the fluid is flowing more quickly around protruding objects increasing friction or drag. Pilots will use this speed to maximize endurance (minimum fuel consumption), or maximize gliding range in the event of an engine failure.

In fluid dynamics, a stall¹¹ is a reduction in the lift coefficient generated by a foil as angle of attack increases. This occurs when the critical angle of attack of the foil is exceeded. The critical angle of attack is typically about 15 degrees, but it may vary significantly depending on the fluid, foil, and Reynolds number. The graph shows that the greatest amount of lift is produced as the critical angle of attack is reached. This angle is 14.5 degrees in this case, but it varies from airfoil to airfoil. In particular, for aerodynamically thick airfoils (thickness to chord ratios of around 10%), the critical angle is higher than with a thin airfoil of the same camber. Symmetric airfoils have lower critical angles. The graph shows that, as the angle of attack exceeds the critical angle, the lift produced by the airfoil decreases (*see fig 5*).

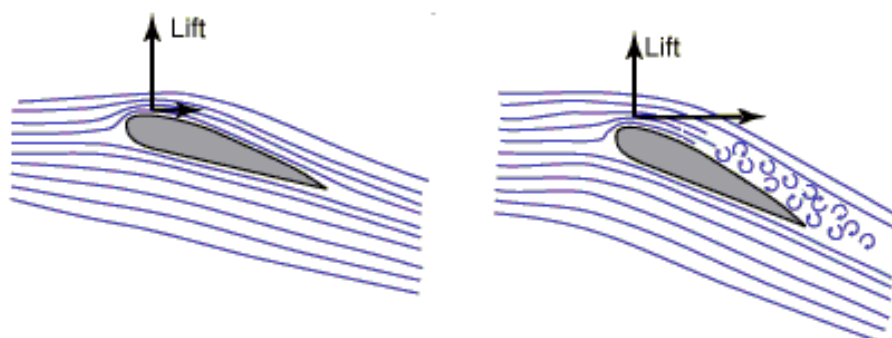


Fig.5 Stall point illustration

¹⁰ Renard, C. (1889). "Nouvelles experiences sur la resistance de l'air". L'Aéronaute. 22: 73–81.

¹¹ Anderson, John David (1997). *A History of Aerodynamics and its Impact on Flying Machines*. New York, NY: Cambridge University Press. ISBN 0-521-45435-2.

3.3. ANALISYS OF 3 BLADED ALOUETTE III ROTOR

Rotor parameters

Diameter	11.02m	Disc area	95.38 m ²
Maximum RPM	353RPM	Disc loading	33.2 kg/m ²

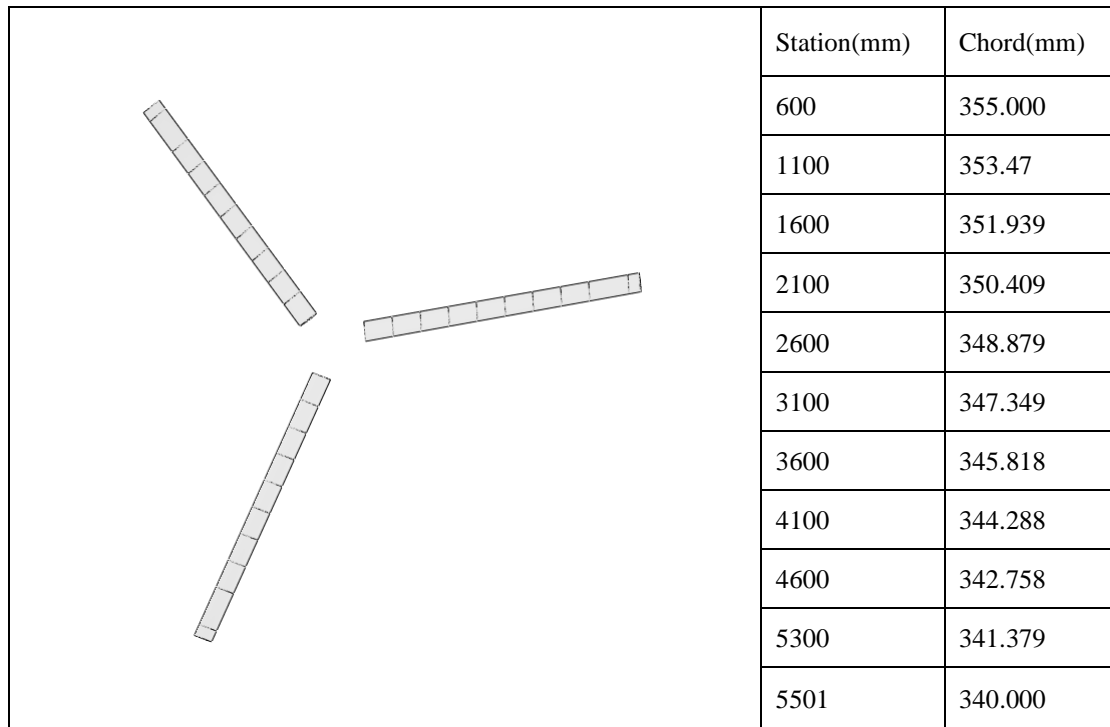


Fig.6 Alouette III original rotor - stations and chord lengths¹²

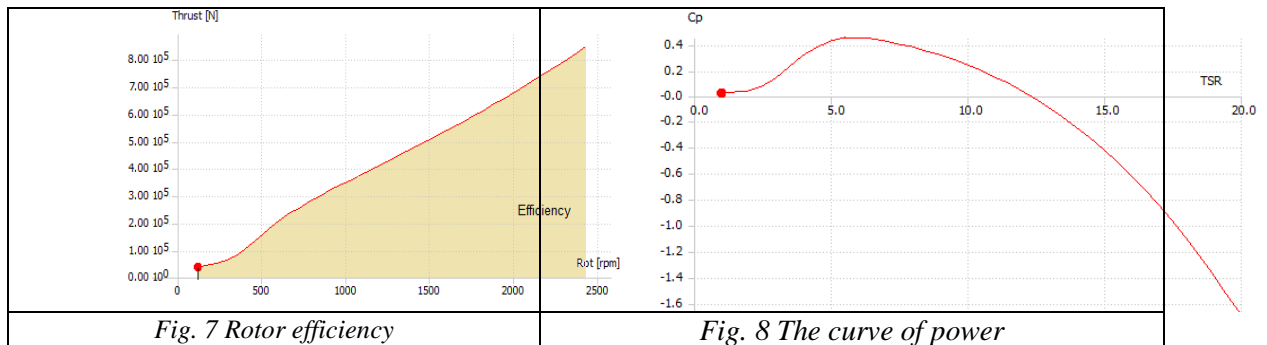
A propeller creates a thrust force out of the supplied power¹³. The magnitude of this force is not constant for a given propeller, but depends on the velocity of the incoming air and the rotational velocity of the propeller itself. Thus tests of propellers usually cover a wide regime of operating conditions. The area under the graph illustrates the efficiency of the propeller

The relationship between the wind speed and the rate of rotation of the rotor is characterized by a non-dimensional factor known as Tip speed ratio TSR. Power coefficient as a function of the TSR for a four bladed rotor determines the curve of power (see fig.8). Maximum power occurs at the optimal TSR¹⁴.

¹² Alouette III Pilot handbook, 92

¹³ Prisacariu V. The aerodynamic analysis of the profiles for flying wings, Journal of Defense Resource Management ISSN 2068-9403

¹⁴ ***XFLR5 guidelines v6.04 p51

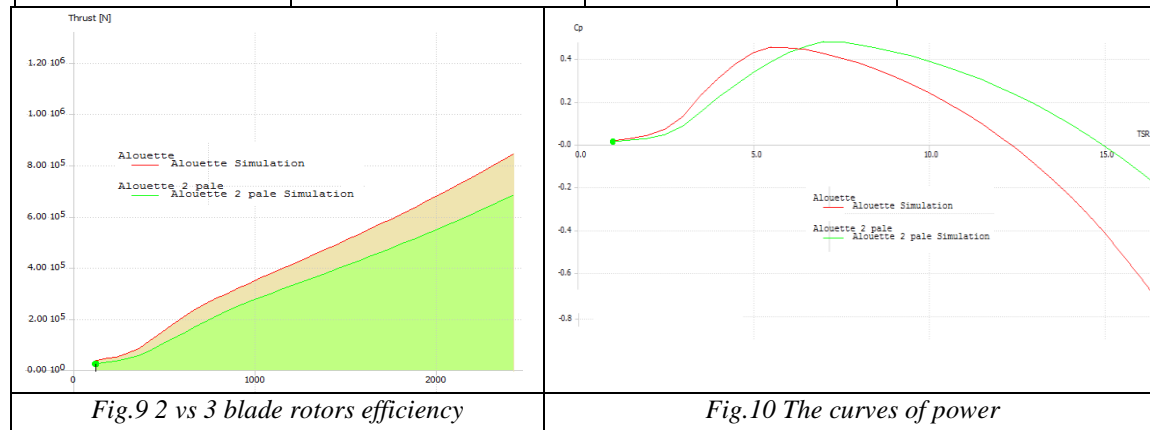


3.4. ANALYSIS OF MODIFIED ALOUETTE III ROTOR

A. 2 Bladed rotor

Simulation parameters

Rho	1.225	Viscosity	1.465
Relax factor	0.35	Max ϵ	0.0001
Reynolds nr.	1'289'000	Velocity	70m/s



Consequences:

Air flow: from 8646m³/minute to 5765m³/minute that means: apx 34% lower

- lower Maximum Takeoff Weight apx 1450Kg
- lower Service Ceiling apx 2150m
- lower Maximum speed apx 75 Kts
- **lower fuel consumption**

B.4 Bladed rotor

Simulation parameters

Rho	1.225	Viscosity	1.465
Relax factor	0.35	Max ϵ	0.0001
Reynolds nr.	1'289'000	Velocity	70m/s

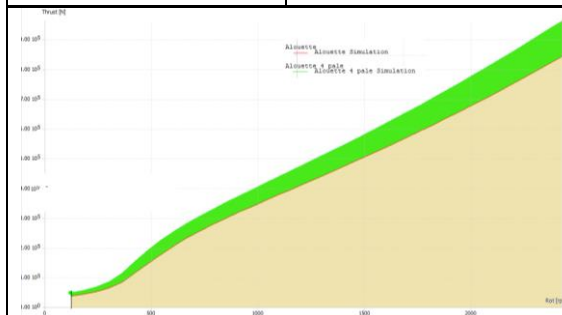


Fig.11 3 vs 4 blade rotor efficiency

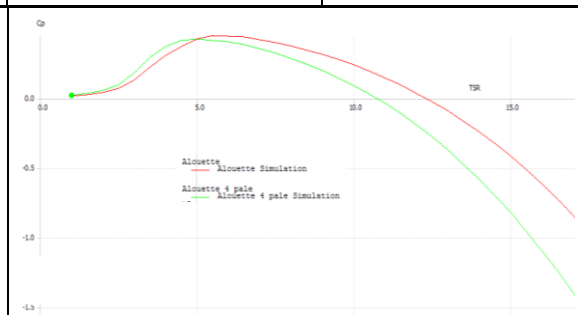


Fig.12 The curves of power

Consequences:

Air flow: from 8646m³/minute to 11528m³/minute that means: apx33% higher

- higher Maximum Takeoff Weight apx 2900Kg
- higher Maximum Speed apx 150Kts
- higher Service Ceiling apx 4200m
- **higher fuel consumption**

CONCLUSION

The effect of the number of the blades; more blades mean higher lift and efficiency, but for this to happen there must be considered a powerful powerplant and/or a higher fuel consumption

The effect of the number of the blades; less blades mean less lift and efficiency, but for this to happen there must be considered a weaker powerplant and/or a lower fuel consumption

The airfoil must preferably have a high critic point to delay the separation of the limit layer.

Author contributions regarding the theme

- Determine blade number influence of the Alouette III main rotor
- Determine NACA 63A611.5 airfoil aerodynamic performances
- Execute a 1:1 model of the rotor using NACA 63A611.5 airfoil and real dimensions

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SYSTEM MODELING OF A CONBUSTION ENGINE BASED ON STRUCTURED ANALYSIS AND REAL TIME METHOD

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Oumayma BEN AMARA²
Mohamed Najeh LAKHOUA³

ABSTRACT:

THIS RESEARCH WORK CONSISTS OF THE ANALYSIS AND THE MODELING OF A COMBUSTION ENGINE BASED ON THE STRUCTURED ANALYSIS AND REAL TIME METHOD (SA-RT). WE EMPHASIZE OUR WORK ON EXPLAINING THE SYSTEM DIAGRAMS OF THE CASE STUDY. THEN, WE WILL HIGHLIGHT TWO MODELS OF THIS METHOD: MODEL OF THE ENVIRONMENT AND MODEL OF THE BEHAVIOR ON THE BASIS OF DIFFERENT DIAGRAMS SUCH AS THE CONTEXT DIAGRAM, THE PRELIMINARY DIAGRAM, THE CONTROL DIAGRAM AND THE STATE / TRANSITION DIAGRAM.

KEY WORDS: COMBUSTION ENGINE, ANALYSIS AND MODELING, SA-RT METHOD.

INTRODUCTION

Le système temps réel réagit dans un temps bien déterminé et spécifié aux fonctionnements qui proviennent de son environnement. En effet, le comportement d'un système informatique est qualifié de "temps réel" lorsqu'il est soumis à l'évolution d'un procédé qui lui est connecté et qu'il doit piloter ou suivre en réagissant à tous ses changements d'états.

Ce type des systèmes produit généralement un résultat de calcul logiquement exact afin d'exécuter une tâche voulue d'où le fait de dépasser le délai qui lui a été accordé défini la défaillance de système. Ce dernier est une condition qui a des répercussions influençant sur la conception et la validation des systèmes temps réels. Il doit être déterministe c'est à dire facile à faire sa conception et prévoir avec certitude son comportement temporel en fonction des contraintes de charges et aussi environnementales. Cette caractéristique doit servir à traiter les informations et respecter les dates d'échéance. Ce qui permet de dire qu'un système

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temps réel ne doit pas être obligatoirement rapide par contre c'est un dispositif qui respecte les contraintes temporelles qui les qualifie⁴.

La méthode SA-RT (Analyse Structurée Temps Réel)⁵ est une méthode très connue sur le plan industriel vue qu'elle est primordiale dans l'analyse fonctionnelle et opérationnelle des applications temps réel. Elle a pour but de décrire non seulement d'une façon graphique mais aussi d'une façon textuelle toute fonction qu'on veut connaître en termes de besoins comme « pourquoi on fait cette application ? ». Cette mise en forme du cahier des charges de l'application est formelle puisqu'elle met en valeur la méthodologie et l'expression.

Cette méthode forme l'une des bases les plus utiles pour la modélisation des systèmes multiphysiques⁶ tels qu'un véhicule électrique ou même les différents types des moteurs⁷ qui sont jusqu'à nos jours la composante fondamentale et la plus importante de l'automobile⁸.

Dans la plupart des systèmes industriels le phénomène de la combustion s'impose. Or, les chercheurs aujourd'hui ont pour objectif de comprendre, prédire et même contrôler l'ensemble des phénomènes qui se passent lors de la combustion. La conception des dispositifs expérimentaux d'un tel système n'est pas seulement difficile mais aussi coûteuse.

Cet article consiste d'étudier et de modéliser un exemple académique de moteur à combustion pour une automobile paru dans le livre « systèmes temps réel de contrôle – commande » tout en identifiant les diagrammes explicatifs de la méthode SA-RT. C'est ainsi que nous discutons un modèle d'environnement et un modèle de comportement.

MATERIEL ET METHODE

Le contrôle/commande d'un moteur⁹ se fait en se basant sur les besoins en rendement, consommation et même la pollution. Plus le véhicule demande beaucoup de consommation de puissance, plus on exerce une force d'appui sur le pédale de l'accélérateur. Donc, pour des résultats satisfaisants nous devons réguler et optimiser les divers paramètres de la combustion mais en contre partie la pollution ne doit pas être aussi importante. On affronte deux cas qui ne sont étudiés que par le calculateur spécifique afin de préciser les différents états du moteur. Soit en lui donnant une prévention sur sa consommation excessive ou la nécessité du changement de mode conduite à cause de la pollution. Or, qu'on parle d'un véhicule électrique on ne parle pas d'un seul calculateur spécifique mais des nombreux calculateurs dédiés à des différentes applications comme le freinage ABS, l'éclairage,... et ils sont liés entre eux à travers un bus CAN dans le but de partager les informations de communication et atteindre un fonctionnement autonome et cohérent. Une captation de l'information se fait à travers les capteurs désignés à préciser les informations en cours de traitement permettant par la suite de réguler les erreurs en donnant les ordres aux actionneurs.

Nous considérons la commande du moteur¹⁰ (figure 1) comme une boîte dont on ne connaît pas sa composition interne mais qui fournit une réponse à travers ce qui été injecté

⁴ Lakhoua M.N., Conception de systèmes temps réel, Editions Universitaires Européennes, Verlag, ISBN: 978-3-639-50760-7.

⁵ Jaulent P., Génie logiciel les méthodes : SADT, SA, E-A, SA-RT, SYS-P-O, OOD, HOOD, Paris 1992.

⁶ Tschirhart D., Commande en temps réel : conception et mise en œuvre d'un exécutif multitâche, Paris 1990.

⁷ Dorseuil A., Le temps réel en milieu industriel, Dunod, Paris 1991.

⁸ Sun Y., Xinhua H., Study on Methods of Warfare Complex System Modeling, International Forum on computer Science-Technology and Applications, 2009.

⁹ Cottet F., Systèmes temps réel de contrôle - commande, Dunod, Paris 2005.

¹⁰ Montois J., Gestion des processus industriels temps réel, Ellipses, France 1999.

en entrée donc la partie commande ne nous intéresse pas mais ce qui nous concerne est de bien modéliser le système donné pour que ça conception soit plus facile à étudier¹¹.

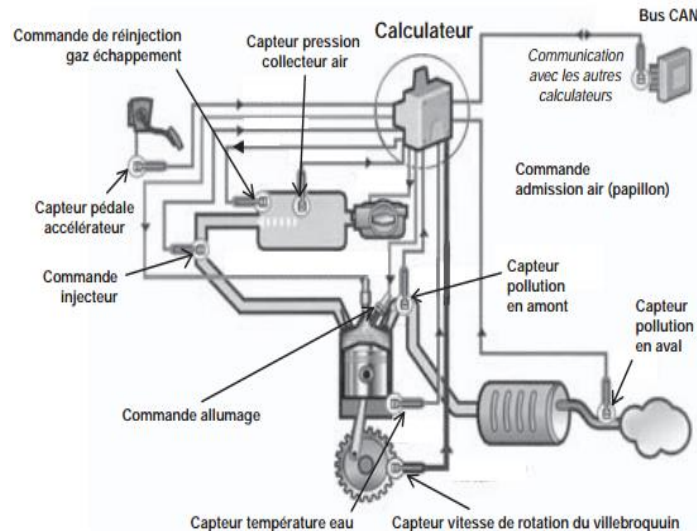


Figure 1 : Représentation du moteur à combustion

La méthode SA-RT était conçue afin de compléter la méthode SA à spécifier les systèmes non-actifs temporellement contraints en ajoutant des outils de décrire parfaitement la dynamique des systèmes dynamiques et en exprimant l'exécution de contrôle de l'exécution des processus de transformation des données¹². Ceci permet de classer les données d'un système avec la méthode SA-RT suivants trois niveaux nécessaires: un premier fonctionnel¹³ qui définit les fonctions et les variables du système ; un deuxième informationnel¹⁴ qui définit les données manipulées par les fonctions ; un dernier dynamique qui définit le contrôle¹⁵ du flux des données et l'activation des fonctions.

RESULTATS DE LA MODELISATION

Dans cette partie, nous présentons les résultats de l'application d'analyse SA-RT d'un moteur à combustion d'une automobile.

Nous commençons notre analyse par le diagramme de contexte (figure 2) qui englobe en un seul schéma les différents composants constituant ce dernier et définit les frontières d'étude à respecter. Généralement, on associe à ces derniers des flots de données entrants et des flots sortants. D'où, les sept capteurs à gauche comportent les données d'entrée et les commandes situées à droite comportent les flots de sortie. On trouve ainsi le Bus CAN qui joue le rôle d'un élément ayant à la fois des flots de données d'entrée et de sortie c'est à dire

¹¹Lakhoua M.N, The need for systemic analysis and design methodology of the medical equipments, IJASS, Inderscience, Vol.8, N°1, 2018.

¹²Hatley D.J., Pirbhai I.A., Stratégies de spécification des systèmes temps réel (SA-RT), Masson, France, 1991.

¹³Soberman M., Génie Logiciel en informatique de gestion, Eyrolles, Paris 1992.

¹⁴Ben Ahmed S., Moalla M., Courvoisier M.: Towards a design methodology for flexible manufacturing systems command combining SA-RT and object Petri nets. In: Proceedings of the IEEE Symposium on Emerging Technologies and Factory Automation ETFA'95, 1995, Vol.1, pp. 83-94.

que c'est un canal de transmission garantissant une liaison bidirectionnelle entre les composants. Donc on représente ainsi la fonction principale du système qui constitue l'application à étudier, par l'évènement "conducteur" qu'on lui attribue les conditions nécessaires qui influent sur le fonctionnement normal. Pour ce cas on parle d'un système qui doit être mis en marche ou freiné.

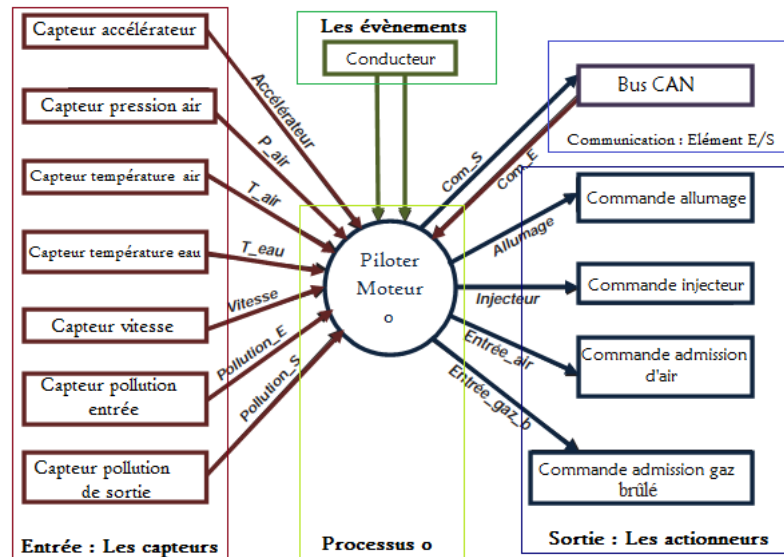


Figure 2 : Diagramme de contexte d'un moteur à explosion

En résumé nous avons une fonction initiale 0 qui est "Piloteur moteur" admettant deux conditions (arrêt et marche). Douze terminaux comportant treize flots de données qui se décomposent en huit entrants (Accélérateur, P_{air}, T_{air}, T_{eau}, Vitesse, Pollution_E, Pollution_S et Com_E) et cinq sortants (Com_S, Allumage, Injecteur, Entrée_{air} et entrée gaz_b). C'est ainsi qu'on constate clairement que le diagramme de contexte nommé ainsi DC définit parfaitement l'interface entre la conception et le client.

Le diagramme préliminaire (figure 3) joue un rôle important dans les étapes qui suivent comme la conception du système à étudier. Dans cette étape, peut dire que les paramètres de la conception sont optimisés en fonction des objectifs et des besoins du client. Donc, c'est une étape très importante pour mieux comprendre le fonctionnement du moteur à travers la modélisation systémique.

Pour bien enrichir notre travail nous allons décomposer le processus fonctionnel initial 0 cité dans le paragraphe précédent en des sous-processus qui se résument des processus fonctionnels de base et un autre de contrôle ayant pour but de découper en une suite ordonnée les opérations de l'ensemble. En réalité cette décomposition, met en valeur le diagramme flots de données par une limite bien déterminée.

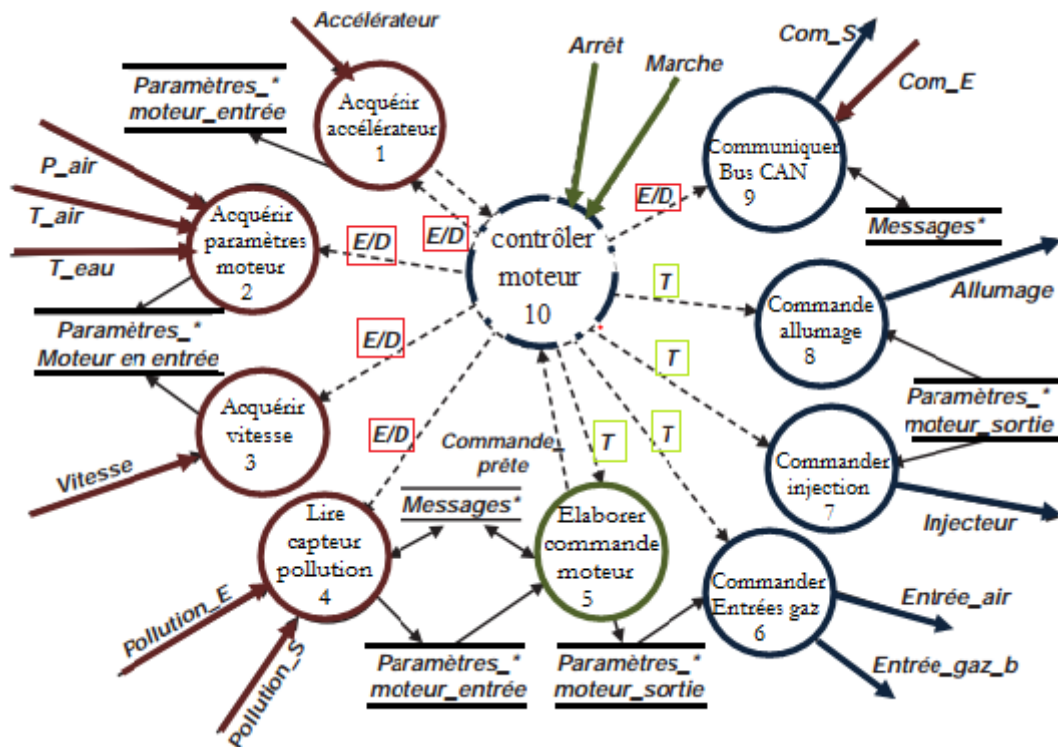


Figure 3 : Diagramme préliminaire du moteur à combustion

Nous pouvons remarquer clairement que ce dernier permet de vérifier la cohérence des flots de données ou des événements entrants et sortants par rapport au diagramme de contexte. On note ainsi que les processus fonctionnels sont liés au processus de contrôle par des flots de contrôle de type Enable/Disable (E/D) ou bien Trigger (T). Les processus fonctionnels 5, 7, 8 et 9 sont déclenchés en même temps. Concernant les paramètres du moteur en entrée et en sortie, ils ne sont que des unités de stockages de données complexes. Une autre unité est conservée pour les messages qui se présentent sous une file de des informations gérés suivant le premier arrivé (FIFO) ou le plus important au niveau d'entrée. Quand à la sortie on ne prend que le résultat du premier traité (FIFO).

Généralement, la liaison entre les divers processus fonctionnels et le processus de contrôle se fait lors de la réalisation du diagramme de état /transition en notant à chaque fois l'évènement nécessaire. Si on donne un ordre de fonctionnement aux processus fonctionnels d'acquisition (1, 2, 3, 4) et on fournit les données utiles et cycliques comme pour notre cas (acquérir accélérateur) qui fournit régulièrement l'évènement "Etat_accélérateur" en déclenchant par la suite l'élaboration de la loi de commande à partir de tous les flots de données d'entrée acquises. Lorsque la commande est prête alors le processus 5 déclenche tous les processus de commande c'est à dire 6, 7 et 9. Enfin, nous obtenons un processus fonctionnel 9 de communication gérant périodiquement les messages au niveau de la réception/émission.

Le diagramme état/transition¹⁶ (figure 4) est un plus simple que les deux présentés en haut. Nous constatons qu'il contient deux états actifs et l'état repos. L'évènement "état accélérateur" interrompt l'état de l'attente périodiquement. Ainsi in distingue la présence d'un état assimilé à l'élaboration de la loi de commande du moteur à combustion.

¹³Marty J.C., Sartor M.: A specification method combining state charts, activity-charts, and SART concepts in FMS study. In: Proceedings of the 20th IEEE International Conference on Industrial Electronics, Control and Instrumentation IECON'94, 1994, Vol. 2, pp.1147-1152.

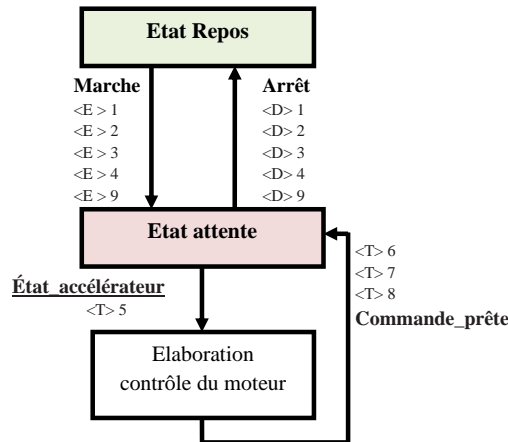


Figure 4 : Diagramme état/transition du moteur

DISCUSSION

Une représentation propre des différents diagrammes de la méthode SA-RT permet d'avoir une idée sur le fonctionnement du système étudié. Pour notre application cette étude nous aide à bien définir les terminaux, les interactions entre eux et les différentes étapes et transition qui les relient afin de réaliser la fonction attendue et qui est définie comme le processus 0.

Le système de contrôle agit sur son environnement à travers des actionneurs, et récupère les informations de l'extérieur grâce aux sept capteurs présentés. Ces capteurs donnent une information au système de contrôle pour différencier à chaque fois la valeur voulue par rapport à la valeur mesurée puis il donne un ordre aux actionneurs pour agir sur le procédé afin d'avoir un fonctionnement correct et monotone¹⁷.

Les tâches sont un centre primordial du système temps réel puisqu'il comporte le programme applicatif trouvé dans le système de contrôle¹⁸ et qui permet la communication entre les tâches, la réalisation de l'acquisition de données en provenance des capteurs, ainsi l'ordre donné pour actionneurs commande à l'aide des actionneurs du moteur à combustion¹⁹.

Le diagramme de contexte contient le processus 0 qui constitue la fonction objectif de notre modélisation "Piloteur Moteur". Il constitue une étape intermédiaire entre tout ce qui est attendu et les premiers cas d'utilisation. Il s'agit d'un processus d'analyse et représente la fonction du système à modéliser en général et les divers acteurs qui interagissent avec ce dernier qui sont les terminaux. Parmi eux on trouve l'événement donnant un ordre de marche ou d'arrêt. Il définit les frontières du système étudié en l'isolant et le délimitant²⁰.

Le diagramme préliminaire accentue les fonctions qui sont en relation avec la fonction objectif. Il montre clairement la circulation des données de la première activité jusqu'à atteindre le but en mettant en valeurs les flux de données entrants et sortants. Les processus

¹⁴Larvet P., Analyse des systèmes : de l'approche fonctionnelle à l'approche objet, InterEditions, Paris, 1994.

¹⁵David R., Alla H., Du Grafcet aux réseaux de Petri, Edition Hermès, Paris, 1992.

¹⁶Lakhoua M.N., Khanchel F., Laifi S., Khazemi S., System analysis of medical equipment for healthcare management, Annals of the Faculty of Engineering Hunedoara 14 (4), 17, 2016.

¹⁷Naoui, A., Bel Hadj Ali, S., Afilal, L. E. & Abdelkrim, M. N. Application of functional specification and operational safety conventional methods for a networked control system suitable qualitative analysis, conference STA, 2014, pp. 44-52.

présentés sont sous forme des verbes (acquérir vitesse, lire capteur pollution, élaborer commande moteur, commander entrées gaz, etc.)²¹.

Le stockage de données est organisé suivant un modèle conceptuel de données (messages, paramètres moteur_sortie, etc.)²².

Les flux de données sont des flèches liant les processus entre eux et liant ces derniers aux entités externes. Ils lient aussi les processus aux dépôts de données en indiquant le sens de circulation des informations²³.

Le diagramme état/transition met en valeur les différents états du système qui est le moteur à combustion. Ces contraintes d'activation (E), de désactivation (D) et celles temporelle (T) montrent que c'est une représentation assimilée à la modélisation par GRAFCET.

Ce qu'on peut retenir de ces diagrammes et leur richesse d'information est qu'un passage au pilotage du moteur doit passer par les étapes suivantes : identification des entités externes ; identification des flux entrants et sortants ; identification des sous processus ; identification des dépôts de données ; traçage des diagrammes.

Le moyen de communication utilisé par les tâches pour l'envoi des données sous forme de messages est le réseau CAN.

Tous ces diagrammes se complètent entre eux pour donner à la fin un modèle descriptif, explicatif et détaillé sur un système multiphysique fonctionnant en temps réel.

CONCLUSION

Un système temps réel peut comporter un ou plusieurs systèmes qui ont pour but de répondre à un objectif bien déterminé dans un temps bien défini. Pour comprendre le fonctionnement des tels systèmes on procède à l'analyse fonctionnelle et opérationnelle par la méthode de modélisation SA-RT.

Dans cet article, nous avons présenté une application de l'analyse systémique à un exemple de littérature d'un moteur de combustion d'une automobile. Cette méthode fournit au chercheur un guide d'acquisition des connaissances grâce à un langage simple combinant la décomposition hiérarchique du système ainsi que des diagrammes contenant les contraintes et les informations nécessaires qui peuvent mener après cette étude à la conception du système.

¹⁸Jimenez F., M. Courvoisier ; A. Garcia ; G. Munoz ; N. Harchani ; M. Al-Mohamed ; D. Esteve, Tools and models for systems design and synthesis of MEMS based on asynchronous circuits, proceedings of IEEE International Conference on Industrial Technology, Vol2, pp. 64 – 69, 2000.

¹⁹Lakhoua M.N, Wertani H, Overview of Conceptual Proceedings Modeling for Complex Systems, CMSAM 2018, Wuhan China, September 27-28, 2018.

²⁰Glaa R, Lakhoua M.N, El Amraoui L, Using SA-RT method and SCADA for the analysis and the supervision of hydrogen circuit, Journal of Electrical Engineering, Vol.16, N°3, 2016.

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LANDMARKS OF SPIRITUAL AUTOBIOGRAPHY FROM THE ORTHODOX SPACE IN THE 19TH AND 20TH CENTURIES

Flavius-Cristian MĂRCĂU¹

ABSTRACT:

THIS IS A BOOK REVIEW OF: MAXIM (IULIU-MARIUS) MORARIU, *REPERE ALE AUTOBIOGRAFIEI SPIRITUALE DIN SPAȚIUL ORTODOX ÎN SECOLELE XIX ȘI XX* [LANDMARKS OF THE SPIRITUAL AUTOBIOGRAPHY IN THE XIXTH AND XXTH CENTURIES, (IAȘI: LUMEN PUBLISHING HOUSE, 2019) AND IT PRESENTS ITS CONTENT AND VALUE FOR THE CONTEMPORARY RESEARCH AND THE INTER-DISCIPLINARY VALUE.

KEY WORDS: JOHN OF KRONSTADT, SILOUANE THE ATHONITE, NICOLAE BERDIAEV, AUTOBIOGRAPHICAL TEXTS, MYSTICS.

Iuliu-Marius Morariu is already known in the scientific space thanks to his previously published books.² Spiritual autobiography was also among the topics frequently approached

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² See, for example: Iuliu-Marius Morariu, *Mystique and autobiography from Romanticism to nowadays - studies in Orthodox Spirituality*, (Saarbrücken: Lambert Academic Publishing, 2016); Iuliu-Marius Morariu, *Stări, momente și personalități din Ortodoxia transilvană – pasaje insuficient reliefate istoriografic* [States, moments and personalities from the Transylvanian Orthodoxy – passages not enough emphasized by the historiography] (Târgu Jiu: Academica Brâncuși Press, 2013); Iuliu-Marius Morariu, *Restitutio Grigore Pletosu*, (Cluj-Napoca: Eikon and Renașterea Publishing House, 2014); Maxim Morariu, *Sfântul Constantin Brâncoveanu - un model pentru tinerii de astăzi* [Saint Constantin Brâncoveanu – a model for today's youth], (Cluj-Napoca: Renașterea Publishing House, 2015); Gavrilă-Tudor Zinveliu, Maxim Morariu, *Noi aspecte ale martiriului Sfinților născuți* [New aspects of Născu's Saints Martyrdom], (Cluj-Napoca: Renașterea Publishing House, 2016); Iuliu-Marius Morariu, *Preoții născuți și „Astra” (1861-1918)* [Născu Priests and ASTRA (1861-1918)], (Cluj-Napoca and Bistrița: Argonaut Publishing House, Charmides Publishing House, 2016); Iuliu-Marius Morariu, *Autobiografia spirituală a lui Dag Hammarskjöld – o abordare teologică* [Dag Hammarskjöld's spiritual autobiography – a theological approach], (Cluj-Napoca: Argonaut Publishing House, 2016); Iuliu-Marius Morariu, *Asociaționismul cultural din zona Bistriței și a Născudului (1850-1918)* [Cultural Associationism in Bistrița and Născu Areas (1850-1918)], (Cluj-Napoca: Argonaut Publishing House, 2017); Iuliu-Marius Morariu, *„Țara Născudului” în Primul Război Mondial - aspecte memorialistice, socio-economice și culturale* [“Născu country” in the First World War – memorialistic, socio-economical and cultural aspects], vol. 1 and 2, (Cluj-Napoca: Argonaut Publishing House, 2018); Iuliu-Marius Morariu, *Rolul tânărului cercetător în Asociațiunea ASTRA* [The role of the young researcher in ASTRA Association], (Dej: Astra Press, 2017); Mihai-Octavian Groza, Gabriela-Maria Nisipeanu, Iuliu-Marius Morariu (coord.), *Sebastian Stanca*

by him in the last years. His investigations were materialised in important studies and articles dedicated to it or to the convergent topics.³ Now, the book entitled: *Repere ale autobiografiei spirituale din spațiul ortodox în secolele XIX și XX [Landmarks of the spiritual autobiography in the XIXth and XXth centuries]*, (Iași: Lumen Publishing House, 2019) comes as a synthesis of his concerns and it is the first important work dedicated to the topic in this area.

Segmented into five big chapters and accompanied by a foreword written by Metropolit Andrei of Cluj (p. 7-12), abstracts in English language (p. 501-504), French (p. 505-510) and Italian (p. 511-515), a detailed bibliographical list (p. 435-500) and an index of names (p. 516-536), the work starts with an introduction (p. 13-36) where the author speaks about the relevance of the spiritual autobiography, the way how it can contribute to the creation of bridges between spiritualities or about its interdisciplinary value. He also evaluates critically the literature dedicated to the topic in other confessional areas or from the philological, psychological or philosophical space.

It is followed by a chapter dedicated to the explanation of the keywords of the demarche (p. 37-70), namely "spiritual" and "autobiography", where the author emphasizes which are the elements that differentiate the investigated genre by all the other autobiographical texts. Afterwards, Iuliu-Marius Morariu presents the landmarks of the spiritual autobiography from the Christian space from Saint Paul, considered the founder of the genre and until nowadays (p. 71-150). He shows there why the aforementioned author and not Saint Augustine must be considered the founder of the genre and how in different protestant backgrounds the spiritual autobiography is used with proselyte purposes (people being stimulated to write about their experience for converting others too).

(1878-1947). *Un cleric cărturar din Sebeșul de altădată [Sebastian Stanca – a cleric from other times Sebeș]*, (Cluj-Napoca: Argonaut Publishing House, 2016).

³ Like: Iuliu-Marius Morariu, "Aspects of Applied Ethics in the Spiritual Autobiographies from the Orthodox Space in the 19th and 20th Centuries," in Camelia Ignătescu, Antonio Sandu, Tomiță Ciulei (eds.), *Proceedings Volume: Rethinking Social Action. Core Values in Practice*, (Iași: Lumen, 2017), 548-557; Iuliu-Marius Morariu, "Aspects of political theology in the spiritual autobiography of Dag Hammarskjöld," in *HTS Teologiese Studies / Theological Studies*, 74 (September-December 2018), no. 4:1-5; Iuliu-Marius Morariu, "Aspects of political theology in the spiritual autobiography of Saint John of Kronstadt (1829–1908)," in *HTS Teologiese Studies / Theological Studies*, 74 (September-December 2018), no. 4:1-5; Iuliu-Marius Morariu, "An interdisciplinary genre in the Theological Literature: the spiritual autobiography and its landmarks for the Orthodox space," in *Journal of Education, Culture and Society*, 8 (January-June 2018), no. 1: 145-150; Iuliu-Marius Morariu, "Aspects of political theology in the spiritual autobiography of Nicolas Berdiaev," in *HTS Teologiese Studies / Theological Studies*, 75, (September-December 2019), no. 4: 1-4; Iuliu-Marius Morariu, "Self-development and autobiography," in *Journal for the Study of Religions and Ideologies*, 18 (Winter 2019), no. 4: 218-222; Iuliu-Marius Morariu, "The relevance of humiliation and body pain in the spiritual autobiographies of Saint Teresa of Avila and Saint Silouan the Athonite," in *Studia Monastica*, 61 (December 2019), no. 2: 409-415; Iuliu-Marius Morariu, "The Spiritual Autobiography in the Eastern space in the second half of the XIXth and XXth century", in *Astra Salvensis*, 3 (December 2014), Supplement no. 1: 166-174; Iuliu-Marius Morariu, Ștefan Josan, "Elements of spiritual autobiography in the literary works of Virgil Gheorghiu", in *Research and Science Today*, 11 (March 201) no. 1: 83-88; Iuliu-Marius Morariu, "Aspects of political theology in the spiritual autobiographies of the Orthodox space? New potential keys of lecture," in *Astra Salvensis*, 5 (December 2017), no. 10: 129-133; Iuliu-Marius Morariu, "Saint Faustina Kowalska and Saint Teresa of Calcutta – two authors of spiritual autobiographies from Catholic space of the 20th century" in *Astra Salvensis*, 7 (June 2019), no. 13: 231-239; Cătălin, Peptan, *Information and intelligence in security equation*, Annals of the „Constantin Brâncuși” of Târgu Jiu, Letter and Social Science, Series 2/2019, 39-45; Iuliu-Marius Morariu, "Educational Aspects in the Spiritual Autobiography of Mother Teresa of Calcutta," in *Astra Salvensis*, 7 (December 2019) no. 14: 307-312.

Then the investigation of the way how the genre developed in the Eastern Orthodox space starts from the one of the three important authors, namely: Saint John of Kronstadt and his diaries,⁴ Saint Silouane the Athonite⁵ and Nicolas Berdiaev.⁶ Each one receives a chapter (p. 151-265; p. 266-368; p. 369-420), and each thematic unity has an introductory sub-unity and conclusions. The author decides also to help the reader coming from another area of research by offering a brief biographical presentation of each author's life and activity in the context of the age where they leaved.

The presentations are followed by some long and well-documented general conclusions (p. 425-434), where the author not only summarize the main aspects approached there, but also offers the landmarks of the phenomenon of spiritual autobiography in the Orthodox space.

The rich bibliography used (in English, Romanian, French, Italian, Spanish or German languages), mostly formed by recent titles, together with the beauty of the approach and the actuality of the topic make Iuliu-Marius Morariu's (hieromonk Maxim) doctoral thesis, published at Lumen's Publishing House, an important book that will be surely used in the future research dedicated to the topic. We can only congratulate the author, wish him luck with future approaches and hope that the work will be soon translated in other languages too, for being useful also for readers that are not Romanian-speakers.

⁴ John Iliytch Sergieff, *My life in Christ, or Moments of spiritual serenity and contemplation, of reverent feeling, of earnest self-amendment, and of peace in God ... Extracts from the diary of the Most Reverend John Iliytch Sergieff ("Father John")*, (London: Cassell and company, 1897); Saint John of Kronstadt, *Viața mea în Hristos [My life in Christ]*, (Bucharest: Sophia Press, 2005); Saint John of Kronstadt, *Adevărurile în care cred [The thruths that I think in]*, (Bucharest: Sophia Press, 2011); Saint John of Kronstadt, *Ultimele însemnări [Last notes]*, (Bucharest, Alexandria: Orthodox Book and Romanian Book Presses, 2006); Saint John of Kronstadt, *Calea pocăinței lăuntrice - jurnal duhovnicesc needitat [The way of inner penitence – spiritual unedited diary]*, (Bucharest: Evanghelismos Press, 2010); Saint John of Kronstadt, *Către păstorii duhovnicești [To the spiritual fathers]*, (Galați and Alexandria: Egumenița and Orthodox Book Presses, 2012); Saint John of Kronstadt, *Cum ne mântuiește Dumnezeu - sfaturi de urmat pentru toată vremea [How does God saves us – advices to follow everytime]*, (Bucharest: Sophia Press, 2012); Saint John of Kronstadt, *Cunoașterea de Dumnezeu și cunoașterea de sine, dobândite prin experiență [Knowledge of God and self-knowledge, received through experience]*, (Bucharest: Sophia Press, 2010).

⁵ Saint Silouane the Athonite, Sfântul Siluan Athonitul, *Între iadul deznădejdiei și iadul smereniei [Between the hell of desperation and the hell of humility]*, (Sibiu: Deisis Press, 2001).

⁶ Nicolas Berdiaev, *Essai d'autobiographie spirituelle*, (Paris: Editions Buchet Castel, 1992).

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27. **Saint John of Kronstadt;** *Calea pocăinței lăuntrice - jurnal duhovnicesc needitat [The way of inner penitence – spiritual unedited diary]*, (Bucharest, Evanghelismos Press, 2010);
28. **Saint John of Kronstadt;** *Către păstorii duhovnicești [To the spiritual fathers]*, (Galați and Alexandria, Egumenița and Orthodox Book Presses, 2012);
29. **Saint John of Kronstadt;** *Cum ne mântuiește Dumnezeu - sfaturi de urmat pentru toată vremea [How does God saves us – advices to follow everytime]*, (Bucharest, Sophia Press, 2012);
30. **Saint John of Kronstadt;** *Cunoașterea de Dumnezeu și cunoașterea de sine, dobândite prin experiență [Knowledge of God and self-knowledge, received through experience]*, (Bucharest, Sophia Press, 2010);
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33. **Saint Silouane the Athonite;** *Sfântul Siluan Athonitul, Între iadul deznădejdi și iadul smereniei [Between the hell of desperation and the hell of humility]*, (Sibiu, Deisis Press, 2001); **Zinveliu, Gavrilă-Tudor, Morariu, Maxim;** *Noi aspecte ale martiriului Sfinților născădeni [New aspects of Năsăud's Saints Martyrdom]*, (Cluj-Napoca, Renașterea Publishing House, 2016);

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INTERFERENCES BETWEEN MORALS AND LAW IN ROMANIAN CONTEXT

Iuliu-Marius MORARIU¹

ABSTRACT:

IN THIS ARTICLE, AUTHOR PRESENTS THE WAY HOW, DURING THE HISTORY, MORALS AND LAW INTERFERED IN ROMANIAN CONTEXT AND SHOWS HOW IN DIFFERENT MOMENTS OF HISTORY, CHURCH WAS THE ONE WHICH, THROUGH THE MORALS ALSO CONTROLLED THE CIVILE LAW. IT ALSO EMPHASIZES THE PROCESS OF DEVELOPMENT OF CIVILE LAW AND ITS SEPARATION FROM THE MORALS IN THE HISTORY AND IT SPEAKS ABOUT THE CONTEMPORARY SITUATION, BUT ALSO ABOUT SPECIAL MOMENTS OF THE ROMANIAN HISTORY LIKE THE COMMUNIST PERIOD. AREAS LIKE POLITICAL THEOLOGY, MEDIAEVAL HISTORY, RELATIONSHIP BETWEEN CHURCH AND STATE AND FIRST ONE'S CONTRIBUTION TO THE APPARITION AND DEVELOPMENT OF MODERN STATE, ARE ALSO FACED THERE, INSIDE AN ARTICLE THAT AIM IS TO BE AN OVERVIEW OF THE WAY HOW MORALS, PRIVATE AND CIVILE LAW INTERFERED DURING THE CENTURIES AND INFLUENCED THE HISTORICAL DEVELOPMENT OF ROMANIAN SPACE. IN HIS DEMARCHE, THE AUTHOR USES INFORMATION PROVIDED BOTH BY HISTORICAL, THEOLOGICAL OR LAW SOURCES, BUT IT DOES NOT NEGLECTS OTHER SOURCES THAT, AT LEAST PARTIALLY, APPROACH HIS TOPIC.

KEY WORDS: PRAVILA, CHURCH, STATE, SECULARISATION, ALEXANDRU IOAN CUZA, SECULAR STATE.

INTRODUCTION

Morals and law have been, since the ancient times, important elements of the social life. While the first one was used in the religious space,² the other one is relevant for the social order and for aspects like social justice or the life and organisation of a state. If the first one uses principles and is related with religion and intrinsic motivation,³ the other one is offers a pack of rules and is also related with a coercive system that sometimes uses punishment for correction of behaviour with negative social effects.

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² Dumitru Stăniloae, *Teologia Morală Ortodoxă, vol. III [Orthodox Moral Theology, 3rd volume]*, (Bucharest: Press of Biblical and Missionary Institute of Romanian Orthodox Church, 1981), 14.

³ Ștefan, Ștefan, *Morala Creștină și Etica Postmodernă. O Întâlnire Necesară [Christian Morals and Postmodern Ethics. A Necessary Encounter]*, (Cluj-Napoca; Cluj University Press, 2009), 20.

But despite of these differences, there must be said that, in the history⁴, there were many moments of interference between the two ones. Therefore if one takes a look on the Byzantine history, will surely see that there were moments when law was seen as practical extensions of morals,⁵ fact that explains why even the religious life developed a branch deeply related with juridical rules, offered so much to the cannon law or influenced the publication of some juridical documents like Justinian's *Eclogue*⁶ or the later legislative Byzantine documents. A similar situation can also be encountered in the Western space, where the relationship between law and morals will be also visible during the Middle Age.

Conscious of this fact, we will try there to speak about the interferences between morals and law in the Romanian context. Placed in the Eastern Europe, Romanian lands have been since the formation of the Mediaeval Kingdoms that were later united in the contemporary country,⁷ at the crossroads of powers like the Ottoman Empire, the Russian or the Austro-Hungarian one. This explains why, while in Moldavia and Wallachia there is a law tradition with a strong Byzantine influence, whose evolution was also related with the history of the Orthodox Church, in Transylvania, there was a different approach, with a smaller Church influence. In order to see how the morals have influenced the development of the law and which were the main points of interference between the two aspects during the history, we will use there books dedicated to the history of the law⁸, history of the Church⁹, canon law¹⁰ and other similar topics. While the influence of Byzantine law on the Romanian context have also been previously investigated,¹¹ we will also try there to not neglect this topic and to bring into debate its most important aspects.

The presentation will try to emphasize the dynamics of this interference between morals and law from the medieval context and until nowadays, when there is a separation between Church and state and moreover, due to a misunderstood manifestation of secularism, often regarded as a problem of political theology¹² the first one is often considered as being too conservative and therefore sent out from the table of public debates.

⁴ Flavius Cristian Mărcău, Mihaela Andreea Ciorei, "The role of intelligence in the fight against terror," in *European Scientific Journal*, IX (2013), no. 2, p. 1-11

⁵ Helene Arhveiler, *Ideologia Politică a Imperiului Bizantin [Political Ideology of The Byzantine Empire]*, (Bucharest; Corint Press, 2002), 42; Ioan Bitoleanu, *Introducere în Istoria Dreptului [Introduction in Law History]*, (Bucharest: Press of Tomorrow's Romany Foundation, 2006), 38; Stelian Brezeanu, *O Istorie a Imperiului Bizantin [A History of Byzantine Empire]*, (Bucharest: Albatros Publishing House, 1981), 5; A. A. Vasiliev, *Istoria Imperiului Bizantin [History of Byzantine Empire]*, (Iassy: Polirom Press, 2010), 18.

⁶ Avram Andea, *Sinteză de Istorie Bizantină [Synthesis of Byzantine History]*, (Timișoara: Mirton Press, 1995), 105.

⁷ For more information about this aspect, see: Ioan Aurel Pop, *Istoria Românilor [History of Romanians]*, Bucharest, Cluj, Chișinău, Litera Press, 2011).

⁸ Mihai T. Oroveanu, *Istoria Dreptului Românesc și Evoluția Instituțiilor Constituționale [History of Romanian Law and the Evolution of Constitutional Institutions]*, (Bucharest: Cerna Press, 1992); George Fotino, "Ce Este Dreptul Românesc? [What Is the Romanian Law?]," in *Analele Facultății de Drept din București*, 12 (1939), no. 1: 174-201.

⁹ Ioan Rămureanu, *Istoria Bisericească Universală [History of Universal Church]*, (Bucharest, Press of Biblical and Missionary Institute of Romanian Orthodox Church, 2004); Nicolae Chifăr, *Istoria Creștinismului, Vol. II [History of Christianity, Second Volume]*, (Iassy: Trinitas Press, 2000).

¹⁰ Ioan Floca, *Drept Canonic Ortodox. Legislație și Administrație Bisericească, Vol. II [Orthodox Canon Law. Church Legislation and Administration, Second Volume]*, (Bucharest, Press of Biblical and Missionary Institute of Romanian Orthodox Church, 1990).

¹¹ Iuliu-Marius Morariu, "Receptarea Dreptului Bizantin în Țările Române [The Reception of Byzantine Law in Romanian Countries]," in *Cetatea Culturală*, 14, (April 2013), no. 4: 81-88.

¹² Iuliu-Marius Morariu, "Aspects of political theology in the spiritual autobiography of Dag Hammarskjöld," in *HTS Teologiese Studies / Theological Studies*, 74 (2018), no. 4: 1-5; Iuliu-Marius Morariu, "Aspects of political

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According to the *Statute for the organization and function of Romanian Orthodox Church*,¹³ which is the majoritarian church in the Romanian space (with more than 86 per cents of faithful), nowadays, between state and Church there is a clear separation. During the history it has not always been the same. Being a *Byzance after Byzance*,¹⁴ the Romanian space known, as already mentioned, especially in Wallachia and Moldavia, strong Byzantine influence.

Therefore there, the first documents with juridical value had a religious influence. This explains why, especially during the Middle Age it is difficult to separate the civil law by the religious one and why in many cases the motivations of a law from the lay space is religious. In an attempt to offer an overview of the canonical and juridical documents released in this space in the aforementioned period, but also to show which was the Greek contribution in this area, a contemporary Romanian canonist shows that:

"Between the collections of laws (names) of the Romanian-Byzantine state and the collections of canons (canones), especially in the form of nomocanones that circulated on the Romanian space, the following were kept as Greek, Slavic and Romanian manuscripts: Alphabetical Syntagma of Matei Vlastaris (1335) - (translated into Slavic language in 1345 or 1348); The Teachings of the Holy Fathers; The nomocanon of Manuil Malaxos (1563); The Law Manual or the Hexabiblos of Harmenopoulos (1345); Syntax of Jacob by Ianina (1645); The Canon of John the Postman; Byzantine agricultural law (8th century); The basilicals, etc.

The legal codes of Romanian-Byzantine origin used by the Romanians have always been adapted to the concrete situations, with the time appearing and a series of compilations, especially in the Romanian language, of which the following have been kept and are known: "Pravila of the priest and scholastic Luca (1581); Pravila of Father Toader from Lower Râpa (1610); Pravila of the Holy Fathers of Codex Neagoianus (1620-1621); The spine of the people (17th century); Pravila in short choice (17th century - before 1632); and many other fragments kept in different libraries still not studied, kept in manuscript form."¹⁵

As it can be seen, it is even difficult to differentiate between religious and pure juridical documents. The "Pravils" were prepared as documents that regularise the life of the society, but they had a strong influence from the moral side. The same aspects can be seen also in other documents with juridical value, like the *Chronicals of Stephen the Great*¹⁶ or *The advices of Neagoe Basarab to his son Teodosius*.¹⁷ Moreover, in the Middle Age, in the two aforementioned Kingdoms, the bishops and priests had also juridical attributions, as

theology in the spiritual autobiographies of the Orthodox space? New potential keys of lecture," in *Astra Salvensis*, 5 (December 2017), no. 10: 129; Maxim Morariu, "O Perspectivă Ortodoxă Asupra Fenomenului Secularizării [An Orthodox Perspective on Secularisation Phenomenon]," in *Altarul Banatului*, 16 (March-June 2015), no. 3-6: 76.

¹³ Romanian Orthodox Church, *Statutul pentru Organizarea și Funcționarea Bisericii Ortodoxe Române [The Statute for the Organisation and Function of Romanian Orthodox Church]*, (Bucharest, Press of Biblical and Missionary Institute of Romanian Orthodox Church, 2008), 5.

¹⁴ Nicolae Iorga, *Bizanț după Bizanț [Byzance after Byzance]*, (Bucharest: Romanian Encyclopaedic Press, 1972).

¹⁵ Ioan N. Floca, *Din Istoria Dreptului Românesc, Vol. 1 [From the History of Romanian Law, First Volume]*, (Sibiu: Archdiocesan Press, 1993), 6-7.

¹⁶ Stephen the Great, *Cronica lui Ștefan cel Mare – Versiunea Germană a lui Schedel [Stephen's the Great Chronical- Schedel's German Version]*, (Bucharest: House of the Schools Press, 1942).

¹⁷ Neagoe Basarab, *Învățăturile lui Neagoe Basarab Către Fiul Său Theodosie [The Teachings of Neagoe Basarab to His Son Teodosius]*, (Bucharest: Roza Vânturilor Press, 1996).

contemporary research shows.¹⁸ If this was the situation in the Wallachian and Moldavian space, in Transylvania, things looked a little bit different. The "Pravils" were also used there,¹⁹ but starting from the 16th century, they had relevance only for the Church space while in the civil life, the rules imposed by the authorities of the Transylvanian Autonomous Principate and later by the Austro-Hungarian or Habsburg authorities will be the normative ones for the lay space.

The emancipation of the law from morals will come later, in the 19th century. It will be Alexandru Ioan Cuza's secularization law²⁰ the one of the moments that will contribute to its initiation.²¹ Still, the total separation between the two will come on 11th of July 1866.²² This will be the moment that marks a definitive separation between moral and possible future practices with law or, in other words, between moral and an ideological interference with law. Adopted under the pressures of King Carol I, freshly installed as king of Romania, the document will have a big relevance not only for the future evolution of the country, but also for the context when it became its fundamental document. But it was a Constitution based on the French model. This explains the clear demarcation between State and Church and the individualization of juridical aspects by the moral ones.

The prerogatives of the state and the one of the Church, but also their relationships will be clearly defined there and in the later outcomes of the document like the Civil or the Penal Code. At the bureaucratic level there will be also changes. For example, if before the document released by Church authority is enough to justify a birth, marriage or a death, since then, in parallel with Church registers, the state will also initiate to have its own documents. Moreover, the Church will not be able anymore to officiate a matrimony without having an official document. Even later, when the Catholic Church will have a Concordat with the

¹⁸ Constanța Vintilă Ghițulescu, *În Șalvari și cu Ișlic. Biserica, Sexualitate, Căsătorie și Divorț în Țara Românească a Secolului al XVIII-lea* [In Șalvari and with Ișlic. The Church, Sexuality, Marriage and Divorce in the Romanian Country of the 18th Century], (Bucharest: Humanitas Publishing House, 2004); Constanța Vintilă Ghițulescu, *Evgheniții*, (Bucharest: Humanitas Publishing House, 2006); Constanța Vintilă Ghițulescu, *Focul Amurului. Despre Dragoste și Sexualitate în Societatea Românească, 1750-1830* [Fire of Love. About Love and Sexuality in the Romanian Society, 1750-1830], (Bucharest, Romania: Humanitas Publishing House, 2013); Constanța Vintilă Ghițulescu, *Patimă și Desfătare* [Passion and Delight], (Bucharest: Humanitas Publishing House, 2015).

¹⁹ Mircea Păcurariu, *Istoria Bisericii Ortodoxe Române* [History of Romanian Orthodox Church], (Bucharest: Press of Biblical and Missionary Institute of Romanian Orthodox Church, 2006), 98.

²⁰ Antonie Plămădeală, *De la Filotei al Buzăului la Nicolae Bălcescu și Andrei Șaguna* [From Philotheos of Buzău to Nicolae Bălcescu and Andrei Șaguna], (Sibiu: Press of Sibiu Romanian Orthodox Diocese, 1997); ***, *Secularizarea Averilor Bisericești (1863): Motivații și Consecințe - Simpozion Național, București, 12 Noiembrie 2013* [The Secularization of Church Fortunes – National Symposium, Bucharest 12th of November 2013], (Bucharest: Basilica Press, 2013).

²¹ In 1863, the Principe of Wallachia and Moldavia, united in 1859, will decide to nationalise the fortunes of the most important monasteries from the two countries and to use the lands for starting an agrarian law, that aim was to help the peasants by offering them half of hectare of land for agrarian purposes. At that moment, most of the Romanian monasteries were dedicated to the Mount Athos or to the Holy Land. For this reason, the abbots were in majority Greeks and the use of the products of those lands (Monasteries like Voroneț had at that time about 50 villages belonging to them) where used by them. Cuza also intended a second phase of the law, that aim was to offer to the peasants also the tools needed to use properly the lands. Unfortunately, in 1866, he was sent into exile at Florence and did not succeed to accomplish his plan.

²² ***, *Constituția din 1 Iulie 1866 cu Modificările Adunărilor Constituante din 1879 și 1884 după Edițiunea Oficială* [The Constitution from 1st of July 1866 with the Changes of the Constituent Assemblies from 1879 and 1884 According to the Official Edition], (Bucharest: Press of the Bookstore Alcala & Co, 1890).

Romanian state, during the interwar period (Moldovan 1942; Runcan 2000),²³ this aspect will remain the same and the topics stipulated there will be related with Church's possessions, educational system for clergyman and other aspects, not with making as it would be in Italy, the matrimonial document released by a priest, to have an official value for the state too.

During the communist period, there will be stipulated an official separation between Church and state.²⁴ In fact, the state will try as much as possible to eliminate Church (will also succeed to do it with the Greek-Catholic Church, partially with the Catholic one and will also persecute many Orthodox priests and bishops that were not thinking according to the "exigencies" of the regime. In this period, more than before, there will not exist anymore any interference between law and morals. The last one will not be anymore used to justify any legislative aspect, and the role played by the religion in the history will not be anymore emphasized in these decades. This can be surely considered the moment of total separation between morals and law, as the one of separation between Church and state. If in previous situations, documents like Nicodim Sachelarie,²⁵ normative for private law will define different law using moral criteria (for example, seeing matrimonial aspects in terms like "sin" and classifying them on basis of elements like the adultery), and some of these aspects will be invoked even later in the interwar period, in cases with ambiguity, during the communist one, this will not happen.

After 1989, although the Church will start to regain its place in society and the need for spiritualisation will become, at least in the first years after the fall of communism, an important and debated topic, morals will not be from now on considered normative for the society. Moreover, little by little, state will start to see the Church as a concurrency and with the help of other institutions seeking for credibility (like mass-media), will contribute to its diminishing. If before the 2000's, the similitudes regarding the morals and law or the role played by the Church or morals in development of a certain juridical aspect will be neglected, after this moment, the secular society will even start to criticise the religious institution and to see it as a promoter of old-fashioned or even anti-social ideas. Therefore, since this moment, the so called lay area or the scientific field will not only neglect the potential moral interferences between morals and law, but will also argue against them. This seems more strange in a context where the scientific discourse is always directed towards interdisciplinarity and the need to create bridges and holistic approaches.

One of the most visible examples and for sure the most recent one, can be considered the referendum for the sustaining of the traditional family, from 2018.²⁶ Promoted by a

²³ Ștefan Moldovan, *Concordatul în Dreptul Internațional și Concordatul Statului Român cu Vaticanul [The Concordat in International Law and the Concordat of Romanian State with Vatican]*, (Sibiu: "Dacia Traiană" Press, 1942); Nechita Runcan, *Concordatul Vaticanului cu România: Considerații Istorico-juridice [The Concordat of Vatican with Romania. Historical and Juridical Considerations]*, (Constanța: Ex Ponto Press, 2020).

²⁴ For more information about the relationship between the Orthodox Church and communist state, see for example: Iulia Conovici, *Ortodoxia în România Postcomunistă. Reconstrucția unei Identități Publice, Vol. 1 [The Reconstruction of a Public Identity: Orthodoxy in Post-communist Romania, 1st Volume]*, (Cluj-Napoca: Eikon Press, 2009); Iulia Conovici, *Ortodoxia în România Postcomunistă. Reconstrucția unei Identități Publice, Vol. 2 [The Reconstruction of a Public Identity: Orthodoxy in Post-communist Romania, Second Volume]*, (Cluj-Napoca: Eikon Press, 2010).

²⁵ Nicodim Sachelarie, *Pravila Bisericească [Church's Rules]*, (Cernica: Credința Strămoșească Press, 1940).

²⁶ For more information about this event and its reception, see also:

https://en.wikipedia.org/wiki/2018_Romanian_constitutional_referendum, accessed on 22. 12. 2019;
<https://www.libertatea.ro/stiri/referendum-pentru-familie-2018-2408195>, accessed on 22. 12. 2019;

coalition of the Christian Churches and denominations from the Romanian space, the initiative aimed to change the Constitution and to make it clear that the family represents the union between a man and a woman (it was so in previous constitutions, until its final revised version from 2011). Although it started from a Christian initiative and it has moral arguments, it was also relevant from the juridical point of view, due to its consequences in this area. Unfortunately, only 21 per cents from the ones who had the right to vote did it²⁷ and its results were invalidated. Strongly criticised by different political representatives as also by some non-governmental organisations and some of mass-media organs and deeply sustained by the Churches and some political parties or NGO's on the other sides, the referendum was often presented as a confrontation between the retrogrades values of the Church and the society or as a testimony of the abjuration of the Church itself from fundamental principles such as that of love or tolerance.

Most of its contesters refused to see the principles that were at the base of the demarche, while the sustaining Churches, most probably from an error of communication, presented it rather as a fight against the ones who are different then as a manifest for an aspect that can be seen in the juridical area since millennia (as in the moral area too). It is not the purpose of this research to present the intrinsic motivations of one side or other and therefore we will not insist there more on this topic. Still, one aspect is as clear as possible, namely the fact that the initiative represented a moment that proved that the moral is not anymore wanted to interfere with juridical space and a testimony that its influence towards the development of a clear way of thinking and understanding the law and offering complementary arguments in its understanding it is not anymore recognised or wanted.²⁸ As a moment where there can be seen the interference between the two important domains, the moment from 2018 surely emphasized the fact that although, morals and law are two different domains with different instruments of thinking and understanding the reality and different purposes, they can be seen in a complementary way and although if today the influence of morals towards law is not anymore recognised, in the past, it was a reality.

CONCLUSION

As we have tried to show in the rows above, the relationships between morals and law knew, in Romanian space, a special dynamics. Therefore, in certain moments of history it was difficult to separate them and the law was rather considered as an outcome of morals than as an independent branch of science. Due to the fact that Romanian space was, as the most important historian from this space says, a "Byzance after Byzance,"²⁹ there can be found many byzantine influences there and the byzantine way of thinking can be also used in order to understand the civil and ecclesiastic mechanisms from Romanian Medieval space.

The later development of juridical life from the pre-modern and modern age, materialised in documents like the *Pravila's*,³⁰ knows also the interference of morals and law. Aspects of civil or private law are seen through the lengths of the morals or justified on its

<https://www.vaticannews.va/ro/mapamond/news/2018-09/romania-referendum-pentru-familie.html>, accessed on 22. 12. 2019; <https://www.digi24.ro/referendum-familie-2018/referendum-schimbare-constitutie-redefinire-casatorie-familie-1008821>, accessed on 22. 12. 2019.

²⁷<https://www.digi24.ro/referendum-familie-2018/rezultate-finale-referendum-au-votat-2110-dintre-alegatori-1010305>, accessed on 22. 12. 2019.

²⁸https://ro.wikipedia.org/wiki/Discu%C8%9Bie:Referendumul_de_modificare_a_articolului_48_din_Constitu%C8%9Bia_Rom%C3%A2niei, accessed on 22. 12. 2019.

²⁹ Nicolae Iorga, *Bizanț după Bizanț [Byzance after Byzance]*.

³⁰ For example: Nicodim Sachelarie, *Pravila Bisericească [Church's Rules]*.

basis. If one takes a look on topics like the matrimonial law and its punishments in the aforementioned period, he will surely see that it is difficult to distinguish between sexual morals and matrimonial law.

The separation between the two ones will start, as we have already mentioned³¹ with the first Romanian Constitution. The fact that the first constitutional Romanian document is based on the French one partially explains this aspect.³² Still, the separation and the impossibility to see interferences between the two ones will become clear in the communist period. After 1989, there will be an increasing tendency not only to separate the two ones, but also not to show anymore the influence exerted by the first one on the second one and even a certain "fight" that will mark, with a certain delay compared with the Occident, the "exit from the religion."³³

In conclusion, it can be said, as we have also tried to show there that, if the law is seen in the Christian mediaeval pre-states from Romanian space, as an outcomes of religion and morals, little by little, the interferences between the two ones will become more and more rare nowadays and the contemporary society will even try to deny the influences of morals on the law and to cancel the ones that are too visible.

³¹ ***; *Constituția din 1 Iulie 1866 cu Modificările Adunărilor Constituante din 1879 și 1884 după Edițiunea Oficială* [The Constitution from 1st of July 1866 with the Changes of the Constituant Assemblies from 1879 and 1889 According to the Official Edition].

³² Due to the fact that in France the Constitution was an emanation of the Revolution and this moment of the history was marked not only by a separation between Church and state, but also by the rejection of the Church and its withdrawal from the state activities.

³³ Marcel Gauchet, *Ieșirea din Religie* [The Exit from Religion], (Bucharest; Humanitas Publishing House, 2006).

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THE IMPACT OF CRIME ON SOCIETY IN THE CURRENT SOCIO-ECONOMIC ROMANIAN CONTEXT

Adrian NICOLESCU¹

ABSTRACT:

CURRENTLY, WE CAN EASILY SEE THAT THE PHENOMENON OF CRIME IS MANIFESTING BOTH IN DEVELOPING OR UNDEVELOPED COUNTRIES AS WELL AS IN DEVELOPED COUNTRIES, NOT TAKING INTO ACCOUNT THE ECONOMIC, POLITICAL AND SOCIAL SITUATION OF THE SOCIETY AS A WHOLE. IN ORDER TO COMBAT CRIME, EFFORTS ARE BEING MADE BY ALL THE ACTORS INVOLVED, AND THE EFFORTS ARE OUTLINED, IN PRINCIPLE, AT THE LEGISLATIVE LEVEL BY ELABORATING AND UPDATING THE NORMATIVE ACTS CONCERNING THIS FIELD AND, NOT LASTLY, BY MODERNIZING THE TECHNIQUES FOR PREVENTING THESE ILLICIT ACTIVITIES, WHICH HARM ALL SOCIAL VALUES PROTECTED BY LAW. IN THIS CONTEXT, WE ARE WITNESSING AN ACCELERATION OF THE PROCESS OF GLOBALIZATION THAT INVOLVES AN EXPANSION OF THE COMMUNICATION NETWORKS, THE INCREASE OF INSECURITY ON ALL LEVELS, THE PROLIFERATION OF CONFLICTS OF ANY KIND, AND ALL THESE WILL GIVE RISE TO THE RAPID INCREASE OF THE PHENOMENON OF CRIME, ESPECIALLY WITH AN ORGANIZED, DIVERSIFIED AND CROSS-BORDER CHARACTER. IT MUST BE KNOWN THAT IT IS NECESSARY TO INCREASE THE DEGREE OF KNOWLEDGE REGARDING THE EVOLUTION AND IMPACT OF CRIME ON SOCIAL AND ECONOMIC DEVELOPMENT ON TODAY'S SOCIETY BY USING LEGAL AND TECHNICAL TOOLS TO COMBAT THIS RATHER COMPLEX PHENOMENON, BEING A CERTAIN FACT THAT AMONG THE IMPORTANT FACTORS THAT AMPLIFY THIS PHENOMENON ARE SOCIAL EXCLUSION, POVERTY AND UNEMPLOYMENT.

KEY WORDS: CRIME, KEY INSTITUTIONS, DETERMINANT FACTORS, SOCIAL ORDER

1. GENERAL CONSIDERATIONS

The expansion of organized crime represents an imminent danger and a clear threat to all the states of the world, regardless of their development status, determining a conclusive analysis and a complex evaluation, in order to adopt the appropriate and connected legislative and administrative measures for limitation and combating crime at international, European and national level. The impact is felt both by the European and global economies, seriously affecting the fiscal revenues of the states. It is noteworthy that in the current European and international context, a manifestation of environmental offenses has been found, which have a special and long-term impact on the living conditions of the communities.

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Certain offenses committed on the environment are irreversible in the sense that the damage can no longer be repaired, neither partially nor wholly. The imminent risks regarding environmental degradation, associated with the activity of cross-border crime networks and economic crime, are properly identified and managed by integrating environmental criminology into environmental governance. In this situation, a greater attention is required on the prevention, detection, investigation and criminal prosecution of the offenses against the environment, not only for the natural persons, but especially for the legal persons, following as much as possible the recovery of the caused damages, but also restoration of the affected areas.

Given that crime is a growing phenomenon with profound and serious consequences for the environment in which we live, discovering, adapting and choosing the most appropriate and effective means of prevention is a continuous and permanent concern for both lawyers and sociologists.

In the literature, criminality is a social problem, since it includes a significant discrepancy between the value reference systems and the expectations of individuals.²

A prudent society will defend not only after the crime has taken place but before it will occur. Thus, all appropriate measures will be taken to prevent the establishment of the conditions for the formation of crime, by engaging in an intense, systematic fight to combat the causes of crime.³

We emphasize that the effects of the crime phenomenon can be significantly reduced by clear prevention and control policies, but under no circumstances can the effects be stopped altogether, given that criminal behavior is a dimension of human conduct.

Taking into account the extent to which the crime is known and the extent to which the criminal law means react against it, it can be divided into real, apparent and legal crime.

The real crime represents the totality of the criminal offenses committed in a territory, in a certain period of time. This means that in practice, there is always a quantitative difference between the number of crimes actually committed and the number provided by the judicial statistics.

The apparent crime comprises the totality of the crimes reported to the judicial authorities and registered as such. This type of crime is different from the real crime, because it cannot be known and quantified for the following reasons - not all the criminal facts are brought to the knowledge of the authorized bodies of the state and registered as such; a final court decision is not pronounced in all cases, regarding all the criminal facts notified after the final investigations; a good part of the facts reported remain with unidentified authors.

The legal crime represents the totality of the criminal acts for which final sentencing decisions have been pronounced.⁴

2. THE CAUSES OF THE SOCIAL PHENOMENON OF CRIME

Currently, the phenomenon of crime is driven by a multitude of factors that dominate today's society, which is constantly changing, and which the authorities must take a quick approach to. Among the most essential generating factors of the phenomenon we list economic factors, demographic factors, socio-cultural factors, family, the impact of mass media.

² Tudor Amza, *Criminologie*, (Bucuresti: Editura Lumina Lex, 1998).

³ Aurel Dincu, *Bazele Criminologiei*, (Bucuresti:Editura Procardia, 1993).

⁴ Ion Chipaila, *Criminologie Generala*, (Craiova: Editura Stech, 2009), 23-24.

The economic factors that determine a criminogenic behavior are unemployment, the standard of living and, last but not least, the economic crises. Unemployment consists of the essential decrease of the incomes for the acquisition of the primary means of existence which determines a certain behavior contrary to the law order. The economic crises lead to a decrease in the standard of living that affects both the production, as well as the level of wages and the unemployment rate. In the absence of a reaction stemming from the state, constantly in social protection, people may be vulnerable in terms of their predilection for crime.

Family plays an essential role in the life of a child. Thus, delinquency studies have shown that, in many cases, the atmosphere in disorganized families, lack of parental authority, control, and their affection as a result of divorce, have determined children to adopt antisocial acts.

Regarding the socio-cultural factors, the specialized literature argued that, "in a broad sense, culture represents the totality of the material and spiritual values created by human society throughout history. Criminology is particularly interested in those cultural factors that play a predominant role in the positive or negative socialization of individuals and which ultimately lead them to commit antisocial facts."⁵

3. DEFINING ELEMENTS OF ORGANIZED CRIME MANIFESTED IN ROMANIA

"At a national level, organized crime manifests itself in many sectors of economic and social life, trying to control areas and financial markets, as well to infiltrate into the real economy by using intimidation and corruption in order to obtain profit and influence. The opening of borders in the region has facilitated the movement of people, goods and capital."⁶

"The organized crime groups in Romania, without being essentially different as a way of organizing and acting from the international ones, have some specific features: they have a specialization and they act on certain criminal segments; their mode of organization is predominantly "cell" type; they act in predetermined geographical areas; they have mobility in identifying new countries where they can carry out their criminal activities; they have permanent concerns in identifying new modes of operation and in reorienting them to new criminal spheres; they use the financial product obtained to carry out new criminal activities; they deal with money laundering and reinvestment in legal activities; they easily recruit new members to replace the old ones in the group structure; those active in the sphere of economic-financial crime target all segments of society, using all available financial instruments and even legislative loopholes; abroad, Romanian organizations are mainly known for their activities in the sphere of human trafficking, cybercrime and drug trafficking."⁷

The phenomenon of crime in Romania has certain peculiarities, so in the field of human trafficking, the counties in Moldova compared to those in the rest of the country, are more exposed, due to the low standard of living and the high unemployment rate. The victims, destined for internal and external trafficking, are especially minor and come from disorganized families, with a low level of education and with a maximum risk of social exclusion.

⁵ Gh. Nistoreanu, C. Paun, Criminologie, (Bucuresti: Editura Europa Nova, 2000), 93.

⁶ <https://intelligence.sri.ro/criminalitatea-organizata-sub-lupa/>. Accessed at 12.11.2019.

⁷ <https://intelligence.sri.ro/criminalitatea-organizata-sub-lupa/>. Accessed at 12.11.2019.

With a significant impact, tax evasion also manifests itself throughout Romania, especially in the area of large urban centers where a large number of companies trading products from China or Turkey are concentrated. Many of these acts of trade are illegal and contrary to the rules in force. Committing such illicit acts, which deviate from the rules of coexistence, are crimes that the criminal law severely punishes and it should not be neglected that these illegal behaviors feed the underground economy, which is becoming increasingly aware of a great diversity of illegal businesses giving birth to an uncontrolled monetary mass.

Computer crime is not to be neglected, it continues its upward, existing and international trend. Romania, along with the other European states, is still a country providing cybercrime, in the fields of computer fraud, credit card fraud, but also computer attacks. The main direction registered in the last period is the one of the computer attacks, Romania being a launching country, the "infrastructure", but also a target. International trends and new modes of operation immediately find their place in Romania, and in this sense, hackers, botnet networks, financial malware and ransomware, can be exemplified.

Last but not least, since the principle of free movement of goods and, in particular, of the persons of Romania is implemented, the latter is on the international map regarding the drug trafficking route, becoming a territory with many implications for storage, delivery as well as drug use. Means and methods of trafficking are constantly changing and adapt rapidly to the demands of the market, which significantly hinders the activity of the bodies empowered to prevent and combat the illicit activities.

In the big urban and university centers in Bucharest, Cluj, Iași, Constanța, Timișoara, there is an acceleration in the drug consumption. In these areas, the central and local authorities make sustained efforts, finding and preventing the trafficking and consumption of drugs crimes in which Romanian or foreign citizens are involved. For organized crime in the European community, because of being a transit country, Romania represents a real alternative for the introduction of cocaine in other European states. It can be noticed that in Romania, the competence of preventing and combating the investigation of organized crime is divided between several authorities that, in principle, do not cooperate efficiently and sufficiently, which results in that in many situations there are overlaps and the causes of the phenomenon are not properly investigated by the competent authorities.

4. MEASURES TO PREVENT AND COMBAT THE PHENOMENON OF CRIMINALITY

In the specialized literature it is highlighted that the definition and evaluation of the concept of criminal policy for crime prevention must take into account three dimensions⁸ : the first refers to the criminal law in force regarding the system of sanctions applied to the delinquent individuals, the second includes specialized institutions for prevention and specialized social control against crime, and the third one includes social reaction to crime and criminality.

Given the fact that total eradication of the effects of crime cannot be completely achieved, all the measures used to limit this phenomenon must take into account the multitude of criminal acts committed throughout the territory, as well as the particularities of the situations in which different persons or even institutions become targets of such crimes.

We believe that all the measures to prevent and combat the phenomenon of crime should be aimed at a more efficient application of existing legislation, and the obligation of

⁸ Radulescu S.M., Banciu D., Sociologia crimei si criminalitatii, (Bucuresti: Casa de Editura si Presa „Sansa” SRL, 1996), 224

the legislature is to complete and permanently improve the legislation on crime so as to keep the pace with the constantly changing reality. At the same time, it should not be neglected that better cooperation and collaboration between the responsible institutions in order to limit the criminal activity would be welcomed.

Also, institutions with significant attributions in the field of crime must orient their activity in two main directions regarding the prevention of this phenomenon. First, the authorities should consider the victims of these crimes by creating complex programs for counseling and assisting the victims, as well as those who have been the perpetrators of a crime. Secondly, they should aim to create the possibility of perfecting its own people who are active in this rather complex field and who are in a difficult position to control ascension and constant change.

With Romania's accession to the European Union, the entire legislative framework had to be harmonized with the legislation of the Member States. Therefore, the legislation of the European community has been transposed into national legislation with the sustained effort of all the actors involved in order to achieve this objective.

With the entry into force of the Lisbon Treaty, all EU Member States have an imperative obligation to strictly follow the directions set out in different fields, in particular in the field of combating crime. The treaty establishes the following areas of crime - terrorism, human trafficking and sexual exploitation of women and children, illicit drug trafficking, illicit arms trafficking, money laundering, corruption, counterfeiting of means of payment, computer crime, organized crime.

"In order to ensure the closeness of laws, regulations and administrative rules of the states in criminal matters, the Treaty gives the right of the European Parliament and the Council to decide, by directives adopted according to the ordinary legislative procedure, on the definition of offenses and sanctions in the fields of criminality which has a cross-border dimension."⁹

Also, through directives, in accordance with the provisions of art. 82, para. 2 of the Treaty on the Functioning of the European Union, the possibility of the European Parliament and the Council to establish minimum norms to ensure mutual recognition of judicial decisions in criminal matters, as well as police and judicial cooperation, regarding the following aspects - mutual admissibility of evidence between Member States, the rights of persons in criminal proceedings, the rights of victims of crime, other special elements of the criminal procedure identified by the Council, in advance, by a decision- has been recognized.

The Treaty of Lisbon outlined a legal framework manifested, in principle, through the efforts made to guarantee the freedom of movement and the prompt European response to the global threats facing today's society. Also, the treaty further strengthened the protection of fundamental rights and democratic control over EU policies on internal security and was the one that made the European Parliament a co-legislator on police and judicial cooperation in the field of organized crime.

The European Parliament and the Council play an essential role in the policy of preventing and combating crime as they outline, in principle, the main powers and competences of Europol, an institution of force in this field. Europol's main mission, as a law enforcement agency of the European Union, is to assist Member States in preventing and combating all serious forms of international crime. Its role is to contribute to a more secure Europe, for the benefit of all EU citizens, by supporting EU law enforcement, by exchanging

⁹<http://www.dragomirlaw.ro/articles/Rolul%20organizatiilor%20internationale%20de%20securitate%20pentru%20prevenirea%20si%20combaterea%20criminalitatii%20organizate.pdf>. Accessed at 13.11.2019

and analyzing crime information. At present, Europol is cooperating to combat the crime phenomenon with 17 countries outside the EU, nine EU bodies and agencies and three other international organizations, including Interpol, which is involved, in many respects, in Europol's operational activity.

“The European Commission considers that the assessment of the threat posed by the serious forms of crime and organized crime from 2017 constitutes a basis for establishing EU priorities in tackling crime for the next four years. Based on these considerations, the Commission invites the Council to approve the inclusion of the following eight types of crime in the list of priorities of the EU policy cycle on serious and internationally organized crime for 2018-2021: cybercrime, drug crime, illegal immigrants introduction, organized crime against property, trafficking in human beings, trafficking in firearms, fraud in the field of VAT and environmental crimes.”¹⁰

5. CONCLUSIONS

Crime is one of the manifestations that inevitably accompany problems such as poverty, lack of resources, lack of opportunities, lack of opportunities, marginalization. Considering that the phenomenon of crime as a social problem that does not take into account the geographical barriers or the levels of development, an American expert in this field characterized it, several decades ago, as a genuine "symptom of the decay of a nation", which synthesizes the main shortcomings of cultural, educational and economic policy.¹¹

Studies by the Rowntree Foundation have shown that economic policies, including welfare and social security programs, do not cause significant effects on youth crime or delinquency unless they have a full impact on a nation's psychology and culture.¹²

In other words, the facts contrary to the social order or even the crimes are not only generated by economic causes, but also by numerous other psychological and cultural variables. The response to the phenomenon of crime is multidisciplinary and involves the activity of a large number of central and local public institutions, as well as citizens or different civic, religious or social organizations existing at local level, so that their sometimes complementary, overlapping or even contradictory activity, may be, as far as possible, reduced or even eliminated.

In conclusion, the phenomenon of crime has a significant negative impact on the socio-economic development of today's society, but this impact is amplified by corruption that has penetrated at all institutional levels. State, through anti-corruption measures, clearly increases the economic efficiency and, implicitly, the administrative efficiency of the law enforcement institutions, and the administrative and political measures for the economic development precisely reduce the impact of crime on the individual, generating legal, but not illegal opportunities in order to obtain income, educational support, social and health programs for vulnerable groups.

Clearly through all these measures the society as a whole prevents any deviations from the law order.

The fight against organized crime is still a real challenge for the authorities that make sustained efforts to stop this phenomenon, which is quite difficult to find. Organized crime is

¹⁰<https://ec.europa.eu/transparency/regdoc/rep/1/2017/RO/COM-2017-213-F1-RO-MAIN-PART-1.PDF>. Raport al Comisiei catre Parlamentul European, Consiliul European si Consiliu. Al saselea raport referitor la progresele inregistrate pentru realizarea unei uniuni a securitatii efective si reale.

¹¹ Walter A. Lunden, *Statistics in Delinquents and Delinquency*, Springfield, (Illinois: Charles C. Thomas, Publisher, 1964), 5.

¹² Rowntree Joseph Foundation, *Studies on Juvenile Delinquency*, (London: Cambridge, 1995).

a decisive element that favors terrorism, giving the actors of this phenomenon the possibility of acquiring weapons and acquiring illicit financial means.

Also, an issue currently faced by the empowered authorities in this field is the fact that "the border between cybercrime and traditional crime disappears to a greater extent as criminals use the Internet both as a way to intensify their activities, as well as a source of purchasing the means and finding new methods of committing crimes. Terrorism, organized crime and cybercrime are therefore interconnected areas, and supporting the fight against organized crime is a key priority for action at EU level within union security. "¹³

¹³<https://ec.europa.eu/transparency/regdoc/rep/1/2017/RO/COM-2017-213-F1-RO-MAIN-PART-1.PDF> .Raport al Comisiei catre Parlamentul European, Consiliul European si Consiliu. Al saselea raport referitor la progresele inregistrate pentru realizarea unei uniuni a securitatii efective si reale.

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RELIGION AND ITS IMPLICATIONS FOR GLOBAL POLITICS

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ABSTRACT:

THROUGHOUT TIME, THE RELIGIOUS PHENOMENON HAS BEEN ONE OF THE MOST CONTROVERSIAL TOPICS OF ANALYSIS AND THE TARGET OF MULTIPLE SOCIAL PERCEPTIONS. STARTING AS THE BINDING AGENT OF THE ARCHAIC COMMUNITIES, WHICH LATER GENERATED VARIOUS TYPES OF COMMUNITIES², TO BEING THE SOURCE OF CONFLICT OR TERRORISM ACTS, RELIGION AND RELIGIOUS BELIEFS HAVE BEEN PRESENT, MORE OR LESS NOTICEABLY, IN ALL THE HISTORICAL STAGES OF THE HUMAN SOCIETY AS A CONTRIBUTING FACTOR IN THE PROCESS OF DEFINING CERTAIN SOCIO-POLITICAL STRATEGIES OF THE WORLD'S NATIONS. VACILLATING FROM VITUPERATION TO APPRECIATION, THE RELIGIOUS PHENOMENON HAS FOLLOWED A SINUSOIDAL PATH, YET IT REMAINED A CONSTANT OF SOCIAL LIFE IN ANY HISTORICAL ERA, AND, MOST OFTEN, A CONSTANT WITHIN POLITICS.

THE PHENOMENON OF RELIGIOUS RESURGENCE IS NO LONGER A NOVELTY, BUT HAS BECOME AN IMPORTANT FACTOR IN VARIOUS AREAS OF SOCIETY. AND THIS GENERATES AT LEAST ONE IMPORTANT QUESTION: HOW DO WE RELATE TO THE RELIGIOUS PHENOMENON IN A POST-MODERN SOCIETY THAT CONSIDERS ITSELF SECULAR AND HUMANIST, WHILE CONTINUING TO BE MULTICULTURAL AND MULTI-RELIGIOUS?

THE THESIS OF THIS STUDY STARTS WITH THE ASSUMPTION THAT THE PHENOMENON OF RELIGIOUS RESURGENCE HAS BROUGHT CHANGES AT THE LEVEL OF INTERNATIONAL RELATIONS, INFLUENCING THE STRATEGIES AND POLITICAL DECISIONS IN THE INTERNAL AND EXTERNAL POLITICS. THE AIM OF THE PRESENT STUDY REVOLVES AROUND THE ASSERTION THAT THERE IS A RELATIONSHIP OF INTERDEPENDENCE BETWEEN THE RESURGENCE OF RELIGION AND THE INTERNAL AND INTERNATIONAL POLITICS. THIS STUDY ENDEAVORS TO DISCUSS THE DIMENSIONS OF THIS RELATION, AS WELL AS A FEW EMPIRICAL ASPECTS.

KEY WORDS: THE RESURGENCE OF RELIGION, INTERNATIONAL RELATIONS, GLOBALIZATION, IMPACT, POLITICS

THE RESURGENCE OF RELIGION. GLOBAL RELIGIOUS REVIVAL

In our contemporary world, it is very difficult to ignore the presence of religion in public affairs. The media portrays numerous cases of people, institutions, and ideas from the religious sphere thus demonstrating it continues to have a major relevance and influence on the political field.³

¹ Lecturer, Agora University of Oradea.

² George Moyser, *Politics and religion in the modern world*, (London and New York: Routledge, 1991), 1.

³ George Moyser, *Politics and religion in the modern world*, 1.

Proof of religious resurgence is already overwhelming and it is not disputable because it is accepted as inherent. Absolutely obvious especially in Africa and Latin America, this re-emergence is also visible in Asia and even Australia, through the increasing numbers of religious topics with each passing year since 2001. The seemingly European negative example, as exempt from the phenomenon of religious resurgence, through its continuous and extreme secular state, has already challenged a careful analysis of present practices.⁴

This wave of religious resurgence has multiple causes. First of all, certain people react to the failure of the secularization process and of the liberal and official religions to fulfill their religious needs. This is a familiar pattern in the history of religions. A second source for the religious rebirth is the continuous failure of justice, the incapacity of making a fair distribution of goods and services, including food and health products. Certain people react against the failure of the humanistic-secular paradigm to confer peace and prosperity, and to provide plausible explanations for inequity, evil and pain.⁵

The religious movements in many areas of the world, present in various religions and gradually drawing in more people and even organizations, are the reason the analysts deemed it necessary to reevaluate the secularization theory. One of the findings is that all the signs of religious rebirth contradict the secularization theory, outlined half-way through the middle of the 20th century. Religion should have gradually become all the more private, with gradually lesser interest for the political problems and a decreasing force (with less impact) both in the society as a whole, and in individual lives. An echo of the expectation (and anticipation) that religion could disappear can be heard in certain multicultural political groups hoping that religious differences won't matter much. In time this position will become difficult to advocate.⁶

The predictions concerning the place religion will take in the public arena of the 21st century are based on the hopes it will become marginalized and even eliminated, or at least limited to the private life. Late modernity predicted the *alienation from religion*, meaning that religion would no longer have control over the social life, being limited to the private life, at best, thus giving way to a society dominated by a secular mindset in which religion lost all its social roles.

*The historicity of the extra-European, and even the European territories, contradicts this diagnosis of religious extinction. Without abandoning the expression, specialists write about the vitality of religions, which are capable of creatively responding to the displacements caused by globalization, and thus offer meaning to the individuals and communities, on the traumatizing path of modernity.*⁷

The prediction was for a secularized era, whereas religion would be ill-suited and irrelevant. Yet the visible reality is different. The religious factor and its religious emergences not only have not disappeared, but have gained amplitude in our contemporary context, encompassing different social levels.

⁴ George Moyser, *Politics and religion in the modern world*, 1.

⁵ Peter Beyer & Lori Beaman, , *Religion, Globalization and Culture*, (Boston: Brill Leiden, 2007), 187.

⁶ Peter Beyer & Lori Beaman, , *Religion, Globalization and Culture*, 187

⁷ Anca Manolescu, *Stilul religiei în modernitatea târzie*, (Iași: Polirom, 2011), 103.

*The classical assumption that modernization generates the unavoidable decline of religion has lost some of its strength. After the fall of communism and the acceleration of globalization, the various forms of religiousness have reentered the heart of political and intellectual debate, while religious engagement is increasing in general.*⁸

The religious resurgence is considered a surprise, in a society that considers itself to be secular. The global rebirth of the religious movements in the 1970s has taken by surprise many Western observers, who presumed that the secularization process, based on the positivist ideas of the progress and modernization of the 19th century, was universal, unidirectional and unavoidable: all societies have become inexorably all the more secular. Within such societies, religious institutions have been progressively marginalized, and their influence on society has diminished.⁹ Although it was believed that secularization would gradually fence in religion, limiting it to the private life, contemporary religious awakenings have created skepticism towards the secularization theory and there can be seen new efforts in adapting it to the new circumstances. The contemporary world is massively religious, characterized by the interplay of secular and counter-secular forces. There are strong religious dynamics in most parts of the world, the Western Europe being an exception in this respect.¹⁰

The causes of the resurgence of religion were connected to the inner needs of the individual:

*... the rebirth of religion is certainly connected to the global search for identity and belonging, community, and new orientation systems to guarantee purpose and significance. The more a society is exposed to modernization people will yearn for a deeper meaning of life, because modernization creates the feeling of displacement and disorientation, causing the collapse of community's values, traditions and lifestyles.*¹¹

The spiritual factor is believed to be essential in the making and perpetuation of a society. Throughout the historical evolution of humankind, certain drives were noticeable, under the influence of one or more systems of thought which, even though they claimed to be secular, functioned by the same principles as the religious systems.

The historical world built by the Europeans during the last 6-7 centuries (beginning with the Renaissance) is today in the process of being shattered all together, a process altering the very axis of the world. Yet this change cannot be observed at the level of economies and states, only religions. Consequently, the problem of our contemporary world cannot be limited to the opposition between capitalism vs. communism, but refers to the break of the constraints (parametrical) described: a) by the capitalist system (as a world system); b) by the noologic positivist conglomerate (nous < gr. spirit, logos < orienting word), as a constitutive part of the great Western culture,

⁸ Camil Ungureanu (ed.), *Religia în democrație. O dilemă a modernității*, (Iași: Polirom, 2011), 5.

⁹ David Zeidan, *The resurgence of religion*, (Boston: Brill Leiden, 2003), 61.

¹⁰ David Zeidan, *The resurgence of religion*, 62.

¹¹ Natalia Vlas, *Globalizarea și religia la începutul secolului XXI*, (Cluj Napoca: Presa Universitară Clujeană, 2008), 136.

that gains a gradually more important position, even triumphing over the whole, especially starting from the 18th century onwards, by overtaking the spiritual lead of the world; c) by the secular systems of legitimizing authority.¹²

Secularization was not capable to solve important issues at the level of international relations. This is why analysts presume that the global resurgence of religion can be interpreted as a result of the failure of the secular, modern state to produce democracy or evolution in the developing countries. These countries have gone through a dilemma during the colonial occupation – should they accept Western countries as models of development and despise and renegade their own culture, with the purpose of gaining equal power – or should they affirm their own cultural and religious traditions and retain their inferior material level.¹³

In the midst of the rapid transformation and the challenges imposed by progress and globalization, the consequences are the individualization of religious and spiritual search for meaning, a search that cannot be limited to the need for safety. As a result of immigration and globalization, in Europe arose new religious communities. In short, while the secularization theory remains open as a scientific assumption, at society level the recent European history didn't take the shape of a teleology of the triumph of secular thinking. We are now witnessing the decline of the traditional church, and in the same time the new positioning of the sacred and spiritual in relation to the private and social life.¹⁴

The resurgence of religion is global in a geographic sense because it is not limited to a certain part of the world, such as South America, Central Asia or Middle East, and, from the perspective of compared politics and compared religion, this phenomenon takes place in different countries, with different political types, and in all the major religions of the world. The global resurgence of religion also takes place in countries with different cultural and religious traditions, as well as in countries with different levels of development.¹⁵

During the last part of the 20th century, there has been a worldwide rebirth of religion. This rebirth brought about an amplification of religious consciousness and the emergence of fundamentalist movements deepening the differences between religions. Yet it did not produce significant changes in the world's percentage of different religions.¹⁶

There is a comeback of religion on a global scale which takes place in the entire world, a comeback which means a challenge to our interpretation of the modern world – what it means to be modern – and it impacts the manner in which culture and religion influence international relations. The global rebirth of religion takes place in the modern world; it is part of a larger crisis, the crisis of modernity in the Western countries. This reflects a much deeper delusion, on a larger scale, toward a modernity which reduces the world and

¹² Ilie Bădescu, *Geopolitică și religie. Insurecții religioase în secolul XXI. Insurecția euxiniană*, , <http://roncea.ro/2010/08/06/prof-ilie-badescu-geopolitica-si-religie-insurectii-religioase-in-secolul-xx-insurectia-euxiniana/>, accesat în 16.10.2013.

¹³ Thomas Scott M, *The Global Resurgence of Religion and the Transformation of International Relations*, (Palgrave Macmillan, 2005), 40-41

¹⁴ Ungureanu, *Religia în democrație...*, 7.

¹⁵ Scott, *The Global Resurgence of Religion...*, 26.

¹⁶ Samuel P. Huntington, *Ciocnirea civilizațiilor și refacerea ordinii mondiale*, (București: Litera, 2012), 85.

everything that can be perceived and controlled through reason, science and technology, and leaves aside the sacred, religion and spirituality.¹⁷

As a result, it was suggested that the global resurgence of religion can be seen as part of the search for authenticity and development in the developing countries. The global resurgence of religion in the developing countries can be seen as a rebellion against the West.¹⁸

The global resurgence of religion can also be interpreted as a fundamentalist and anti-modern reaction to the unavoidable and inexorable spread of modernity and globalization. The phenomenon can be understood as part of a larger picture, the already-existing criticism of modernity on a world level of authenticity and development. A postmodern perspective starts by accepting the fact that the disaffection with modernity has shown us that the Illuminist promises of freedom, autonomy and understanding through reason and knowledge were unwarranted. This approach shares the same perspective with the artists, theologians, and cultural critics who admit the limitations of the world delusion. This tendency was predicted by George Simmel, over a century ago. He was worried that the growing attachment to things would constantly devalue our world. For all these reasons, the 20th century could be the last modern century. A truly multicultural international society is formed for the first time, taking seriously the cultural and religious pluralism – this is one of the most important aspects of the 21st century's international politics.¹⁹

The global resurgence of religion may be defined as an increase of performances and religious persuasion, a growing importance of religious beliefs, practices, and declamations, in private and public life, as well as a growing role of religious people, non-state groups, political parties and communities, organizations, in internal politics, and all this happens in a manner of significant implications for international politics.²⁰

THE IMPLICATIONS AND CONSEQUENCES OF RELIGIOUS RESURGENCE ON INTERNATIONAL POLITICS

The idea that religion plays a major role in many conflicts worldwide is accepted. Despite this, it is uncertain which conceptual frame should be adopted in order to analyze the rebirth of religion, religious ideas and transnational religious movements in international relations. The scholars who are concerned with the global rebirth of religion in international relations have adopted a variety of views on religion, and placed religion in a variety of theoretical conceptions of international relations.²¹

Researchers in international relations have approached religion as if it were a part of a larger problem (even one of identity), that of understanding the power of ideas, systems of beliefs or ideologies in international relations. People's ideas, their beliefs, what they consider to be right or wrong, strongly shape their behavior. The emphasis on religion as being a set of ideas and a form of ideology underlines the manner in which the differences of religious ideas – religious differences – perpetuate the potential for conflict and make existing conflicts much harder to solve.²² One of the reasons is the fact that religions involve

¹⁷ Timothy Fitzgerald, *Religion and Politics in International. The Modern Myth*, (London:Continuum International Publishing Group, 2011), 180.

¹⁸ Scott, *The Global Resurgence of Religion...*, 41-42.

¹⁹ Fitzgerald, *Religion and Politics...*, 181.

²⁰ Scott, *The Global Resurgence of Religion...*, 26.

²¹ Thomas Scott, *Religion and International Conflict*, in K.R. Dark, *Religion and International Relations*, (Macmillan Press Ltd, 2000), 1.

²² Thomas Scott, *Religion and International Conflict*, 1.

basic values, which define what is good and wrong, values considered an absolute truth and, often times, a universal truth. Usually, the religious people claim that these values and beliefs should be accepted by everyone in the world. Self-identification with religion and devotion to it spring from the natural tendency to perceive the values of one's own religion as being superior to other systems of beliefs.²³

Religious conflicts are a type of ideological conflict and as such they are much harder to solve, since they exclude the possibility of compromise or coexistence. Ideas, unlike territorial disputes, and economic conflicts over commerce, money and resources, cannot be separated.²⁴

The use of religion and religious beliefs in politics differs from the secular political ideologies, because the moral commitments and the political options that emerge from religious beliefs, institutions and practices are associated with the Absolute. This implicates that the religious values and beliefs may add an additional degree of efficiency in the expectations from people.²⁵

The second way the religion was understood in the International Relations is as a primary source of individual and social identity. This approach considers religion to be a main quarry of differentiation between groups. A system of religious beliefs offers its followers an important source of identity. There is a certain core essentialism and determinism in the very nature of religion, because the religious differences are immutable and fundamental, and much more important than the differences imposed by ethnicity, class or gender.²⁶

In the modern world, religion is essential, probably even the central force that motivates and mobilizes people. What actually matters for them is not the political ideology or economical interests. Even more than the ethnicity, the religion makes a definitive and exclusive discrimination between people.²⁷

The third way the religion was perceived in the International Relations is a version of the idea that religion is a form of ideology. The religion is therefore a type of transnational idea, and it could simply be called *transnational religion*. The ideas become transnational when people from different countries have a similar belief system, moral code, or they believe in a special international law, or some international regulations. The proletarian internationalism, the anti-racism and a basic commitment regarding the human rights, are all transnational ideas aiming to create multinational or multi-ethnic states.²⁸

The fourth way the religion is perceived in the International Relations is as a form of soft power. Unlike the hard power (military or economical power), the soft power is the force of the attractive ideas. When the ideas are attractive (or even the opposite, when they are repulsive, e.g. racism and anti-Semitism), they become capacities of attitude that form the intangible elements of power for the International Relations players. They inform (or sometimes can infuriate, in case of racism or Islamic and Hindu fundamentalism) the popular beliefs, the perceptions and attitudes of some elective constituencies. When this happens, the transnational ideas become a form of soft power. People – individuals, citizens, believers and

²³ Kegley, C. and Wittkopf, E., *World Politics: Trend and Transformation*, (New York, 1997), 181–186.

²⁴ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 2.

²⁵ Barker, E., *The Cage of Freedom and the Freedom of the Cage*, in Barker, E. (ed.), *LSE on Freedom*, (London, 1995), 103–118.

²⁶ Scott, *apud* K.R. Dark (ed.), *Religion and International Relations*, 4.

²⁷ Huntington, *Ciocnirea civilizațiilor...*, 91.

²⁸ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 5–6.

political activists – adhere to these ideas and believe they should influence the nations' behavior in the worldwide politics.²⁹

The transnational religions can also offer basis of action for the non-state actors, transnational performers or non-governmental organizations, and this is the fifth way in which the impact of religion is manifested in the International Relations, method widely studied by analysts. The transnational actors can influence the international relations by using force or the power of ideas. By force, movements of national liberation, rebel or terrorist groups, the monopoly of the state regarding the usage of force in the international system is challenged. The transnational actors can also influence the international relations through ideas and their power. The ideas represent – or are considered as such by the individuals and the international community – the soft power of the ideas played in time, ideas that give shape to the values and norms of the international system. The transnational environmental groups (like Greenpeace) represent the environmentalism at a worldwide level, while the human rights groups (such as Amnesty International or The International Committee of the Red Cross) represent the human rights. This gives them the possibility to influence the political agenda, and the vocabulary of the political debates. Therefore, they can influence the parameters of the possible political results. This is the reason why some transnational actors have a bigger impact on the world stage and receive a major attention in the external affairs from the leadership of the states than those who are weak in the international system.³⁰

The sixth way in which religion was analyzed in the International Relations is that it is perceived as a civilization or a cultural area. The crucibles of the great religions are tightly connected with the main locations of the great ancient Asian civilizations. This was the starting point for one of the most influent method of interpreting the religion in the international realm, before the Second World War.³¹ Huntington revived this tradition of analyzing the civilizations based on religion, for the period of time after the Cold War. He declared that the East-West axis as a division of the world during the Cold War was replaced with the theory of a clash of civilizations. Civilizations determine the greatest differences within humanity and therefore, it is considered that cultural differences will be the main source of future conflicts in the world.³²

The revival of religion is a contingent, circumstantial, and situational force. This is the reason why the religious conflicts depicted as a reaction to globalization are considered indeed linked to the increasing political and economical power of the marginalized groups in the international relations, instead of bringing the religion in the political realm.³³

THE IMPACT OF RELIGION ON INTERNATIONAL POLITICS

Is religion a threat for international stability, or can it be used as an instrument to promote peace? The influence of religion on international politics can be seen from many perspectives: from religious conflict to the contribution of religion to international peace and stability. When religious institutions are controlled by the state, such as the Orthodox Church of Cyprus or the post-soviet Orthodox Church of Russia, the state politics can become more uncompromising. When religion is mixed with nationalism, as is the case of the Orthodox

²⁹ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 7.

³⁰ Said A., *et all.*, *Concepts of International Politics in Global Perspective*, 4th edn, (Englewood Cliffs: N. J., 1995), 188–191.

³¹ Joll J., *Two Prophets of the Twentieth Century: Spengler and Toynbee*, *Review of International Studies* 11, 1985, 91–104.

³² Huntington, *Ciocrnirea civilizațiilor...*, 22–49.

³³ Peter Beyer, *Religion and Globalization*, (London, 1994), 1–5.

Church of Serbia, the state politics can approve actions of ethnic cleansing and actions that generally violate the human rights. Seen from a different angle, religion can offer increased resistance and independence to communities and individuals. As examples of cases where religion prevailed political or state abuses there is *The Confessing Church* in Nazi Germany or the German Democratic Republic, the Catholic Church of the communist Poland, and the anti-apartheid Christian churches of South Africa.³⁴

Some questions arise when we approach the relationship between religion, on one side, and international politics on the other: How does the 'global renaissance' of religion impact the principles, rules, and norms of the international society?³⁵ Does the transnational religion imply a new transnational ideology, one that would create obedience towards the state? Does this ideology bring new beliefs and values that are incompatible with the rules, principles and norms of the international society?³⁶

The resurgence of religion has been also analyzed from the perspective of its relationship with a series of issues that are unrelated to religion. First of these is the *field of international politics*. To properly evaluate the role of religion in international politics, there has to be a distinction between political movements which are truly inspired or based on religion, and those that use religion as a legitimate tool in their quest of fulfilling a political agenda based on non-religious interests.

The second issue related to the religious resurgence is the *peace and war* debate.³⁷ Although it would be ideal to say that religion is a force working in the interest of peace, things are not so. More accurately, it is very probable that religion is a tool often creating and amplifying wars and conflicts between and within the nations of the modern world. Thus, when analyzing the impact of the religious resurgence within international politics, both aspects have to be taken into account.

Another matter interacting with the resurgence of religion is the *economic development*.³⁸ This is best described in the writings of Max Weber, *The Protestant Ethic and the Spirit of Capitalism*, which shows that certain values nourished the development of the modern economy.³⁹

Moreover, the religious resurgence interacts with the area of *human rights and social justice*.⁴⁰ The religious institutions are regarded as the authors of many human rights, some of those having important political consequences. In any instance, it has to be taken into account the fact that various religions have different perspectives towards the human rights' meaning.

Among the main allegations related to religious resurgence, is that it is and can be a source of conflict. This is because it promotes new beliefs incompatible with the rules, practices, and norms of the international society, such as territorial integrity, sovereignty, and non-intervention. The international society is based on European values and norms, and it was more or less created through the expansion of the European states – through colonialism

³⁴ E. Barker, *The Cage of Freedom and the Freedom of the Cage*, apud Barker, E. (ed.), *LSE on Freedom*, (London, 1995), 103–118.

³⁵ J. N. Rosenau, and Czempel, E-O. (eds.), *Governance without Government: Order and Change in World Politics*, (Cambridge, 1992), 61–62.

³⁶ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 14.

³⁷ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 15.

³⁸ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 16.

³⁹ Max Weber, *Etica protestantă și spiritul capitalismului*, (București: Humanitas, 1993).

⁴⁰ Max Weber, *Etica protestantă și spiritul capitalismului*, p. 17.

and imperialism – across the globe. What was once an international European society is now a worldwide international society.⁴¹

RELIGION AND POLITICAL ACTIONS

As an empirical reflection towards this study, the following paragraphs emphasize some realities and aspects related to the decisional process, starting with the implications religion has as a social actor.

Secularization and liberalization tended to limit religion to the private sphere or sector, thus making the theological aspects irrelevant in considering the relationships between states. In contrast, the role of religion in International Relations is now a broader subject of study. Case studies reveal that external policy is affected by the state religion and by the communications made possible through the networks of 'transnational believers'.⁴²

From another perspective, *religion is a profoundly political influence in public matters and it should not be regarded as a set of theological problems.*⁴³ It is thus considered that religion is *political*, even in the absence of a theologically-generated political conflict. Religion has a social and interpretative purpose or function in fulfilling the need for transcendence. Theology, which articulates the main frame of ideas that belong to a religion, is focused on this function.⁴⁴

The involvement of religion in politics is also seen in the social protection policies, through actions that complete and compensate the lack of state services. It also proposes different or alternative social strategies in overcoming certain social problems.

The link between religion and politics can be palpably and unmistakably seen in the USA, where Christianity had an important contribution regarding political decisions. In matters of external policy, Christians were more relevant in the middle of the '90s.

*Generally, it is considered that the role of the 'Christian rights' in the external policies of the USA has increased over the last years, thanks to certain events. First of all, the election of George W. Bush as the president of USA is strongly tied to this movement. Second of all, their influence is strongly related to the significant number of voters (43%) and to the fact that the Christian rights became a force whose claims are generally taken into consideration by public people. Moreover, the influence of Christians on the external policy is also due to their alliance to neo-conservators.*⁴⁵

As examples, there are some situations where Christians had a direct involvement in international politics, one of them before the Bush administration: during the Cold War, Christians tried to influence the USSR toward religious freedom. They also had various diplomatic initiatives, one of them being *International Religious Freedom*, for signing certain acts against human trafficking (2000). In 2004, under evangelical influence, the North

⁴¹ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 18.

⁴² Harriet A. Harris, *Theological Reflections on Religious Resurgence and International Stability: a Look at Protestant Evangelicalism*, in K.R. Dark (editor), *Religion and International Relations*, (Macmillan Press Ltd 2000), 29.

⁴³ Rubin Barry, *Religion and International Affairs*, in Johnston, D. and Sampson, C. *Religion, The Missing Dimension in Statecraft*, (New York, 1994), 20-34.

⁴⁴ Harris, in K.R. Dark (ed.), *Religion and International Relations*, 32.

⁴⁵ Vlas, *Globalizarea și religia...*, 199-200.

Korean Human Rights Act was signed. Other such examples are the interest of the Bush family in the eradication of AIDS in Africa, freedom of religion in China, etc.⁴⁶

The way Christians were involved in political actions is described by analysts as important in matters of human rights, playing an important role in the following aspects: the end of the civil war in North Sudan – USA efforts in ending the longest civil war in Africa was a result of a constant Christian campaign; the peace treaty of 2005 was mediated by the American ex-senator John Danforth, an Episcopalian.⁴⁷

CONCLUSIONS AND CLOSING ARGUMENTS

The global rise of religion describes the ways in which religion and politics intersect throughout the world. This phenomenon is referred to as *the religion reconstruction* in the global era. A focus on the remodeling of religion can offer a better understanding of the way the methods of social and cultural change are put together thanks to globalization in order to bring a long-term cultural change in internal and international politics.⁴⁸

Religion is often perceived as a competitor in the battle for people's attention and allegiance. Same as the transnational beliefs, religion is considered a set of laws that sit above the state's law or international treaties.⁴⁹ The transnational religion is also considered to be a way of undermining diplomacy – one of the main institutions of the international society. This is due to the fact that religious conflicts cannot be taken into account during diplomatic negotiations.⁵⁰

Even if religion can solve complex conflicts, through religious legitimacy, it is still up to the politics to solve tensions among social communities.⁵¹ The analysts suggest that religious conflicts should not be approached unilaterally:

*There will be need of a holistic approach regarding religion and security. What is more important is that we should not limit our religion and security-related research to threats. Religion is not only part of the problem. It is also part of the solution.*⁵²

There is also another way to express the challenge that transnational religion creates regarding principles, rules, and society norms.⁵³

The best way to understand religions is to consider them interpretative communities, when talking to their members and interacting with their traditions in order to determine their contemporary faith and social life relevance. Different cultural views about religious authority regarding the inter-gender relationships amplified the conflicts in developing countries.⁵⁴

The relationship between politics and religion, between the global resurgence of religion and the international politics is debated under two opposing views: from considering

⁴⁶ Vlas, *Globalizarea și religia...*, 200-208.

⁴⁷ Vlas, *Globalizarea și religia...*, 209.

⁴⁸ Scott, in K.R. Dark (ed.), *Religion and International Relations*, 27.

⁴⁹ J. Goldstein, *International Relations*, 2nd edn, (New York, 1996), 204.

⁵⁰ Johnson D, *Introduction: Beyond Power Politics*, in Johnson, D. and Sampson, C. (eds), *Religion, The Missing Dimension of Statecraft*, Oxford, 3.

⁵¹ M. P. Holt, *The French Wars of Religion, 1562–1629*, Cambridge, 1995, Introduction and chapter 6.

⁵² Robert A. Seiple, Dennis R. Hoover, *Religion & Security. The new nexus in international relations*, (Rowman & Littlefield Publishers, INC. 2004), 2.

⁵³ Scott, *apud K.R. Dark (ed.), Religion and International Relations*, 20.

⁵⁴ Scott, *apud K.R. Dark (ed.), Religion and International Relations*, 21.

the positive role of religion to viewing it as a conflict generator. Both sides have to be disappointed by facts: when evaluating this role, there is no detailed alternative, but a declaration can be made – those neglecting religion in their business conducts are exposing themselves to a great danger.⁵⁵

⁵⁵ Berger , *The Desecularization of the World*, 18.

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NEUROENDOCRINE CELL HISTOLOGY CHANGES IN THE EVOLUTION OF ULCERATIVE COLITIS

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ABSTRACT:

BACKGROUND AND AIM: NEUROENDOCRINE CELLS (NECS) HAVE BEEN IN FOCUS RECENTLY IN SEVERAL STUDIES ON PATIENTS WITH INFLAMMATORY BOWEL DISEASE SHOWING INCREASED NUMBERS IN THE CRYPTS AND SOMETIMES IN THE MUCOSAL LAMINA PROPRIA. THE AIM OF THIS STUDY WAS TO ASSESS HOW NEC HISTOLOGY CHANGES IN ULCERATIVE COLITIS (UC) PATIENTS OVER TIME AND THE POTENTIAL IMPLICATIONS THESE ALTERATIONS MAY HAVE.

MATERIAL AND METHODS: WE RETROSPECTIVELY SEARCHED FOR UC PATIENTS WITH MULTIPLE PRESENTATIONS IN THE PATHOLOGY DEPARTMENT OF ELIAS UNIVERSITY EMERGENCY HOSPITAL IN THE LAST THREE YEARS AND IDENTIFIED 9 PATIENTS WITH COLONIC BIOPSIES TAKEN AT TWO OR THREE DIFFERENT TIMES IN THE EVOLUTION OF THE DISEASE. NECS WERE DETECTED BY IMMUNOHISTOCHEMISTRY USING CHROMOGRANIN A ANTIBODY. WE COUNTED THE NEC PER CRYPT AND EVALUATED THE PRESENCE OF LINEAR HYPERPLASIA.

RESULTS: WE IDENTIFIED A DEFINITE INCREASE IN NECS IN MOST UC PATIENTS, PARTICULARLY AT THE ONSET OF THE DISEASE, FOLLOWED BY A SIGNIFICANT DECREASE OVER TIME AS DEMONSTRATED BY THE MODERATE NEGATIVE CORRELATIONS DETECTED BY PEARSON'S TEST BETWEEN THE DURATION OF DISEASE AND BOTH THE MEAN ($R_p = -0.517$, $P = 0.014$) AND MAXIMUM NUMBER OF NECS PER CRYPT ($R_p = -0.557$, $P = 0.007$). LINEAR HYPERPLASIA IN THE HOTSPOT SHOWED A SIMILAR DECREASING TREND, BUT WITHOUT STATISTICAL SIGNIFICANCE ON OUR SAMPLE ($R_p = -0.388$, $P = 0.074$).

CONCLUSIONS: THERE IS AN INCREASE OF NECS IN UC PATIENTS, HALF OF THEM SHOWING LINEAR HYPERPLASIA. FINDINGS OF NEC HYPERPLASIA AT THE ONSET OF DISEASE COULD HELP WITH THE INITIAL HISTOLOGICAL DIFFERENTIAL DIAGNOSIS OF UC WHEN THE CLASSICAL HISTOLOGICAL ASPECTS ARE NOT PRESENT.

KEY WORDS: ULCERATIVE COLITIS, NEUROENDOCRINE CELL HYPERPLASIA, CHROMOGRANIN A

INTRODUCTION

Ulcerative colitis (UC) is a chronic burdening disease that can lead to colectomy when the lesions are severe and do not respond to treatment. The main acknowledged

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histology changes induced by chronic inflammation in colonic and rectal mucosa in this disease are crypt distortion, basal plasmacytosis, diffuse mucosal inflammatory infiltrate with lymphocytes, plasma cells and eosinophils⁴. All these changes may diminish or even completely resolve in some patients with the help of medication, but relapse usually occurs. Changes in neuroendocrine cells (NEC) numbers and distribution has been in focus recently and several studies have shown increased NECs in patients with ulcerative colitis and inflammatory bowel disease in general^{5,6}. Increased numbers of Chromogranin A (CgA) positive cells in colonic crypts^{7,8,9,10}, NEC micronests^{8,11} and NEC benign and malignant tumors^{12,13,14} have been reported. However, to our knowledge, no study has focused on the NEC dynamic histological changes in the course of evolution of disease in UC patients, which could help predict clinical evolution.

The aim of this study was to determine how NEC histology changes in ulcerative colitis patients over time and the potential implications these alterations may have. Also, we intended to identify the histological parameters that would best describe these changes.

MATERIAL AND METHODS

We searched retrospectively for ulcerative colitis patients with multiple colonic biopsies taken at different moments in the evolution of the disease that were evaluated histologically in the pathology department of “Elias” University and Emergency Hospital in the last three years.

⁴ Magro et al., “Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: Definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders,” *J. Crohn’s Colitis*, vol. 11, no. 6, pp. 649–670, 2017, doi: 10.1093/ecco-jcc/jjx008

⁵ El-Salhy et al., “Gastrointestinal neuroendocrine peptides/amines in inflammatory bowel Disease,” *World J. Gastroenterol.*, vol. 23, no. 28, pp. 5068–5085, 2017, doi: 10.3748/wjg.v23.i28.5068.

⁶ Massironi et al., “Chromogranin A and other enteroendocrine markers in inflammatory bowel disease,” *Neuropeptides*, vol. 58, pp. 127–134, 2016.

⁷ Meianu et al., “P047 Neuroendocrine cells densities alterations in colonic mucosa of patients with inflammatory bowel disease,” *J. Crohn’s Colitis*, 2019.

⁸ Wong, B. K. Larson, and D. Dhall, “Neuroendocrine proliferations in inflammatory bowel disease: differentiating neuroendocrine tumours from neuroendocrine cell micronests,” *Histopathology*, vol. 74, no. 3, pp. 415–423, 2019.

⁹ Gunawardene, Corfe, and Staton, “Classification and functions of enteroendocrine cells of the lower gastrointestinal tract,” *Int. J. Exp. Pathol.*, vol. 92, no. 4, pp. 219–231, 2011.

¹⁰ Nascimbeni et al., “Solitary microcarcinoid of the rectal stump in ulcerative colitis,” *Neuroendocrinology*, vol. 81, no. 6, pp. 400–404, 2005.

¹¹ Kanada et al., “Microcarcinoid arising in patients with long-standing ulcerative colitis: histological analysis,” *Human Pathology*, vol. 64, pp. 28–36, 2017.

¹² Derikx et al., “Is the prevalence of colonic neuroendocrine tumors increased in patients with inflammatory bowel disease?,” *Int. J. Cancer*, vol. 139, no. 3, pp. 535–542, 2016.

¹³ Shigaki et al., “Immunohistochemical analysis of chromogranin A and p53 expressions in ulcerative colitis-associated neoplasia: neuroendocrine differentiation as an early event in the colitis-neoplasia sequence,” *Hum. Pathol.*, vol. 44, no. 11, pp. 2393–2399, 2013.

¹⁴ Costa et al., “Adenocarcinoma is not always the diagnosis – colon neoplasia in patient with long-standing ulcerative colitis under long-term prednisone maintenance therapy,” *Clin. Res. Hepatol. Gastroenterol.*, vol. 43, no. 4, pp. 362–364, 2019.

Histological examination

The slides were stained by hematoxylin and eosin. The diagnosis of ulcerative colitis was confirmed using the acknowledged histological criteria¹⁵. Mucosal inflammation was evaluated using two histological scoring systems – Nancy index and Geboes score.

Immunohistochemistry

Immunohistochemistry was performed on all slides using Cell Marque Chromogranin A (LK2H10) mouse monoclonal antibody, dilution 1:100, following the immunohistochemistry protocol for paraffin-embedded sections.

Analysis

We counted and described the distribution of CgA positive cells (manually and by computed analysis) within colonic crypts and evaluated their presence in the mucosal lamina propria.

The histological slides were either scanned using Aperio slide scanner or examined conventionally on the optical microscope. On the digital slides, we performed image analysis on the digital slides using QuPath software¹⁶. Each crypt was defined as a single annotation, then positive cell detection for DAB stain command was applied. The results were manually checked.

The cut-off for defining NEC hyperplasia was a count of ≥ 3.2 NEC/crypt^{17,18}. Linear hyperplasia was defined as NEC hyperplasia consisting of 5 or more contiguous CgA positive cells.

A „hotspot“ was defined as the area of 10 crypts showing the maximum number of CgA positive cells on a slide.

Statistical tests were done using IBM SPSS 20 software.

RESULTS

Patients

We identified 9 patients, 5 with two presentations, and 4 patients with three presentations respectively, corresponding to 22 cases (28 histological slides). The relevant demographic, clinical and endoscopical parameters, along with histological scores of inflammation activity are presented in Table1.

The majority of the patients had moderate or severe lesions at the first presentation, and a slight decrease of both endoscopical and histological scores of inflammation at further examinations. They also had a rather extensive colonic involvement (either left colonic or pancolonic).

Most of the patients were under conventional treatment, and 1, and 2 respectively were under biological therapy at the first and second presentations.

¹⁵ Magro et al., “Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: Definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders,” *J. Crohn's Colitis*, vol. 11, no. 6, pp. 649–670, 2017, doi: 10.1093/ecco-jcc/jjx008

¹⁶ Bankhead et al., “QuPath: Open source software for digital pathology image analysis,” *Sci. Rep.*, vol. 7, no. 1, p. 16878, 2017.

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¹⁸ Nascimbeni et al., “Solitary microcarcinoid of the rectal stump in ulcerative colitis,” *Neuroendocrinology*, vol. 81, no. 6, pp. 400–404, 2005.

Upon colonoscopy, biopsies were taken mainly from the areas with the most severe lesions. 28.5% were labeled as originating from the sigmoid, 28.5% from the rectum, 7.14% from the descending colon, 3.57% from the transverse colon, and 3.57% from the ceacum. For 25% of the biopsies the segment of origin was not specified.

Table 1. Clinical, endoscopic and histological aspects of the patients.

	Presentation 1	Presentation 2	Presentation 3
Age (median)	30 [18, 56]	31 [19, 57]	37 [28, 58]
Gender	7 males, 2 females	7 males, 2 females	3 males, 1 female
Duration of disease (median)	9 weeks [1, 73]	22 weeks [11, 94]	13 weeks [4, 83]
Montreal classification		3 E2, 6 E3	
Mayo partial score	1 Mayo 1 3 Mayo 2 5 Mayo 3	1 Mayo 0 6 Mayo 2 2 Mayo 3	3 Mayo 2 1 Mayo 3
Treatment			
5-ASA	6	5	1
Azathioprine	2	3	0
Corticoids	4	4	1
Biological agents	1	2	1
Histological inflammation			
Nancy Index <2	1	3	1
Nancy Index ≥3	8	6	3
Geboes grade <3.2	0	2	0
Geboes grade ≥3.2	9	7	4

Histological aspects

Although nitrocellulose paper was not routinely used by colonoscopists, most of the biopsies were oriented. Nevertheless, 22.72% of the histological slides had at least partial lack of orientation.

All the colonic biopsies taken at the first presentation in our department showed either mild or marked architectural alterations of the crypts. At the second presentation, 44.44% of the patients showed normalization of the crypt architecture, but still had increased mucosal inflammatory infiltrates of various levels. At the third presentation, only one patient showed normal crypts, the others showing marked crypt distortion.

Immunohistochemical staining for CgA

NEC hyperplasia, defined as a mean of ≥ 3.2 NECs/crypt, was detected in 68.18% of the colonic biopsies. The mean density of NECs was 4.18 CgA positive cells/crypt. Linear hyperplasia was present in 54.55% of all biopsies (Figures 1-4).

On the slides we evaluated, there were no proliferations of NECs within the lamina propria on multiple sections.

Figure 1. Chromogranin A immunohistochemical stain, 5x. The crypt architecture is distorted in this hotspot and both single-cell and linear neuroendocrine hyperplasia is present, mainly in the lower half of the crypts. Arrows indicate linear hyperplasia.

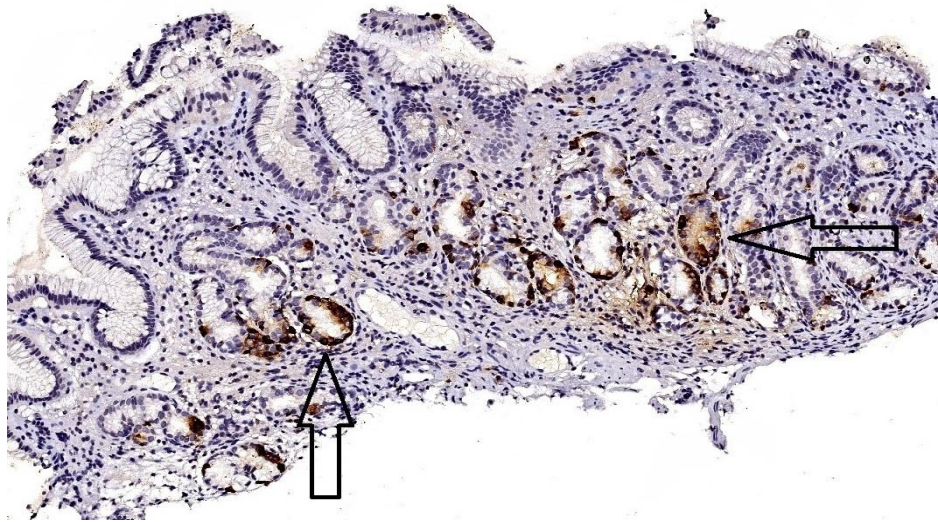


Figure 2. Chromogranin A immunohistochemical stain, 5x. Crypts show ramifications and loss of orientation. Neuroendocrine cell hyperplasia can be seen also in the upper half of the crypts (linear hyperplasia is highlighted by arrows).

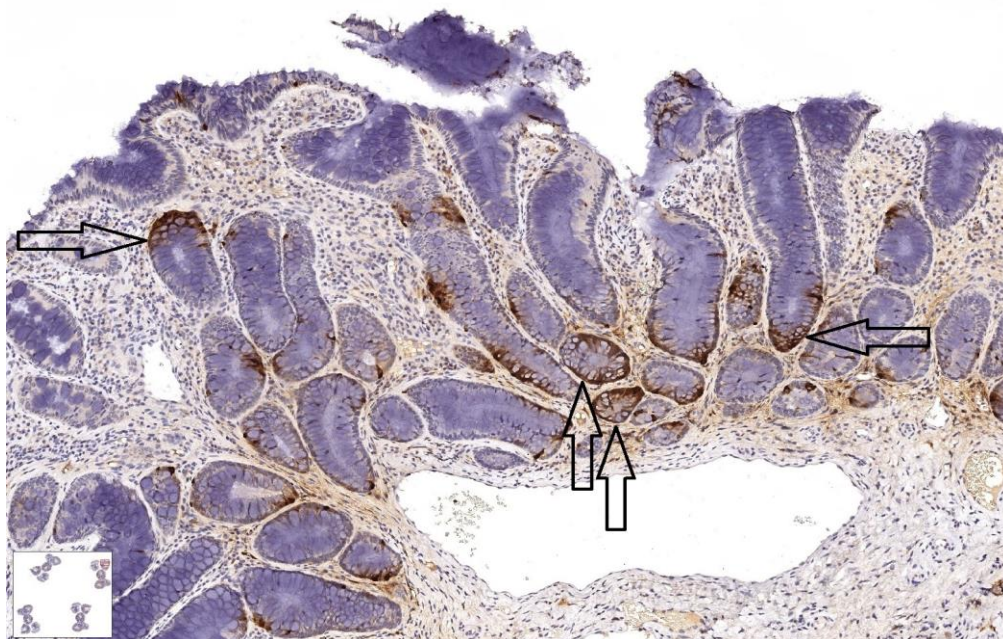
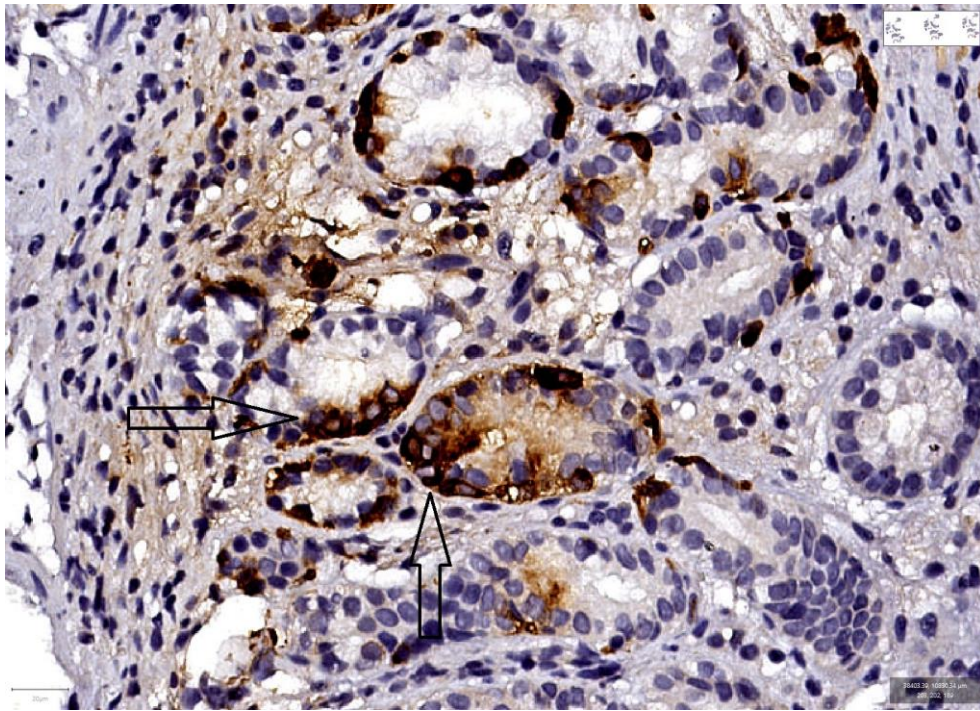


Figure 3. Chromogranin A immunohistochemical stain, 40x. Strong immunohistochemical stain is seen in hyperplastic neuroendocrine cells within colonic crypts (arrows indicate linear hyperplasia).



NEC changes with disease duration

All but one patient (88.88%) had NEC hyperplasia at least at one moment in the evolution of disease.

We observed a decrease over time in the NECs per crypt in the examined ulcerative colitis patients (Figures 1 and 2).

There was a statistically significant, moderate negative correlation by Pearson's test between both the mean and maximum number of NECs per crypt and duration of disease (Table 2).

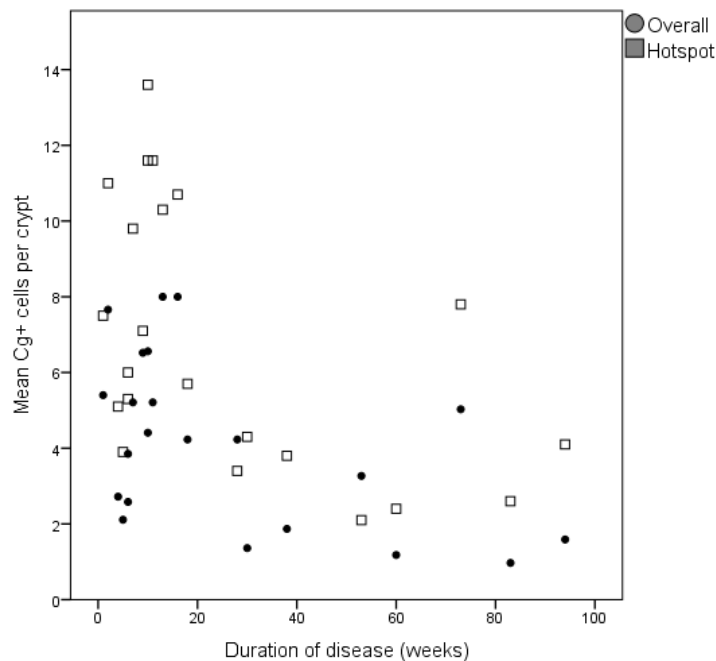


Figure 1. Dynamics of the mean NECs per crypt with duration of disease

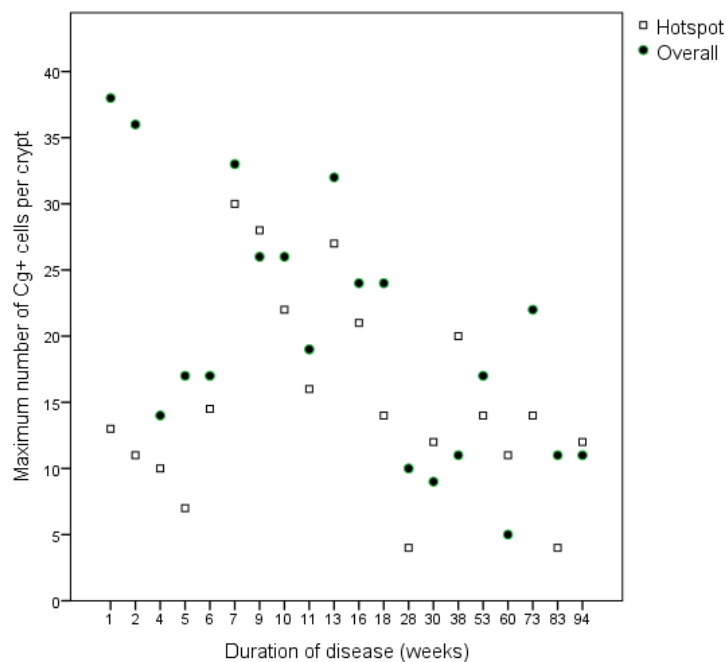


Figure 2. Dynamics of the maximum numbers of NECs per crypt with duration of disease

On the other hand, the mean number of crypts with linear hyperplasia of NECs on the biopsies was more constant over time (Figure 3), as opposed to the mean number of single-cell NEC hyperplasia showed above (Figure 1), which dramatically decreased with disease duration.

However, most of the crypts showing linear hyperplasia were clustered in the hotspots. The number of crypts with linear hyperplasia in the hotspot appears to decrease as

well with disease evolution over time, but is not statistically significant in the patients we studied ($p=0.074$), possibly because of the reduced sample (Table 2).

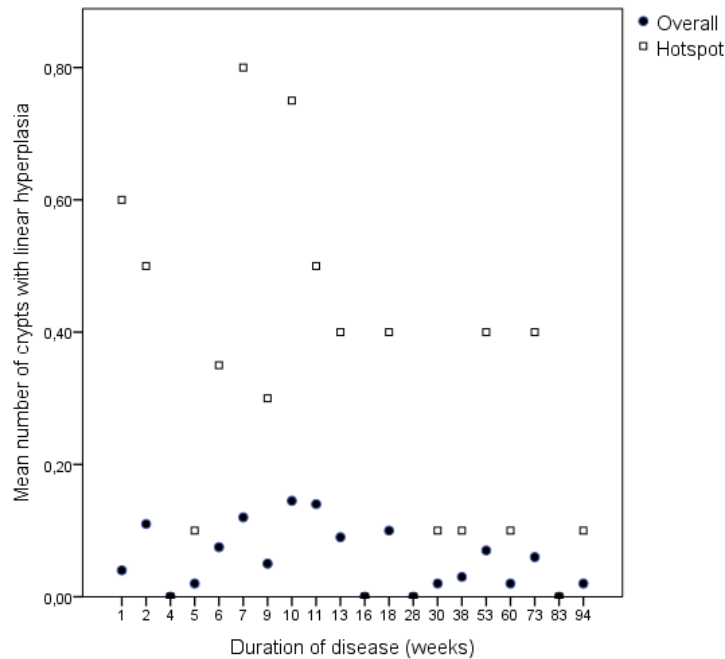


Figure 3. Dynamics of the mean number of crypts with linear hyperplasia NECs with duration of disease

Table 2. Pearson's correlation tests between duration of disease and histological variables

Variable	r_p	p value
Mean number of NECs per crypt overall	-.517	.014
Mean number of NECs per crypt in hotspot	-.518	.014
Maximum number of NECs cells per crypt overall	-.557	.007
Maximum number of NECs per crypt in hotspot	-.355	.105
Mean number of crypts showing linear hyperplasia of NECs overall	-.376	.084
Number of crypts showing linear hyperplasia of NECs in hotspot	-.388	.074

Discussions

In this study we identified a definite increase in NECs in most ulcerative colitis patients, a finding that confirms previous studies mentioned in the introduction section. This increase particularly manifests at the onset of the disease and is followed by a decrease over time, with the increase of disease duration.

We observed that changes in the hotspot reflect the overall changes on the histological sections. Thus, we believe that examining the immunohistochemical staining for CgA in the hotspot is reliable for detecting NEC hyperplasia, both single-cell and linear. This approach appears less time consuming than assessing NEC numbers/crypt on the whole slide and was not considered by other studies in the literature, to our knowledge.

We also found that the mean and maximum numbers of NECs per crypt are reliable histological parameters for evaluating NEC hyperplasia. Assessing the maximum number per crypt on the histological slide also seems more practical and less time consuming.

Linear hyperplasia is also a very helpful tool, though not statistically significant in our sample possibly because of its small size, especially because it is very easy to identify on the immunohistochemical stain. Since linear hyperplasia was most often clustered, using the hotspot method could be the easiest and most efficient way to detect it.

Findings of NEC hyperplasia at the onset of disease could help with the initial histological diagnosis, as these changes were not reported in infectious or ischemic colitis in the literature. This is a new direction we would like to follow in a future study.

CONCLUSIONS

In our study, neuroendocrine cells generally showed increased numbers in ulcerative colitis patients, similar to previous data in the literature. We showed that the mean and maximum number of Chromogranin A positive cells per crypt can be reliably used for assessing the level of NEC hyperplasia.

Also, we found that neuroendocrine cell linear hyperplasia is a striking feature in many patients with UC and this histological parameter, when present, highlights the area with the most numerous neuroendocrine cells (the hotspot).

The presence of neuroendocrine cell hyperplasia at the onset of ulcerative colitis could be a promising feature in the histological differential diagnosis and deserves future attention.

ACKNOWLEDGEMENTS

All authors equally contributed in the research and drafting of this paper.

All authors report no potential conflict of interest.

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MANAGEMENT OF GESTATIONAL DIABETES- A REVIEW OF CURRENT LITERATURE

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ABSTRACT:

GESTATIONAL DIABETES MELLITUS (GDM) IS DEFINED AS GLUCOSE INTOLERANCE WHICH LEAD TO HYPERGLYCAEMIA OF VARIABLE DEGREES OF SEVERITY WITH FIRST ONSET OR FIRST RECOGNITION DURING PREGNANCY^{55,59}. GDM IS ONE OF THE MOST COMMON MEDICAL DISORDERS OF PREGNANCY WITH AN SIGNIFICANT IMPACT ON THE MATERNAL-FETAL HEALTH. DUE TO THE EPIDEMY OF OBESITY, INCREASING MATERNAL AGE AND DECREASING PHYSICAL ACTIVITY, GDM'S PREVALENCE INCREASED BY 10-100% OVER THE PAST 30 YEARS. THE INTERNATIONAL DIABETES FEDERATION (IDF) REPORTS THAT ONE IN SIX (16.8%) PREGNANCIES ARE AFFECTED BY DIABETES GLOBALLY AND 86.4% OF CASES ARE DIAGNOSED WITH GDM²⁷. HYPERGLYCEMIA DURING PREGNANCY INCREASES PERINATAL MORBIDITY AND MORTALITY IN MOTHERS AND CHILDREN WITH A HIGH RISK OF DEVELOPMENT OBESITY, METABOLIC SYNDROME AND TYPE 2 DIABETES MELLITUS (T2DM) LATER IN LIFE.⁹ THERE IS A NEED TO FOCUS ON PREVENTION, SCREENING, EARLY DIAGNOSIS AND MANAGEMENT OF GDM IN ORDER TO AVOID THIS TRANSGENERATIONAL VICIOUS CIRCLE. THE AIM OF THIS REVIEW IS TO SUMMARIZE THE LAST DATA ABOUT THE MANAGEMENT OF GESTATIONAL DIABETES.

KEY WORDS: GESTATIONAL DIABETES, PREVALENCE, SCREENING, DIAGNOSE, MANAGEMENT OF GESTATIONAL DIABETES

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I. INTRODUCTION

Gestational diabetes (GDM) is defined as glucose intolerance with first recognition and onset during pregnancy. During pregnancy, maternal insulin resistance increases in order to ensure an adequate nutrient supply to the developing foetus. Hyperglycaemia develops if there is an insufficient insulin synthesis and secretion⁷. Nutrition management is an important key in the medical care of the patient diagnosed with GDM in order to control blood glucose throughout the pregnancy⁸. It is necessary to complete a nutrition assessment of mother in order to obtain the medical and obstetrical history, anthropometric and laboratory data, lifestyle, and food preferences. In order to reduce the risk of developing diabetes later in life, it is of great importance to have lifestyle changes⁹. A meal plan should be realized in order to assure adequate nutrients and promote an optimal weight gain, normoglycemia with a specific amount of carbohydrate per day and the absence of ketonuria. Follow-up visits are necessary in order to evaluate nutrient intake and parameters such as weight gain, blood glucose control, prevention of ketosis and compliance.

A. Prevalence

Prevalence of GDM is estimated to be around 7% of all pregnancies worldwide. It is difficult to have a clear estimation because the prevalence is reported differently due to the lack of an universal diagnostic criteria and screening procedures. GDM is associated with important maternal and fetal complications such preeclampsia, shoulder dystocia and birth injury, macrosomia, primary caesarean delivery, preterm delivery and foetal and neonatal mortality. Women with a history of GDM have a seven fold increased risk of type 2 diabetes mellitus compared to women who have not had GDM. Rates of type 2 diabetes mellitus after a diagnosis of GDM vary depending on the population and length of follow up, but the greatest risk is in the first five years and it have been reported to be as high as 70%¹⁰. Research has shown that lifestyle changes can prevent or delay progression to type 2 diabetes mellitus for these women¹¹. An early diagnosis of GDM represents an opportunity for intervention to reduce the development of type 2 diabetes mellitus because the prevalence of type 2 diabetes mellitus is increasing rapidly.

B. Risk Factors

During the first prenatal visit it is important to determine risk of developing GDM. The risk can be classified as low, average, or high. Low risk implies the following characteristics and does not require a routine screening¹².

- Without history of family diabetes (first degree relatives- parents, siblings)
- Normal pre-pregnancy body mass index

⁷ Powe CE, Allard C, Battista MC, et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. *Diabetes Care* 2016;39(6):1052-1055.

⁸ Brand-Miller J., Hayne S., Petocz P., Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care*. 2003;26:2261–2267.

⁹ Egan AM, Simmons D. Lessons learned from lifestyle prevention trials in gestational diabetes mellitus. *Diabet Med* 2019;36(2):142-150.

¹⁰ Eades, C. E., Cameron, D. M., & Evans, J. M. M. (2017). Prevalence of gestational diabetes mellitus in Europe: A meta-analysis. *Diabetes Research and Clinical Practice*, 129, 173–181

¹¹ Egan AM, Simmons D. Lessons learned from lifestyle prevention trials in gestational diabetes mellitus. *Diabet Med* 2019;36(2):142-150.

¹² Zhang C., Rawal S., Chong Y.S. Risk factors for gestational diabetes: is prevention possible? *Diabetologia*. 2016;59:1385–1390.

- No previous history of abnormal glucose tolerance
- No history of adverse pregnancy outcomes associated with GDM
- Not a member of an ethnic group with a higher prevalence of GDM

Average risk implies the following characteristics. The presence of one or more of them recommend screening for GDM between the 24th and 28th weeks of gestation:

- <25 years of age and obese
- Family history of diabetes in first degree relatives
- Member of an ethnic/racial group of high prevalence (Hispanic American, Native American, Asian American, African American, Pacific Islander)

High risk implies the following characteristics and the presence of any of them recommend a screening for GDM as soon as possible:

- Significant obesity
- Family history of diabetes
- GDM in previous pregnancy and history of adverse outcomes History of glucose intolerance
- glucosuria

If GDM is not diagnosed, blood glucose testing should be repeated at 24-28 weeks or at any time the patient has symptoms or signs that are suggestive for hyperglycemia.

II. SCREENING AND DIAGNOSIS

The tests utilized for diagnosis are the 75g 2-hour OGTT (recommendations of National Institute for Health and Care Excellence (NICE), American Diabetes Association (ADA)) and the 100g 3-hour OGTT (recommendation of American Association of Obstetricians and Gynecologists (ACOG))¹³. Using a 75 g 2-hour OGTT, gestational diabetes is diagnosed if one or more values is equal, or exceeds the cut off values: FPG (5.1 mmol/l [92 mg/dl]), 1-h plasma glucose (10 mmol/l [180 mg/dl]), and 2-h plasma glucose (8.5 mmol/l [153 mg/dl]). These cut-off values were chosen arbitrary by the IADPSG [an international consensus group with representatives from multiple obstetrical and diabetes organizations including the American Diabetes Association (ADA)] based on the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study. The aim of HAPO study was to clarify risks of adverse outcomes associated with a degree of hyperglycaemia. In this study 25,505 pregnant women were enrolled and tested by a 75g 2-hour OGTT within 24 to 32 weeks. It was noted the association between glucose values and the likelihood of large for gestational age, primary caesarean delivery, fetal insulin levels and neonatal adiposity. An odds ratio of 1.75 times the mean for the outcomes of increased neonatal body fat, large for gestational age and cord serum C-peptide greater than the 90th percentile was arbitrarily chosen for the proposed new diagnostic criteria by the IADPSG. The OGTT should be performed after fasting overnight for 8-14 hours, and not reducing the usual carbohydrate intake for the preceding several days. In 2010, IADPSG published new recommendations for the screening and diagnosis of GDM and their recommendation was an universal screening for gestational diabetes. They state that at the first antenatal visit, pregnant women should be screened for GDM using standard criteria to diagnose diabetes in non pregnant state. In this way we identify the women with overt diabetes ("pre-existing diabetes") based on any of the following criteria: fasting plasma glucose level (FPG) ≥ 7.0 mmol/l (126 mg/dl), a casual plasma glucose of 11.1 mmol/l (≥ 200 mg/dl), or HbA1c ≥ 6.5 . Confirmation of the diagnosis

¹³ ACOG Practice Bulletin No. 190 summary: gestational diabetes mellitus. Obstet Gynecol 2018;131(2): 406-408

need an OGTT. If early screening is negative, the IADPSG recommends that at 24–28 weeks of gestation perform a 2-hour (h), 75-g OGTT “one-step approach”¹⁴.

III.COMPLICATIONS

Women with GDM are predisposed to develop pre-eclampsia and experience perineal trauma or caesarean delivery. Although in majority of cases glucose homeostasis return to normal postpartum, GDM is a strong risk factor for type 2 diabetes in later life. Offspring of women with GDM are more likely to have a higher birth weight with associated complications such as neonatal hypoglycaemia, jaundice, birth trauma and even stillbirth. Long term complications can be intellectual impairment, metabolic syndrome, obesity and diabetes¹⁵.

IV.NUTRITION MANAGEMENT

Nutrition management represents the key of treatment during GDM for blood glucose control. During nutrition management of GDM, specific caloric and nutrient recommendations are determined and adapted to individual assessment and self monitoring of blood glucose. Plasma glucose monitoring and daily food journal provide information for insulin and meal plan adjustments¹⁶. According to the American Diabetes Asssociations, all women with GDM should receive nutritional counselling, individualization of medical nutrition therapy (MNT) depending on maternal weight and height. MNT should include an adequate calories and nutrients intake according to the needs of pregnancy and maternal blood glucose goals¹⁷. The most important complication correlated to maternal hyperglycemia, specially maternal postprandial hyperglycemia is fetal macrosomia. Studies has shown that a control of postprandial glucose levels reduces macrosomia, neonatal hypoglycemia, and cesarean delivery as compared to managing preprandial glucose levels alone. Therapy for pregnant women with GDM should be targeted to treat 1-2h postprandial glucose. ACOG and ADA recommendations are: fasting glucose < 95 mg/dl, 1-hour postprandial glucose < 140 mg/dl, 2 h- postprandial glucose < 120 mg/dl.

A. Weight gain recommendations

Lifestyle modification is the first strategy of prevention and management of GDM, which includes nutrition therapy and physical activity. It should be implemented prior to pregnancy, during pregnancy, and postpartum. Nutritional therapy is an individualized food plan that limits the amount of carbohydrate and offers adequate nutrition to maintain an adequate weight gain. Through nutritional education, women can understand the quantity and quality of food needed. Carbohydrate, protein, and fat intakes should account for 50–

¹⁴ Benhalima K, Mathieu C, Van Assche A, et al. Survey by the European Board and College of Obstetrics and Gynaecology on screening for gestational diabetes in Europe. *Eur J Obstet Gynecol Reprod Biol* 2016;201:197–202; Di Cianni G., Volpe L., Casadidio I. Universal screening and intensive metabolic management of gestational diabetes: cost-effectiveness in Italy. *Acta Diabetol*. 2002;39:69–73.

¹⁵ Mitanchez D., Yzydorczyk C., Siddeek B., Boubred F., Benahmed M., Simeoni U. The offspring of the diabetic mother–short- and long-term implications. *Best Pract Res Clin Obstet Gynaecol*. 2015;29:256–269.

¹⁶ Brand-Miller J., Hayne S., Petocz P., Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care*. 2003;26:2261–2267.

¹⁷ Kgosidialwa O, Egan AM, Carmody L, et al. Treatment with diet and exercise for women with gestational diabetes mellitus diagnosed using IADPSG criteria. *J Clin Endocrinol Metab* 2015;100(12):4629-4636.

60%, 15–20%, and 25–30% of the daily dietary total energy, respectively¹⁸. Potential beneficial factors for dietary structure include fruit, green leafy vegetables, poultry and fish, nuts, fiber, or a Mediterranean diet¹⁹. Fiber intake per day needs to be ≥ 28 g. Food with a high GI (glycemic index) lead to higher postprandial values, while food with a low GI may reduce postmeal glycemic excursion, birth weight, and the frequency of insulin use²⁰. Total weight gain during pregnancy varies widely among women but the current weight gain recommendations according to the Institute of Medicine are based on pre-pregnancy BMI²¹.

Pre-pregnancy BMI Category	Total Weight Gain (kg)	First Trimester Total (kg)	Second Trimester (kg/week)	Third Trimester (kg/week)
Low (BMI<18.5)	12,5-18	2.3	0.49	0.49
Normal (BMI 18.5-24.9)	11.5-16	1.6	0.44	0.44
High (BMI 25-29.9)	7-11.5	0.9	0.30	0.30
Obese (BMI>29)	<7			

Source: Institute of Medicine „Nutrition during Pregnancy. Part 1: Weight Gain Part 2: Nutrient supliments”
National Academy Of Sciences, Washington DC. 1990

B. Caloric Requirements

The ideal calorie intake per day is 1800–2000 kcal and should not be <1500 kcal because it will increase the risk of ketonemia who affect the development of the offspring's nervous system²². The caloric requirements are different for each trimester. During the first trimester the energy needs are the same as for nonpregnant women, 30 kcal/kg of ideal pre-pregnant body weight. Thomas- Dobersen recommendations are 36 kcal/kgc for the second trimester and 38 kcal/kgc of ideal body weight or prepreganant body weight for third trimester. Jovanic- Peterson recommendations (using a euglycemic diet with 40 % of calories from carbohidrates) are a calorie intake of 30 kcal/kg of current weight recommended for normal pre-pregnant weight, 24 kcal/kgc of current weight for overweight, 12-15 kcal/kgc for obese women during their second and third trimester. It has been documented that women with GDM who followed an euglycemic diet, in 75 % cases obtained normal glycemia.

¹⁸ Bider-Canfield Z, Martinez MP, Wang X, et al. Maternal obesity, gestational diabetes, breastfeeding and childhood overweight at age 2 years [published online ahead of print March 8, 2016]. *Pediatr Obes*. doi:10.1111/ijpo.12125.

¹⁹ Brand-Miller J., Hayne S., Petocz P., Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care*. 2003;26:2261–2267.

²⁰ Kgosidialwa O, Egan AM, Carmody L, et al. Treatment with diet and exercise for women with gestational diabetes mellitus diagnosed using IADPSG criteria. *J Clin Endocrinol Metab* 2015;100(12):4629-4636.

²¹ Zhang C., Rawal S., Chong Y.S. Risk factors for gestational diabetes: is prevention possible? *Diabetologia*. 2016;59:1385–1390.

²² Egan AM, Dennedy MC, Al-Ramli W, et al. ATLANTIC-DIP: excessive gestational weight gain and pregnancy outcomes in women with gestational or pregestational diabetes mellitus. *J Clin Endocrinol Metab* 2014;99(1):212-219.

C. Carbohydrate

An optimal macronutrient composition for dietary management of gestational diabetes mellitus (GDM) is essential to improve perinatal outcomes. It is important to provide adequate calorie intake to promote fetal/neonatal and maternal health, achieve glycemic goals, and promote appropriate gestational weight gain. The guidelines recommendation is a minimum of 175 g of carbohydrate, a minimum of 71 g of protein, and 28 g of fiber. Carbohydrate (CHO) is the primary nutrient which affects the postprandial glucose levels and the amount and type of carbohydrate are essential for optimal blood glucose levels. A glycemic control reduces the need for insulin and controls weight gain and infant birth weight²³. Data reported that a low CHO diet could minimize postprandial glucose excursions and decrease the need for insulin therapy²⁴. This diet leads to an increase in dietary fat when protein intake is constant. Data has shown that outside of pregnancy, diets high in fat, particularly saturated fat, promote insulin resistance. An increasing of maternal insulin resistance during pregnancy leads to an increased substrate delivery to the fetus and worse fetal hyperinsulinemia. Studies have shown that maternal triglycerides (TG) and free fatty acids (FFA) can be used by the placenta and may be a stronger predictor of excess fetal fat development than maternal glucose. There is a focus in literature on diet in and outside of pregnancy, particularly on the quality of CHO in terms of its glycemic index or ability to increase blood glucose. CHOs that are digested more slowly and attenuate postprandial hyperglycemia can be an option for diet therapy in GDM that avoids the need for CHO restriction. Moses et al. demonstrated that women who consume LGI carbohydrates require less insulin compared to those who consume HGI (high glycemic index) carbohydrates.

D. Fat

Fat content in the diet of a pregnant woman usually ranges from 30 % to 40 % of total calories, but large amounts of fat should be avoided to prevent excessive weight gain, which can lead to insulin resistance. The acceptable macronutrient distribution range for fat is 20-35% of total energy, the same as for nonpregnant women. The type of fat in the diet plays an important role in the glucose response to a meal, independent of the carbohydrate content. The guidelines recommend 7-10% of total energy intake should come from saturated fat, trans fat should be reduced and cholesterol intake should be less than 200 mg/day²⁵.

E. Protein

The diet of well-nourished women in the preconception period and throughout most of pregnancy has a significant effect on birth weight. High intakes of protein and fat during pregnancy may impair development of the fetal pancreatic beta cells and lead to insulin deficiency in the offspring²⁶. Data has shown that moderate protein intake is optimal during pregnancy. Protein meals and snacks do not have important consequences on blood glucose

²³ Brand-Miller J., Hayne S., Petocz P., Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care*. 2003;26:2261–2267; Kgosidialwa O, Egan AM, Carmody L, et al. Treatment with diet and exercise for women with gestational diabetes mellitus diagnosed using IADPSG criteria. *J Clin Endocrinol Metab* 2015;100(12):4629-4636.

²⁴ Powe CE, Allard C, Battista MC, et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. *Diabetes Care* 2016;39(6):1052-1055.

²⁵ Zhang C., Tobias D.K., Chavarro J.E. Adherence to healthy lifestyle and risk of gestational diabetes mellitus: prospective cohort study. *BMJ*. 2014;349:g5450. [PMC free article]

²⁶ Powe CE, Allard C, Battista MC, et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. *Diabetes Care* 2016;39(6):1052-1055.

excursions and can be added for additional calories in place of carbohydrate foods. The recommendations for protein intake are 1,1 g/kg/day or 15-20% of total daily calories.

V. CLINICAL OUTCOMES

Nutrition management in combination with intensive monitoring represent a key to delivery a healthy infant²⁷.

A. Blood glucose monitoring

The use of self-monitoring blood glucose (SMBG) allows to evaluate the nutrition management recommended and emphasize the importance of an appropriate amount and type of food that are likely to produce normoglycemia. For women treated with insulin, evidence indicates that postprandial monitoring is superior to preprandial monitoring. The targets of glucose monitoring recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus are:

- Fasting glucose <95 mg/dL (5.3 mmol/L) and either
- One-hour postprandial glucose <140 mg/dL (7.8 mmol/L) or
- Two-hour postprandial glucose <120 mg/dL (6.7 mmol/L).

B. Food records

Detailed food journals are useful to make adjustments to the meal plan or to the insulin regimen and also help the patient to become aware of individual blood glucose response to particular types and amounts of food. These also indicate the patient's level of understanding and compliance with the recommended meal plan.

C. Urinary ketone testing

Testing urinary ketone on the first morning specimen may be useful in detecting insufficient caloric or carbohydrate intake in women treated with caloric restriction²⁸.

D. Glycosylated haemoglobin

In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, increasing levels of glycemia were associated with worsening outcomes. Observational studies have shown the lowest rates of adverse fetal outcomes in association with A1C <6–6.5% (42–48 mmol/mol) early in gestation. Due to physiological increases in red blood cell turnover, A1C levels fall during normal pregnancy. Because HbA1C represents an integrated measure of glucose, it may not express accurate postprandial hyperglycemia, which lead to macrosomia. HbA1C may be useful but it should be used as a secondary measure of glycemic control in pregnancy, after self-monitoring of blood glucose. In the second and third trimesters, A1C <6% (42 mmol/mol) has the lowest risk of large-for-gestational-age (LGA) infants, preterm delivery, and preeclampsia. In conclusion, a target of <6% (42 mmol/mol) is optimal during pregnancy if it can be achieved without significant hypoglycemia. A1C levels may need to be monitored more frequently than usual (e.g., monthly) due to the alteration in red blood cell kinetics during pregnancy and physiological changes in glycemic parameters.

²⁷ Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358(19):1991-2002.

²⁸ Buhling KJ, Elze L, Henrich W, et al. The usefulness of glycosuria and the influence of maternal blood pressure in screening for gestational diabetes. *Eur J Obstet Gynecol Reprod Biol* 2004;113(2): 145-148.

VI. PHARMACOLOGICAL THERAPY

When lifestyle modification is insufficient to maintain normoglycemia in women with GDM, it is necessary to introduce drug treatment²⁹. Current medication treatments of hyperglycemia during pregnancy include insulin therapy and oral antidiabetic agents (OADs) and they are added when women with GDM are unable to achieve or maintain blood glucose levels and/or when fetal growth rate is above normal. Insulin is the first-line agent recommended for treatment of GDM in the U.S. OADs are not recommended as first-line treatment for GDM because they are known to cross the placenta and there are no sufficient³⁰ data on long-term safety for offspring.

A. Insulin therapy

While the majority of women with GDM will reach their glycaemic targets with lifestyle changes, 15–30% women will require additional intervention. This intensification of treatment should occur if glycaemic goals are not reached in 1–2 weeks, or at diagnosis if the plasma fasting glucose level is ≥ 7.0 mmol/L. In pregnancy complicated by GDM can be used either multiple daily injections or insulin pump technology. The physiology of pregnancy necessitates frequent titration of insulin in order to match with the changing requirements. It is important to have daily and frequent self-monitoring of blood glucose. Literature has shown that none of the currently available human insulin preparations do not cross the placenta. Insulin is a traditional, safe, and effective medication treatment of GDM. Many kinds of insulin preparations are available, such as rapid-acting insulin (e.g., regular human insulin), intermediate insulin (e.g., neutral protamine hagedorn), and long-acting insulin (e.g., insulin detemir). Rapid-acting insulin usually works from 30-min or 1-h post subcutaneous injection, reaching its peak effectiveness between 2 and 4 h, and the effect can last for about 6–8 h. Intermediate insulin works for 1–2 h post subcutaneous injection, reaching its peak effectiveness between 4 and 8 h, and its effect can last for about 12–18 h. Long-acting insulin works for 3–4 h post subcutaneous injection, reaching its peak effectiveness between 8 and 10 h, and its effect can last as long as 20 h. Thus, it is beneficial to combine these insulin preparations to simulate the daily physiological insulin secretion. Insulin administration should start with a small dose, which should be gradually increased, and the insulin type and regimens should be individualized. Therapy is associated with an increased risk of hypoglycaemia is important to educate the patient before initiating. Two key randomized, controlled trials, which identified women with GDM from 24 to 28 weeks of gestation reduces analysed the frequency of adverse outcomes. Firstly, the Australian Carbohydrate intolerance Study in Pregnant Women (ACHOIS) trial group found that treating GDM reduces serious perinatal morbidity and may also improve the woman's health-related quality of life. Subsequently, Landon et al. in a randomized controlled trial noted that treatment of GDM reduced the risk of foetal overgrowth, shoulder dystocia, caesarean delivery and hypertensive disorders which were pre-specified secondary outcomes. There was no effect on the primary outcome, a composite of stillbirth or perinatal death and neonatal complications, including hyperbilirubinemia, hypoglycaemia, hyperinsulinemia and birth trauma³¹.

²⁹ Egan AM, Simmons D. Lessons learned from lifestyle prevention trials in gestational diabetes mellitus. *Diabet Med* 2019;36(2):142-150.

³⁰ Zhang C., Tobias D.K., Chavarro J.E. Adherence to healthy lifestyle and risk of gestational diabetes mellitus: prospective cohort study. *BMJ*. 2014;349:g5450. [PMC free article]

³¹ Dornhorst A. A comparison of glyburide and insulin in women with gestational diabetes mellitus. *Diabet Med*. 2001;Suppl 3:12–14; Rowan J.A., Hague W.M., Gao W., Battin M.R., Moore M.P., MiG Trial

B. Oral Hypoglycemic agents

The choice of pharmacologic therapy is also under debate. Study has shown that compared with insulin, glibenclamide was associated with higher birth weights and neonatal hypoglycaemia. Compared with insulin, treatment with metformin resulted in less maternal weight gain but a lower gestational age at delivery. Another study reported a high probability that metformin use is associated with reduced risk of pregnancy-induced hypertension compared with insulin. In the Metformin in Gestational Diabetes (MiG) trial, metformin was not associated with an increase in neonatal complications compared with insulin, and rates of severe neonatal hypoglycaemia were lower in those women receiving metformin. However, follow-up on data from the MiG trial participants revealed that children of mothers who received metformin had higher skinfold measurements but no difference in body fat percent by body composition measures or neurodevelopmental outcomes at 2 years old compared with offspring of those randomized to insulin. It should be noted that almost half the women randomised to metformin also received insulin to manage hyperglycaemia. A smaller proportion of infants have been followed up to age 9 years and those exposed to metformin were larger by multiple measures including weight, arm and waist circumferences and waist:height. These data suggest that metformin may interact with foetal environmental factors to influence offspring outcomes in the long term. There are no data regarding longterm outcomes for those treated with glibenclamide during pregnancy³². There are some women with GDM who need medical therapy and who, due to cost, language barriers, comprehension, or cultural influences, are not be able to use insulin safely or effectively in pregnancy. Oral agents may be an alternative in these women after a discussion of the known risks and the need for more long-term safety data in offspring. However, due to the potential for growth restriction or acidosis in the setting of placental insufficiency, metformin should not be used in women with hypertension, preeclampsia, or at risk for intrauterine growth restriction³³.

B1. Metformin

Metformin is a biguanide which inhibit hepatic gluconeogenesis and stimulate glucose uptake in the peripheries³⁴. Metformin was associated with a lower risk of neonatal hypoglycemia and less maternal weight gain than insulin in systematic reviews but it crosses the placenta so in umbilical cord blood levels of metformin are as high or higher than simultaneous maternal levels. In the Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU) study's analyses of 7- to 9-year-old offspring, the 9-year-old offspring exposed to metformin in the Auckland cohort for the treatment of GDM were heavier and had a higher waist-to-height ratio and waist circumference than those exposed to

Investigators Metformin versus insulin for the treatment of gestational diabetes. *N Engl J Med.* 2008;358:2003–2015.

³² Balsells M., García-Patterson A., Solà I., Roqué M., Gich I., Corcoy R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. *BMJ.* 2015;350:h102; SMFM Statement: Pharmacological treatment of gestational diabetes. *Am J Obstet Gynecol* 2018;218(5): B2-B4. 37. Dashora U, Rafique S, Tharayil G, et al. The feasibility and impact of implementing NICE guidance on diabetes control during delivery. *Br J Diabetes* 2017;17(3).

³³ Kalafat E, Sukur YE, Abdi A, et al. Metformin for prevention of hypertensive disorders of pregnancy in women with gestational diabetes or obesity: systematic review and meta-analysis of randomized trials. *Ultrasound Obstet Gynecol* 2018;52(6): 706-714.

³⁴ Benhalima K, Mathieu C, Damm P, et al. A proposal for the use of uniform diagnostic criteria for gestational diabetes in Europe: an opinion paper by the European Board & College of Obstetrics and Gynaecology (EBCOG). *Diabetologia* 2015;58(7): 1422-1429.

insulin³⁵. This was not found in the Adelaide cohort. In two randomized control trials of metformin use in pregnancy for polycystic ovary syndrome, a follow-up of 4-year-old offspring demonstrated higher BMI and increased obesity in the offspring exposed to metformin. A follow-up study at 5–10 years showed that the offspring had higher BMI, weight-to-height ratios, waist circumferences, and a borderline increase in fat mass.

B2. Sulfonylureas

It is known that sulfonylureas cross the placenta and are associated with increased neonatal hypoglycemia. Concentrations of glyburide in umbilical cord plasma are approximately 50–70% of maternal levels. Glyburide was associated with a higher rate of neonatal hypoglycemia and macrosomia than insulin or metformin in a 2015 meta-analysis and systematic review. Studies has shown that glyburide failed to be found noninferior to insulin based on a composite outcome of neonatal hypoglycemia, macrosomia, and hyperbilirubinemia but long-term safety data for offspring exposed to glyburide are not available. Glibenclamide is a sulfonylurea that binds to pancreatic beta-cell adenosine triphosphate potassium channel receptors and increases insulin secretion and may be used at 2.5-20 mg per day in divided doses, although the dose–response relationship in pregnancy is not clear.

VII. PHYSICAL ACTIVITY

An important adjuvant therapy in management of diabetes in pregnancy, particularly in GDM, could be the practice of moderate exercise because is effective in controlling weight gain and improving glucose homeostasis by increasing insulin sensitivity. Women with GDM should be advised to take regular exercise to improve glucose control. Studies reported that exercise intervention reduced the incidence of GDM by 28% [95% *CI*: 9–42%; relative risk (*RR*) = 0.72, *P* = 0.005] compared with the control. Halse et al. showed that exercise during pregnancy may help to maintain daily postprandial normoglycemia in women with diet-controlled GDM. Unfortunately there is no unified and clear guideline for physical activity during pregnancy. Many organizations such as the American College of Obstetricians and Gynecologists, the Canadian Diabetes Association, and the Sports Medicine Australia recommend that for women without contraindications to exercise, an accumulated time for moderate exercise of ≥ 30 min on most, if not all, days of the week (at least 150 min/week) is needed during pregnancy and the postpartum period. Pregnant women need to undergo a comprehensive physical assessment, and obtain professional and individualized exercise guidance, before start a exercise therapy. Aerobic activities and strengthening exercises involving large muscle groups are recommended. It should be avoided sports with risks of falling, trauma or collisions. Women need to monitor fetal activity and their blood glucose levels before and after exercise to ensure the safety of exercise and prevent the occurrence of hypoglycemia. Healthy eating and exercise habits should continue after delivery³⁶.

³⁵ Rowan JA, Rush EC, Plank LD, et al. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7-9 years of age. *BMJ Open Diabetes Res Care* 2018; 6(1):e000456.

³⁶ Committee Opinion No 650 Summary: physical activity and exercise during pregnancy and the postpartum period. *Obstet Gynecol.* 2015;126:1326–1327; Evenson K.R., Barakat R., Brown W.J. Guidelines for physical activity during pregnancy: comparisons from around the world. *Am J Lifestyle Med.* 2014;8:102–121; Halse R.E., Wallman K.E., Newnham J.P., Guelfi K.J. Home-based exercise training improves capillary glucose profile in women with gestational diabetes. *Med Sci Sports Exerc.* 2014;46:1702–1709; Keshel T.E., Coker R.H. Exercise training and insulin resistance: a current review. *J Obes Weight Loss Ther.* 2015;5:S5–003;

VIII. POSTPARTUM FOLLOW-UP

The postpartum period is also important in the management of GDM because both the mother and the offspring are at increased risk of future obesity, T2DM, hypertension, and metabolic syndrome. The guidelines recommend to have a postpartum follow-up at 4–12 weeks after childbirth and all women with hyperglycemia during pregnancy should have a 75-g OGTT in order to evaluate their blood glucose levels. If the diagnostic criteria for diabetes or pre-diabetes are met at this point, the mother should be advised to see an endocrinologist and make follow-up visits every 1–3 years. Women with a history of GDM should ideally have an intrapartum interval more than 1 year and plan to get pregnant. They need also to undergo the 75-g OGTT prior to or at least in the early stage of next pregnancy. Lifestyle intervention is also the most fundamental and effective method for postpartum management. Ratner et al. randomized 350 women with recently diagnosed GDM to standard lifestyle and placebo or metformin therapy, or to lifestyle intervention group, and found that in the fourth year after childbirth, lifestyle intervention and metformin therapy can both reduce the incidence of diabetes by approximately 50% from that with the standard lifestyle and placebo. The data also has shown that breastfeeding can also reduce the risk of type 2 diabetes in women with GDM. Gunderson et al. conducted a prospective, observational cohort study of women with a history of GDM to evaluate lactation and the 2-year incidence of diabetes after GDM pregnancy. In their study, the incidence of diabetes after GDM pregnancy was inversely associated with lactation intensity. The conclusions was that the longer the breastfeeding is, the lower is the 2-year incidence of diabetes after GDM pregnancy. Bider-Canfield et al. indicated in a study that breastfeeding for ≥ 6 months is associated with a decreased risk of childhood overweight at age 2 years³⁷.

IX. PREVENTION

Current recommendations for women with GDM to prevent the onset of type 2 diabetes include diet, weight reduction or weight maintenance and participating in regular physical activity³⁸. Data has shown that lifestyle modification reduce diabetes development by 50 % or more. It has been documented that dietary modifications of lowering fat and carbohydrate intake in combination with physical activity can reduce the risk of developing GDM in subsequent pregnancies. It is important to plan and prepare before pregnancy because usually women of reproductive age do not have regular physical examination or know their blood glucose levels. Thus, sometimes, hyperglycemia is already present at conception and studies have shown that hyperglycemia during organogenesis increase the risk of spontaneous abortions and congenital anomalies. All women are encouraged to adopt good dietary and lifestyle habits before pregnancy, especially those who are underweight or overweight/obese. As a woman's body mass index (BMI) prior to pregnancy is of high importance, both low and high BMIs are closely related to poor pregnancy outcomes. Zhang et al. found that adherence to a low-risk lifestyle (healthy body weight, healthy diet, regular exercise, and non-smoking) before pregnancy is associated with a low risk of GDM .

Kgosidialwa O, Egan AM, Carmody L, et al. Treatment with diet and exercise for women with gestational diabetes mellitus diagnosed using IADPSG criteria. *J Clin Endocrinol Metab* 2015;100(12):4629-4636.

³⁷ Carmody L, Egan AM, Dunne FP. Postpartum glucose testing for women with gestational diabetes mellitus: improving regional recall rates. *Diabetes Res Clin Pract* 2015.

³⁸ RatnerRE, ChristophiCA, MetzgerBE ,etal. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *J Clin Endocrinol Metab* 2008;93(12):4774-4779.

X. CONCLUSION

In conclusion, GDM is associated with a higher risk of adverse health outcomes for both mothers and offspring, during the perinatal phase and also in the long term. It is important to give importance to the prevention and management of GDM throughout pregnancy, prior to pregnancy and postpartum. Nutrition intervention and physical activity should be the primary and major strategies. If lifestyle modification alone fails to maintain normoglycemia, insulin should be considered. Postpartum care plays also a critical role in the prevention of future chronic non-communicable diseases.

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BIOCHEMICAL PARAMETERS IN ACUTE PANCREATITIS

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ABSTRACT:

BACKGROUND

ACUTE PANCREATITIS REPRESENT AN INFLAMMATORY DISEASE WITH DIFFERENT GRADES OF SEVERITY, RANGING FROM MILD TO SEVERE PRESENTATIONS.THERE ARE A LOT OF BIOMARKERS USED IN DIAGNOSIS AND PROGNOSIS OF ACUTE PANCREATITIS.

OUR AIM WAS TO EVALUATE DIFFERENT BIOCHEMICAL PARAMETERS AT TWO MOMENTS OF PANCREATITIS:ADMISSION AND DISCHARGE.

METHOD:WE INCLUDED 100 PATIENTS.ALL THE PATIENTS WERE EVALUATED AT ADMISSION AND DISCHARGE.DATA ON BIOCHEMICAL PARAMETERS SUCH AS AMYLASE, LYPASE WERE COLLECTED.

RESULTS:WE HAVE OBTAINED SIMILAR RESULTS LIKE IN THE STUDIES FROM LITERATURE REGARDING DIAGNOSIS OF ACUTE PANCREATITIS USING AMYLASE, LIPASE, LEUKOCYTES, BILIRUBIN, LACTATE DEHYDROGENASE.

KEY WORDS: AMYLASE, LIPASE, ACUTE PANCREATITIS

INTRODUCTION

Acute pancreatitis is a common inflammatory disease which can vary from mild to severe presentation⁸.Early predictors of establishing the severity of the disease are lack⁹.

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Diagnosis of acute pancreatitis can be clinical by abdominal pain, biochemical by serum enzymes such as amylase, lipase and morphological alterations by abdominal ultrasound, computed tomography.¹⁰

There are a lot of causes of acute pancreatitis, but the most two important are gallstones and alcohol.^{11,12} For a good diagnosis there is necessary to have at least 2 of 3 criteria, such as abdominal pain, high levels of serum enzymes (amylase, lipase) and imagistic features.

To predict the severity of the disease, clinical signs, laboratory markers and imagistic tests have to be taken into account. Both lipase and amylase alone don't have the ability to diagnose and predict the severity of the disease.¹³ Although the sensitivity and specificity of the amylase aren't so high, the enzyme is widely used in clinical practice.^{14,15,16}

A cut -off of three folds of the upper limit of reference has increase the sensitivity and specificity of both amylase and lipase tests in diagnosis of acute pancreatitis.^{17,18,19,20}

The aim of the study was to compare the values of different biochemical parameters used in diagnosis of acute pancreatitis at admission and discharge.

MATERIALS AND METHODS

Our study included 100 patients who was admitted at the Department of Gastroenterology with acute pancreatitis.

Laboratory tests (including the complete blood count, total cholesterol, transaminases, bilirubin, alkaline phosphatase levels) were performed to all the patients after a clinical examination. We measured two values at different moments (admission and discharge) at the same patients.

The results were presented as mean±standard deviation for numeric variables and as absolute numbers and percentage for categorical variables, using Shapiro Wilk test. Statistical

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analysis was performed by using R programming soft, version 3.5.3. (2019-03-11) Copyright (C) 2019. The statistical significance was considered for a p value <0.05.

Patients' characteristics are summarized in table 1 (baseline characteristics) and table 2 (laboratory parameters).

RESULTS

The baseline characteristics of the study patients are presented in Table 1. The mean age was 58.07 ± 15.10 years with male predominance (65% of the patients).

The majority patients were from the urban environment.

We represent the values of number of leukocytes, thrombocytes, haemoglobin, cholesterol, triglycerides, transaminases, bilirubin, alkaline phosphatase (see Table 2).

We compare the values of amylase, lipase, leukocytes, bilirubin, lactate dehydrogenase at admission and discharge. (table 3, 4, 5, 6 and 7).

Table 1. Baseline characteristics

Patient characteristics	No = 100
Age – Mean \pm S.D	58.07 ± 15.10
Sex	
M – No. (%)	65 (65.00)
F – No. (%)	35 (35.00)
Residency	
City – No. (%)	75 (75.00)
Rural – No. (%)	25 (25.00)

Table 2. Laboratory parameters

Leukocytes – Mean (IQR)	10855.00 (7600.00)
Trombocytes – Mean \pm S.D	268450 ± 114454
Lymphocytes – Mean \pm S.D	1355.00 ± 581.33
Granulocytes – Mean \pm S.D	9481.70 ± 4995.70
Basophil – Mean (IQR)	65.00 (205.00)
Monocytes – Mean (IQR)	800.00 (580.00)
RDW – Mean \pm S.D	34.92 ± 15.36
Hb – Mean \pm S.D	13.83 ± 2.18
Cholesterol – Mean \pm S.D	181.44 ± 73.38
TGL – Mean (IQR)	100.50 (51.00)
AST – Mean (IQR)	40.50 (85.00)
ALT – Mean (IQR)	34.00 (112.00)
TB – Mean \pm S.D	1.51 ± 1.49
DB – Mean \pm S.D	0.62 ± 0.94
AF – Mean (IQR)	92.00 (97.00)
GGT – Mean (IQR)	148.50 (395.00)

Table 3. The distribution of amylase

Amylase	Admission	Discharge	
Mean ± S.D	649.52 ± 660.03	110.44 ± 98.99	
Mediana (IQR)	446.50 (681.50)	84.00 (70.00)	
Min to Max	29.00 la 3112.00	31.00 la 664.00	
Skewness	1.50	3.08	
Mean Admission	Mean discharge	P value	Mean difference[IC95%]
649.52	110.44	< 0.0001	547.89 [408.90 la 686.88]

Table 4.The distribution of lipase

Lipase	Admission	Discharge	
Mean ± S.D.	1423.24 ± 1888.62	129.10 ± 152.65	
Mediana (IQR)	586.00 (1679.00)	76.00 (95.00)	
Min to Max	3.00 la 9110.00	4.00 la 902.00	
Skewness	1.96	3.09	
Mean Admission	Mean Discharge	P value	Mean difference [IC95%]
1423.24	129.10	< 0.0001	1273.83 [883.46 la 1664.19]

Table 5.Distribution of leukocytes

Leukocytes	Admission	Discharge
Mean ± S.D	11.85 ± 5.30	8.30 ± 3.20
Mediana (IQR)	10.76 (7.62)	7.56 (3.70)
Min to Max	3.40 la 28.92	2.20 la 18.42
Skewness	0.95	1.07

Medie Admisie	Medie Externare	Valoare p	Medie Diferente[IC95%]
11.85	8.30	< 0.0001	3.55 [3.10 la 5.15]

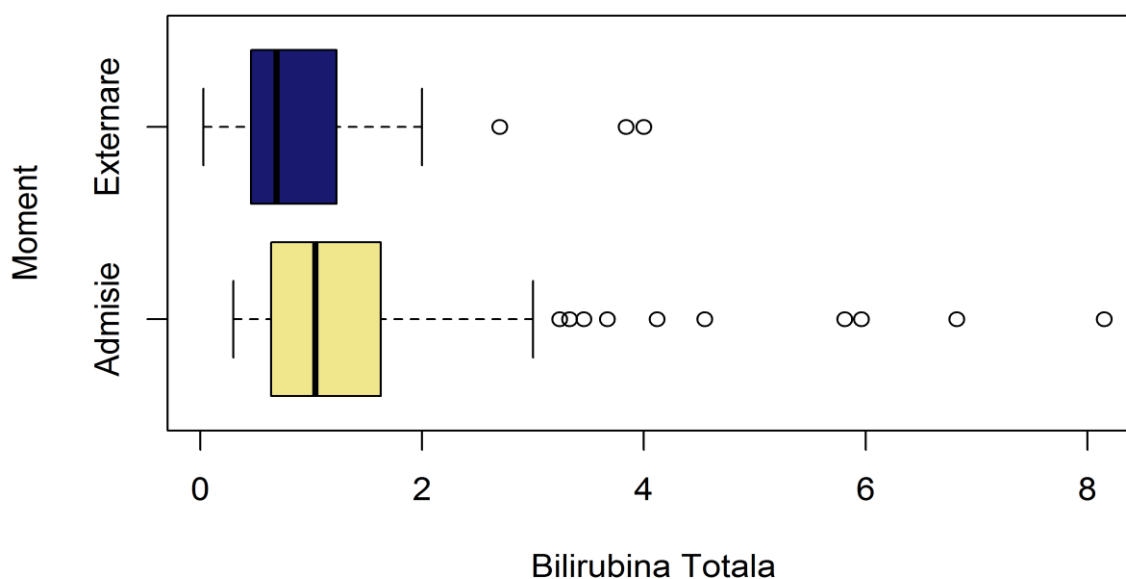
Table 6.Distribution of lactate dehydrogenase

LDH	Admission	discharge	
Mean ± D.S	324.66 ± 229.03	212.82 ± 116.48	
Mediana (IQR)	282.00 (191.00)	189.50 (179.50)	
Min la Max	75.00 la 1221.00	0.26 la 448.00	
Mean Admission	Mean discharge	P value	Mean difference [IC95%]
324.66	212.82	0.0260	111.84 [24.02 la 327.31]

Table 7. Distribution of total bilirubin

Total bilirubin			Admission	Discharge
Medie ± D.S			1.51 ± 1.49	0.97 ± 0.86
Mediana (IQR)			1.04	0.69
Min la Max	0.30 la 8.15	0.03 la 4.00	(1.00)	(0.77)
Skewness	2.35	2.02		
Mean Admission	Mean discharge		P value	Mean difference[IC95%]
1.51	0.97		< 0.0001	0.54 [0.35 la 0.81]

Comparatie Bilirubina Totala



DISCUSSION

In our study we evaluate different values of some biochemical markers at the same patient in two moments: admission and discharge.

In the literature, the importance of lipase is more than of amylase, this one being preferred in diagnosis of hyperlipidemic acute pancreatitis.^{21, 22}

²¹ G. Yin, X. Cang, G. Yu, G. Hu, J. Ni, J. Xiong, Y. Hu, M. Xing, C. Chen, Y. Huang, M. Tang, Y. Zhao, G. Cheng, R. Wan, S. Wang, X. Wang, Different clinical presentations of hyperlipidemic acute pancreatitis: a retrospective study, *Pancreas* 2015,44 (7) : 1105–1110

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Some studies showed that lipase test is better in diagnosis of alcoholic pancreatitis than amylase test.^{23, 24}.

The results of our study were similar to other studies. The value of amylase recorded at admission decrease at discharge with a significant statistical value of $p < 0.0001$. We obtained also a statistical significance with a p value < 0.0001 regarding the value of the lipase in two different moments: at admission with a high level and at discharge with a low, even normal level.

Other biochemical markers such as bilirubin and number of leukocytes were measured at admission and at discharge and we have noticed the decreasing of the value for both of them with a statistical significance of p value < 0.0001 .

We can conclude that these common biochemical parameters such as amylase, lipase, leukocytes, bilirubin have a real value in diagnosis of acute pancreatitis.

ACKNOWLEDGMENTS

All authors equally contributed of the research of this paper.

All authors report no potential conflict of interest.

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DEMOGRAPHIC, CLINICAL, BIOCHEMICAL, PERIOPERATIVE ASPECTS IN COLORECTAL CANCER PATIENTS, 2002-2014

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ABSTRACT:

BACKGROUND AND AIMS: COLORECTAL CANCER (CRC) IS A NEOPLASM WITH INCREASING INCIDENCE IN THE LAST 20 YEARS, WITH IMPROVED OPERABILITY RATES, PERIOPERATIVE MORTALITY AND HIGHER SURVIVAL RATES, BUT WITH THE PERCENTAGE OF RECURRENCE OF THE DISEASE NOT IMPROVED DURING THE LAST 2 DECADES. THE PURPOSE OF THIS STUDY WAS TO EVALUATE PATIENTS WITH COLORECTAL TUMORS HOSPITALIZED, INVESTIGATED AND OPERATED DURING 13 YEARS, IN A SINGLE CENTER AND TO OBSERVE THEIR EVOLUTION. PATIENTS WITH THE DIAGNOSIS OF CRC HOSPITALIZED IN DR. I. CANTACUZINO HOSPITAL BETWEEN 2002-2014 WERE EVALUATED ON THE BASIS CLINICAL, BIOLOGICAL, ANATOMOPATHOLOGICAL DATA OBTAINED FROM PATIENTS SHEET AND ELECTRONIC DATABASE.

KEY WORDS: COLORECTAL CANCER, NODE STATUS, POSTOPERATIVE COMPLICATIONS, RECURRENCE

Abbreviations:

CRC - colorectal cancer
CC - colon cancer
RC - rectal cancer
EEA - end to end anastomosis
ESA - end to side anastomosis
PC - peritoneal carcinomatosis

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INTRODUCTION

Neoplastic disease is a major worldwide public health problem, prospective studies suggesting that cancer mortality will increase in the coming years, due primarily to the increase in life expectancy of the population, but also through the effect of population demographic development on frequency of cancers (population migration, effect of diet and environmental factors). Colorectal cancer (CRC) is a neoplasm located in the first places as an incidence both internationally and nationally. Among the technical advances that patients currently benefit from it, we can mention: population screening on risk, endoscopic interventions, minimally invasive interventions, mechanical suture devices, new classes of antibiotics, new classes of chemotherapy, immunohistochemistry techniques, multi-organ interventions in experienced clinics, leading to lower perioperative morbidity rates and associated general mortality, but with unchanged values of postoperative relapses over the last 20 years. In 2016, the mortality rate of this neoplasm was reduced below half compared to 1970, and the overall survival rates are 65%, depending on various factors, in particular the tumor stage⁵.

Early recurrence is defined as tumor recurrence occurring less than 2 years after the initial tumor resection⁶, although there are authors who consider that a 3-year interval would be more appropriate, considering that in the first 2 years postoperatively, local or distant recurrence would in fact constitute insufficient initial evaluation and staging of the neoplasm. CRC relapse is defined as local recurrence or near the initial tumor or at the level of the same organ, as well as metastasis to the adjacent or distant tumor tissue.

PATIENTS AND METHODS

This is a retrospective study in a single center taken between January 2002 and December 2014. The research project aimed to evaluate different patient related factors-demographic, clinical, biochemical, histopathological and perioperative complications and outcomes.

Ethics

The retrospective analysis of the data has been approved by Ethics Committee of the institution within which the work was undertaken and it conforms to the international provisions.

RESULTS

Between the years 2002-2014, during 13 years, the average number of interventions performed on colon and rectum were about 110 interventions/ year, representing 3.74% of the total number of interventions performed in the Dr. I. Juvara Surgery Department of Dr. I. Cantacuzino Hospital, but in increasing percentage until the study end (from 2.85% to 5.28%). It should be mentioned that the pathology operated in the Surgery Department is varied, comprising interventions of the hepato-biliary and pancreatic, abdominal wall surgery, digestive oncological surgery, genital, interventions performed open and laparoscopic, by case, also diabetic foot interventions or on mammary gland. The 1533 patients with surgical interventions on the colon and rectum required 1-6 operations (with an

⁵ Cancer Facts & Figures, 2019, American Cancer Society, <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf>, last modified June 2019

⁶ McArdle CS, Hole DJ. Outcome following surgery for colorectal cancer: analysis by hospital after adjustment for case-mix and deprivation. Br J Cancer.2002;86:331-5

average of 1.17 interventions/ patient), within the same hospitalization or in iterative hospitalizations, the most common for postoperative or recurrent complications, local or at a distance.

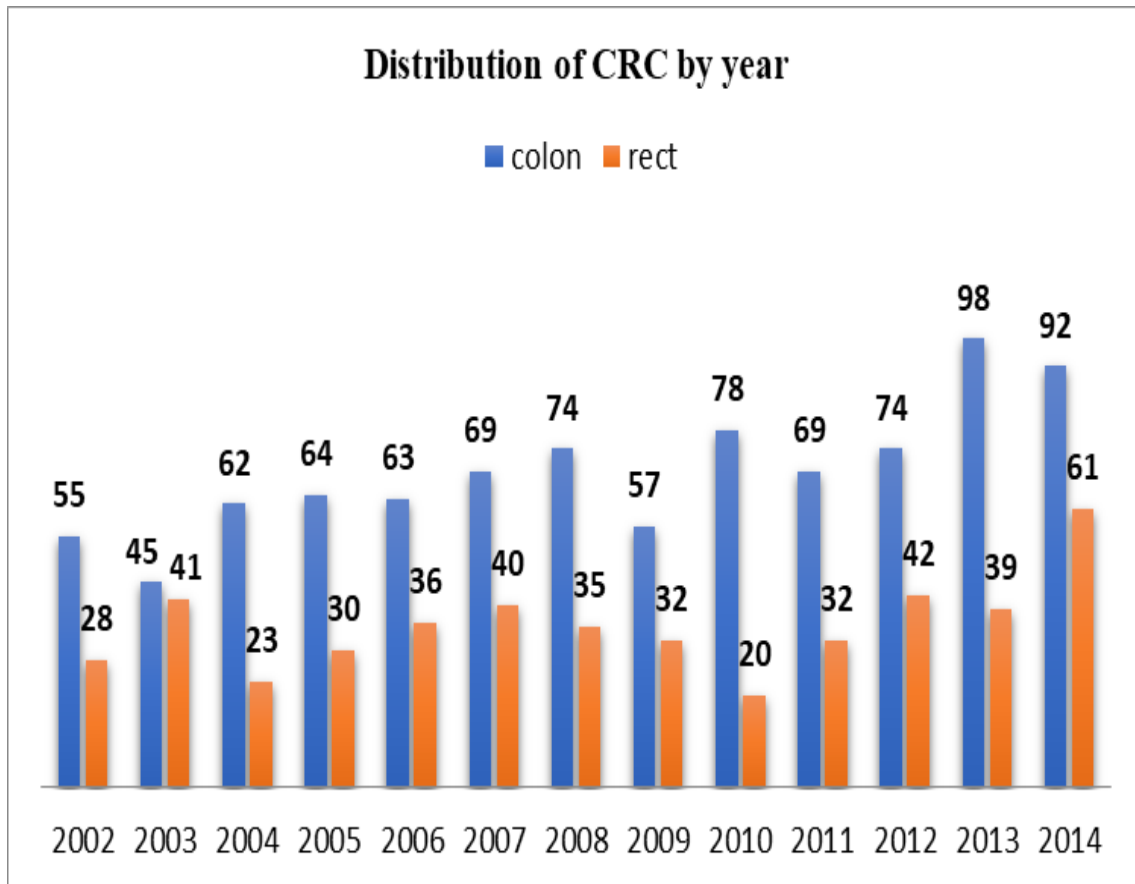
We found a series of patients difficult to fit into a category, due to the lack of continuity of investigations or lack the data available for follow-up - of these, only 3% returned to the Surgery Department to the Medical or Gastroenterology Departments. These patients, who accidentally presented to the doctor or clinic, often after a rectal bleeding episode or due to a colonoscopy to investigate intestinal transit disorders, were in a very small number, difficult to include in subsequent analysis. There have been found the cases with surgical interventions performed on colon tumor without postoperative histopathological confirmation (without a malignancy confirmation), trans-anal polypectomies/colotomy-polypectomy and colon suture, and patients with malignant recto colonic polyposis, totaling a total of 98 patients. We also excluded a number of 23 cases, surgery performed without identifying a tumor formation per se ("false image"), in cases which suspicion was supported by imaging investigations (radiological, tomographic) or endoscopic.

We noticed in the selected group the presence of 8 cases of surgery in patients with known inflammatory bowel disease (Crohn's disease) or with complicated diverticular disease, 3 cases with intestinal lymphoma or gastro intestinal stromal tumor with colonic localization, and 17 cases of other neoplasms with invasion of the digestive tract, respectively colon, which required segmental colectomies or hemicolectomies. Multiple primary cancers may occur in an individual due to genetic predisposition, exposure to environmental factors, secondary to chemotherapy or radiation, or due to immunological deficiencies. Of the associated neoplasms in the selected group, we mention: lung (2 cases), cervical (2 cases), gastric (5 cases), laryngeal (1 case), breast (5 cases), malignant melanoma (1 case), ovary (1 case), lymphoma, multiple myeloma (4 cases), prostate (2 cases) histiocytoma and cerebral glyosarcoma (one case each). In an article published in 2002, based on the study of The Thames Cancers Registry (UK) database, which includes 1.5 million patients with CRC followed from the time of diagnosis till death, from 1961 to 1995, it found the onset of a second primary neoplasm in about 5% of them. Neoplasms induced by chemotherapy or radiotherapy occur in predictable time intervals from primary CRC treatment, thus 1-5 years for acute myeloid leukemia and 10-25 years for solid tumors⁷.

Following the observations in pervious paragraphs we obtained a number of 1359 of patients, and their yearly distribution is presented in Graphic 1. It can be observed the progressive increase in the number of cases, at the beginning approximately 90-100 / year, exceeding 150 at the end of the study.

⁷ H S Evans, H Moller, D Robinson, C M Lewis, C M J Bell, and S V Hodgson

The risk of subsequent primary cancers after colorectal cancer in southeast England, Gut. 2002 May; 50(5): 647-652



Graphic1. Distribution of CRC cases by year

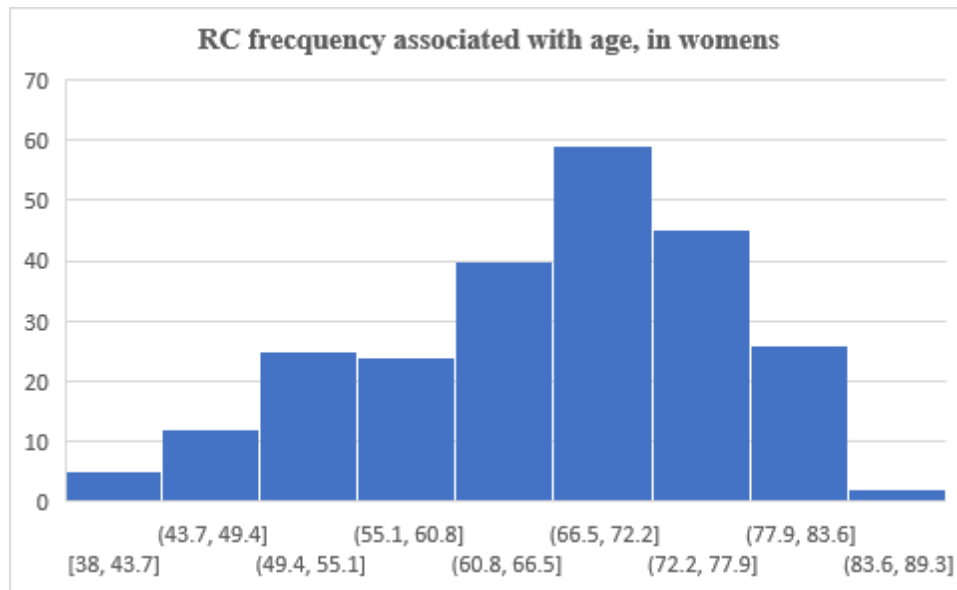
DISCUSSION

Age and gender

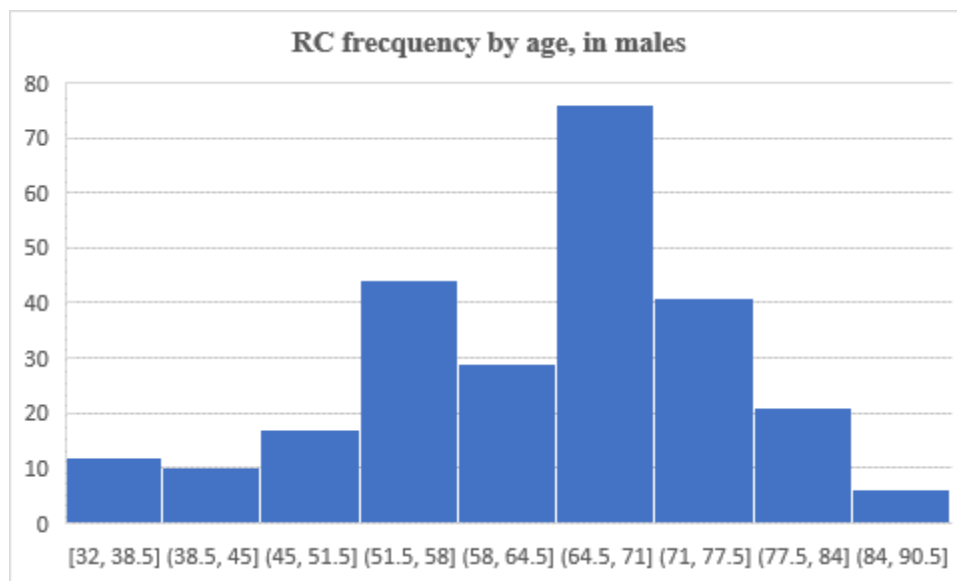
Most patients with CRC are elderly person at the moment of diagnosis, but frequently we are dealing with younger patients under 50 years, time at which the disease evolves for a long time and rectal bleedings were attributed to the hemorrhoidal disease, so that these patients come late to doctor (stage III-IV). In the case of the young patients, tumors are located distal from splenic angle more frequent, and rectal tumors occur in up to 39% of these cases⁸.

For RC, in the group herein, we found an increasing frequency by age, with a maximum peak between 66 to 72 year in female gender and similar to male with a maximum peak of frequency between 64 to 71 age (Graphic 2,3). We noticed a similar peak between 51 to 58 for men, but with a smaller representation. We also found that 14, 4% of male patients are younger than 50, while only 8,3 % female patients are under 50 years age.

⁸ Elizabeth A Myers, Daniel L Feingold, Kenneth A Forde, Tracey Arnell, Joon Ho Jang, and Richard L, Colorectal cancer in patients under 50 years of age: A retrospective analysis of two institutions' experience, Whelan World J Gastroenterol. 2013 Sep 14; 19(34): 5651–5657

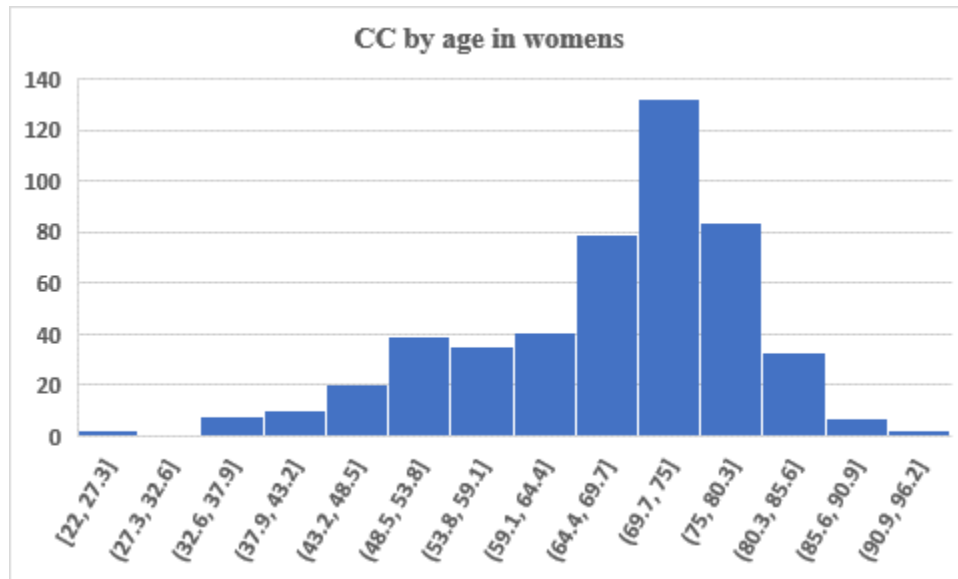


Graphic 2: RC frequency by age, in women

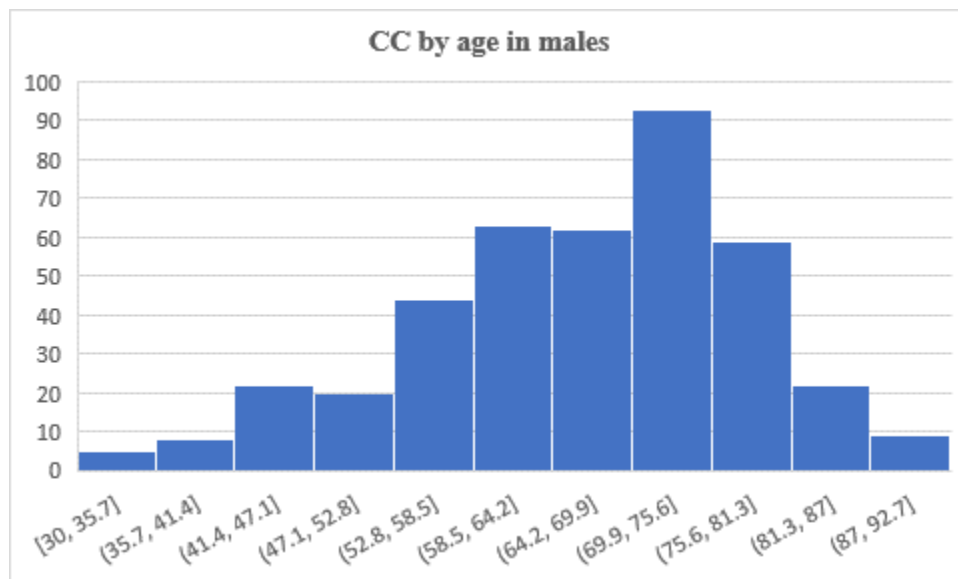


Graphic 3: RC frequency by age, in males

In the group of patients with CC there are no important differences in terms of distribution by gender in the studied group, with a similar mean age (67,44 vs. 67,21), and also for patients under 50 years age (11,67% vs. 11,41%). (Graphic 4, 5)



Graphic 4. CC frequency by age in women



Graphic 5. CC frequency by age in males

There are studies which suggest that women over 65 years of age have higher mortality rates and a shorter 5-year survival⁹. The causes that would produce this effect are not known, but observational studies indicate socio-cultural factors for certain populations, which are related to diet, hormonal status; also, women develop more frequent tumors in the right (proximal) colon that cause more aggressive forms of the disease, compared to those in the left (distal) colon¹⁰. In the right colon there are more frequent flat tumors, more difficult

⁹ Sung-Eun Kim, Hee Young Paik, Hyuk Yoon, Jung Eun Lee, Nayoung Kim, and Mi-Kyung Sung, Sex- and gender-specific disparities in colorectal cancer risk, World J Gastroenterol. 2015 May 7; 21(17): 5167–5175

¹⁰ Hansen IO, Jess P., Possible better long-term survival in left versus right-sided colon cancer - a systematic review, Dan Med J. 2012; 59: A4444; Rene Warschkow, Michael C Sulz, Lukas Marti, Ignazio Tarantino, Bruno M. Schmied, Thomas Cerny, and Ulrich Guller, Better survival in right-sided versus left-sided stage I - III colon cancer patients, BMC Cancer. 2016; 16: 554

to detect by colonoscopy, as opposed to the polypoid formations, which are more frequent in the left colon¹¹. CRC screening is not differentiated by sex, but the sensitivity of the Hemoccult test, frequently used, is different in women and men¹². However, there are articles in the literature that have found that recurrence occurs earlier and more frequently in young patients, and especially in men¹³.

BMI, nutritional status

It is a well-known fact that obesity is a risk factor for CRC, as well as for the death associated with neoplasia. The negative association between BMI and recurrence risk was not observed in female patients, but men with BMI > 35 kg/m show a reduction in disease-free interval, compared to normal-weight patients. Also, the underweight patients have a decreased time interval until the moment of recurrence, and a stronger association with the male gender¹⁴.

In the group of patients from 2002-2014, based on the data available from the electronic archive and the observation sheets, we found the association with diabetes mellitus at 10.15% for RC and 9.00% for CC. Is a known fact that diabetes mellitus and CRC show similar nutritional risk factors as promoters of the disease. Obesity (BMI > 35) was identified in less than 1.5% of cases, and malnutrition or neoplastic cachexia in less than 2% of cases, when it was associated with all advanced stages, with secondary hepatic determinations, and most commonly in rectal tumors on elderly. We looked for the presence of nutritional factors, because the literature described that the risk of more frequent postoperative complications is associated with obesity and cachexia (anastomosis fistula).

Another factor that can influence the postoperative evolution, as well as the risk of recurrence, is the preoperative anemia, which we objected in 12.2% cases of RC and 15.7% cases of CC. In our group, secondary anemia in varying degrees was observed in all cases with secondary hepatic determinations (stage IV).

In the studied group we also identified associated cardio-vascular pathology (9.65% RC, 14.32% CC), liver cirrhosis / VHC (1.52% CR, 2.07% CC), symptomatic gallbladder lithiasis (1.84% cases). Cholecystectomy, as concomitant intervention, did not changed the rate of postoperative complications or the risk of recurrence.

Location of tumor

Primary tumor localization appears to be a prognostic factor, cancers located at/or below the peritoneal segments (rectum and sigmoid) have 5-year survival rates lower than for proximal tumors. Similar to the rectum, distal tumors have a more reserved prognosis¹⁵.

In terms of distributions of colon tumors, we noticed the preponderance at the level of the sigmoid/rectosigmoid junction (42%), followed by the localization at the caecum or

¹¹ Kaku E, Oda Y, Murakami Y, Goto H, Tanaka T, Hasuda K, Yasunaga M, Ito K, Sakurai K, Fujimori T, et al, Proportion of flat- and depressed-type and laterally spreading tumor among advanced colorectal neoplasia, Clin Gastroenterol Hepatol. 2011; 9:503–508

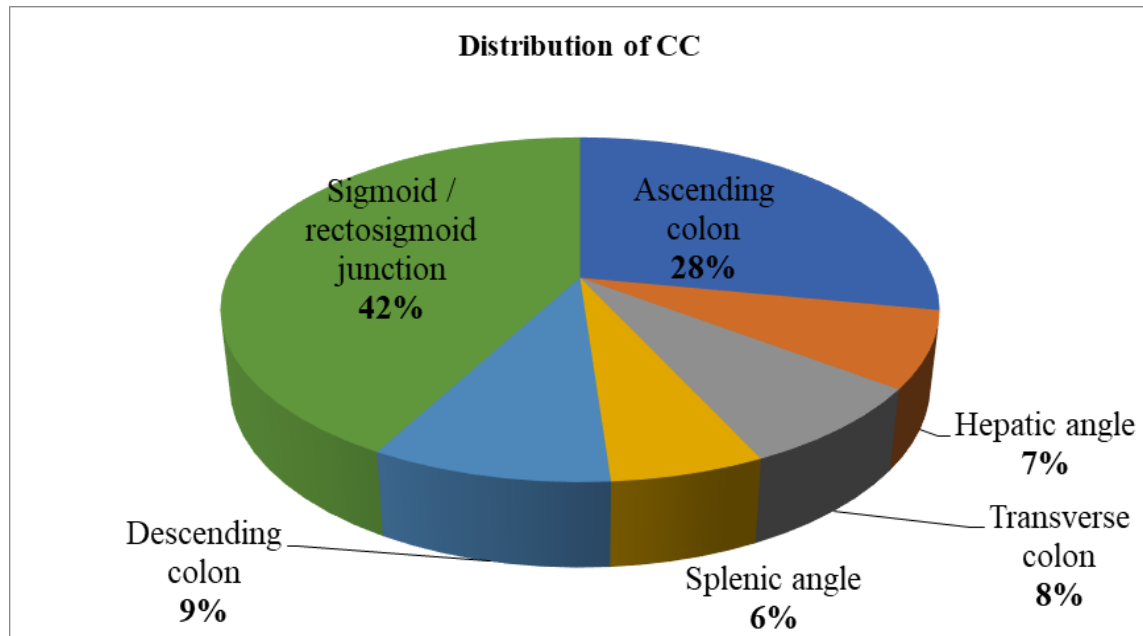
¹² Brenner H, Haug U, Hundt S, Sex differences in performance of fecal occult blood testing, Am J Gastroenterol.2010;105:2457–2464

¹³ Aghili M, Izadi S, Madani H, Mortazavi H, Clinical and pathological evaluation of patients with early and late recurrence of colorectal cancer, Asia Pac J Clin Oncol. 2010 Mar;6(1):35-41

¹⁴ Frank A Sinicrope, Nathan R Foster, Greg Yothers, Al Benson, Jean Francois Seitz, Roberto Labianca, Richard M. Goldberg, Aimery DeGramont, Michael J O'Connell, and Daniel J Sargent, Body Mass Index at Diagnosis and Survival Among Colon Cancer Patients Enrolled in Clinical Trials of Adjuvant Chemotherapy, Cancer. 2013 Apr 15; 119(8): 1528–1536.

¹⁵ Halvorsen TB, Johannesen E, DNA ploidy, tumour site, and prognosis in colorectal cancer, Scand J Gastroenterol. 1990;25(2):141–8

ascending colon (28%), descending colon (9%), transverse (8%), hepatic and splenic angle (7%, 6%). Articles from literature highlights a similar distribution¹⁶.



Graphic 6. Distribution of CC

The surgical interventions performed for CC were according to the tumor location, the biological and nutritional status of the patient and the intraoperative aspect (right/enlarged ileo-hemicolectomy with ileo-transverse EEA or ESA, segmental ileo-colectomy with ileo-ascending ESA, segmental colectomy splenic or hepatic angle with EEA, transverse colon segmental colectomy with EEA, left/wide hemicolectomy with transverse-sigmoid EEA, left hemicolectomy with colostomy, Hartmann's recto-sigmoid resection or with colorectal EEA or ESA, subtotal ileo-hemicolectomy with ileo-sigmoid ESA). We found 26 cases of synchronous tumors, either preoperative (colonoscopy) or intraoperative, which determined the extent of exertion. The most frequent associations were of rectal and sigmoid tumors (8 cases), followed by the ascending-hepatic, transverse-descending and other localization, without a significant association (transverse-sigmoid, hepatic-angle, caecum-sigmoid, sigmoid- hepatic/ splenic angle, sigmoid-ascending, sigmoid-descending, sigmoid-transverse-hepatic angle).

In the series herein the distribution of neoplasia in the rectum showed that 52,55% of the tumors develop in lower part, followed by 37,75% in the superior segment and 9,69% in the anorectal region. In the case of patients with RC, the following surgical procedures were performed: with a curative intention (64.7%), continuous colostomy (18.18%), colostomy and tumor biopsy (7.48%), trans anal tumor biopsy (8.02%), exploratory laparotomy (1.6%).

Surgery was performed with a curative intention on 298 patients, depending on the tumor localization; abdominoperineal amputation, anterior Dixon low resection and Hartmann operations were performed.

¹⁶ Kari Hemminki, Irene Santi, Marianne Weires, Hauke Thomsen, Jan Sundquist, Justo Lorenzo Bermejo, Tumor location and patient characteristics of colon and rectal adenocarcinomas in relation to survival and TNM classes, BMC Cancer 2010, 10:68

Stage, TNM

In the case of CC, relatively few tumors were identified in T1, T2 stage, most being T3 or T4. Node status N0 was identified in 38,12% of cases, majority. It should be mentioned that the dissection and identification of the lymph nodes on the postoperative specimen was done by the Histopathology Department. Similarly, in the case of RC most were T3 tumors and N1 status were predominant.

In this retrospective group, we detected 234 patients with stage IV. Of these, 87 patients with rectal cancer had distant metastases (18,85 %) with a mean age of 62.33 (32-75 years), respectively 147 patients with colon cancer with distant metastases (16,33 %) with mean age of 65.77 (36-91 years). There were few cases of young patients (under 55 years old or younger) whose first presentation in the Clinic detected the presence of secondary hepatic metastases concomitantly with the CRC diagnosis. Most commonly we found hepatic localization (100%), preoperatively detected by imaging investigations and / or an intraoperative identification, followed by pulmonary localization (M2, 4 cases), ovary (M2, 2 cases), bone (M2 vertebral, 1 case). Over 50% of cases with secondary hepatic metastases showed peritoneal carcinomatosis +/- ascites.

CRC in emergency

The patient admission for CRC can be precipitated by obstruction, perforation and, less often, by bleeding. For right colon tumors, right hemicolectomy or bypass may be taken into consideration, and for left and right colon tumors, external derivation along with stenting, represents alternatives, depending on the particularities of the case. Stenting is recommended by many authors, as a first step of therapeutic approach, due to the decreased morbidity and mortality associated with an emergency colonic intervention. The technical success of the stenting was reported at 89-96%, and the clinical success at 85-92%. The mortality related to the procedure is about 1.5%, and the complications can be stent migration (4.4-11.8%), perforation (2.5-4.55) and obstruction (7.3-12%)¹⁷.

In the retrospective study less than 5% of patients were admitted in an emergency complication. The causes of the sudden emergency hospitalization in colonic cancers were intestinal occlusion (3.69%), in decreasing order of frequency of localization, in the rectosigmoid, ascending colon, followed by transverse and caecum. For rectal cancer, occlusive phenomena at admission and emergency surgical intervention occurred in 4.06% of cases. There have also been cases of tumor perforation with localized or generalized peritonitis (caecum, splenic angle, descending and ascending colon) as well as a patient with pelvic abscess in the case of a large, superinfected, neglected rectal tumor.

We have observed frequently that occlusive phenomena were manifestations at admission and indication for emergency intervention in patients with local recurrence, especially in RC and those with PC.

We did not identify cases of severe bleeding in the studied group that required emergency surgery, possibly due to the fact that Dr. I. Cantacuzino Hospital did not have an emergency surgical or interventional endoscopy department at that time.

Postoperative complications

We chose to evaluate the postoperative complications, according to the Clavien-Dindo classification, excluding those of the first and second grade, without a major impact on

¹⁷ Katsanos K, Sabharwal T, Adam A, Stenting of the Lower Gastrointestinal Tract: Current Status Cardiovasc Intervent Radiol 2010, Jun;34(3):462-73

the subsequent evolution. For colon cancer degree III b, IV complication (total 7.16%) were, as follow: anastomotic leak with peritonitis (3.69%), postoperative bleeding or hematoma, postoperative paralytic occlusion (1.61%), evisceration, acute mesenteric ischemia (2 cases, one requiring total colectomy). Two cases of grade V complications: a case of transverse segmental colectomy with anastomotic fistula and a subphrenic abscess in a right hemicolectomy case.

Anastomotic leak was the most frequent complication, the other postoperative complication occurred in a smaller percentage, several cases in each group, including the wound infection that required surgery under general anesthesia; the deaths occurred during the same hospitalization, postoperatively, after subsequent surgeries, in patients with multiple comorbidities.

For the rectal cancer according to the same classification we found in 9.13% of the patients operated, complications III b and IV degree: postoperative paralytic occlusion (the most common reason for early postoperative reintervention), few cases of postoperative bleeding at the rectal operative site, segmental intestinal necrosis, anastomosis necrosis, evisceration, perineal cellulitis, localized or generalized peritonitis, enteral fistulas.

Recurrence

Depending on the locations and the dedicated surgery, the recurrence in the CC were located as follows: sigmoid/rectosigmoid (13.42%), hepatic angle (7.69%), descending colon (7.14%), caecum-ascending colon (5.56%). The overall recurrence in the group with patients (CC) operated between 2002-2014 was 8.45% in a time interval of 1 to 7 years after the intervention with the curative intention.

The recurrence observed during the studied time of RC was 10.74% (1 to 7 years). Several authors have observed that the risk of recurrence increases as the tumor is located more distally, especially, below the level of peritoneal segment¹⁸.

Different patient related factors - demographic, clinical, histopathological and outcomes are summarize in the tables 1, 2.

¹⁸ Berrino F, De Angelis R, Sant M, Rosso S, Bielska-LasotamM, Coebergh JW, Santaquilani M, Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EURO CARE-4 study, Lancet Oncol. 2007; 8:773-783; Alan White, Lucy Ironmonger, Robert JC Steele, Nick Ormiston-Smith, Carina Crowford, Amanda Seims, A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK, December 2018, BMC Cancer 18: 906; Lan YT, Chang SC, Yang SH, Lin CC, Wang HS, Jiang JK, Chen WS, Lin TC, Chiou SH, Lin JK, Comparison of clinicopathological characteristics and prognosis between early and late recurrence after curative surgery for colorectal cancer, Am J Surg. 2014 Jun;207(6):922-30

Age and gender	Male Average 61.23 (min=32; max=89) 14.4 % < 50 years	
	Female Average 59.7 (min=43; max=89) 8.3 % < 50 years	
Distribution of tumors	Upper rectum	37.75 % (173)
	Lower rectum	52.55 % (241)
	Anorectal	9.69 % (44)
Tumor (T) status	T1	1.64 % (8)
	T2	25.41% (115)
	T3	46.72 % (213)
	T4	27.05 % (123)
Node (N) status	N0	29.93 % (138)
	N1	40.27 % (185)
	N2	29.71 % (136)
Stage	I	13.11 % (60)
	II	22.95 % (105)
	III	45.08 % (207)
	IV	18.85 % (87)
Recurrence	1 – 7 years	10.74 % (50)

Table 1. Patient related factors in RC

Age and gender	Male Average 67. 44 (min=30; max=92) 11.67 % < 50 years	
	Female Average 67.21 (min=22; max=91) 11.41 % < 50 years	
Distribution of tumors	Sigmoid/rectosigmoid	42 % (378)
	Caecum, ascending colon	28 % (252)
	Descending colon	9 % (81)
	Transverse colon	8 % (72)
	Hepatic angle	7 % (63)
	Splenic angle	6 % (54)
Tumor (T) status	T1	2.03 % (19)
	T2	13.00% (117)
	T3	48.37 % (438)
	T4	35.78 % (326)
Node (N) status	N0	38.12 % (343)
	N1	33,12 % (298)
	N2	28.78 % (259)
Stage	I	11 % (99)
	II	27 % (243)
	III	45.67 % (411)
	IV	16.33 % (147)
Recurrence	Sigmoid/rectosigmoid	13.42 %
	Hepatic angle	7.69 %
	Descending colon	7.14 %
	Caecum, ascending colon	5.56 %

Table 2. Patient related factors in CC

CONCLUSION

The average number of interventions performed on colon and rectum for neoplastic disease were in increasing number until the study end (from 2.85% to 5.28%), according to increasing prevalence. In terms of distributions of colon tumors, we noticed the preponderance at the level of the sigmoid/rectosigmoid junction, followed by the localization at the caecum or ascending colon. The distribution of neoplasia in the rectum showed that majority of the tumors develop in lower part, followed by those in the superior segment. There are still many young patients, especially men, with stage III, IV CRC tumors, despite numerous screening programs and awareness campaigns. The causes of the sudden emergency hospitalization in colonic cancers were intestinal occlusion. Anastomotic leak was the most frequent complication, the other postoperative complication occurred in a smaller percentage. The recurrence rate observed during the studied time for both, CC and RC, are still high.

CONFLICTS OF INTEREST

Authors declare no conflict of interest in relation to our study and the publication of this article. No financial support has been received for this work.

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The risk of subsequent primary cancers after colorectal cancer in southeast England, *Gut.* 2002 May; 50(5): 647–652.
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ACUTE DIARRHEA WITH ROTAVIRUS IN CHILDREN

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ABSTRACT:

ROTAVIRUS DIARRHEA IS A REALITY PRESENT IN PEDIATRIC CASES, OF THE HIGHEST ACTUALITY. THE MORE SEVERE EVOLUTION OF THE DISEASE IN INFANTS MAKES THIS AGE GROUP VERY VULNERABLE TO EVENTUAL HOSPITALIZATION.

INCREASING INFORMATION AND INCREASING ADHERENCE TO VACCINATION IS THE SOLUTION TO REDUCING OR ELIMINATING DISEASE-CAUSING DEATHS.

KEY WORDS: BABY, DIARRHEA, ROTAVIRUS

Rotavirus infection is the most common cause of severe acute diarrhea AD in infants and young children. In previous years, there have been reported worldwide 27,000-60000 child deaths to 125 million infected children. The introduction of vaccination, currently in the alternative scheme, not included in the National Mandatory Vaccination Program,

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significantly reduced the morbidity and mortality of the disease⁷. There is no longer so strict the fact that the diarrhea with rotavirus is important during the cold season⁸.

Etiologically, the agent discovered in 1973 in the stool and duodenal biopsy of children with diarrhea is an RNA virus of the Reoviride family, with 11 double-stranded segments.

The preferred place of confinement is at the level of the intestinal villi, where they invade and destroy the villi, then affecting both the digestion and the absorption process. This is the explanation for the installation of secondary lactose intolerance, usually self-limited for a period of 1-2 weeks.

The younger the child, the higher the severity of the infection (between 3 months and 2 years)⁹.

In infants, there is an increased likelihood of complications of AD with acute dehydration syndrome ADS due to rapid short-term hydroelectrolytic losses, relative to the total increased water content of the immature organism and body surface area. The apparition to diarrhea of vomiting, fever will accelerate the rate of loss of H₂O and electrolytes and thus the severity of the disease¹⁰.

Under 3 months the infants are protected by the transplacental antibodies transmitted and by the natural nutrition (the secretory piece "j" produced in the mammary gland connects 2 secretory IgA molecules with protective role, barrier in the digestive and respiratory mucous membranes).

Clinically the disease is manifested by: vomiting that occurs before diarrhea with 12-24 hours, fever, liquid diarrhea, colicative abdominal pain. Symptoms appear after an incubation period of up to 2 days after infection.

Infants and young children (under 2 years of age) may have febrile or seizure-related fever, associate with lethargy, torpor. The impossibility of oral rehydration at these ages will indicate hospitalization for the therapy administered iv.

Immunity after infection is durable for one serotype, the disease may occur for others, being known 7 types of rotavirus (A-G), based on the antigenic properties of VP6 protein. Groups A, B, C cause the disease in humans and the group A with serotypes G1-G4 and G9 are of the greatest clinical importance.

According to the WHO, around 2.4-2.5 million hospitalizations and over 500,000 deaths/year are reported worldwide in children under 5 years.

Diarrhea stools are frequent, liquid, explosive, acidic, with a discolored appearance, usually with a variable number of 8-20 stools/day. There are children with diarrhea of holeriform aspect with more than 30-40 stools/day, sometimes accompanied by bloody streaks, important erythema, even slightly rectal prolapse. There are also extradigestive signs: rhinorrhea, cough (in 20-50% of cases), otitis media (20%) or even rare cases have been reported: encephalitis, aseptic meningitis, pneumonia, myositis, polio-like paralysis,

⁷ Tate JE, Burton AH, Boschi-Pinto C, Parashar UD; World Health Organization–Coordinated Global Rotavirus Surveillance Network. Global, regional, and national estimates of rotavirus mortality in children <5 years of age, 2000–2013. *Clin Infect Dis*. 2016;62 Suppl 2:S96–105. doi: 10.1093/cid/civ1013

⁸ Dennehy PH. Rotavirus Infection: A Disease of the Past? *Infectious Disease Clin North America*. 2015;29(4):617–35

⁹ Penelope H, Dennehy M (2012) Rotavirus infection an update on management and prevention. *Advances in pediatric* 59: 47-74. Introduction to diarrhea (2014) *Integrated Management Of Childhood Illness (ICMI)*; module 4. Switzerland, Publications of the World Health Organization, pp. 7-23

¹⁰ Offit PA, Clark MF. Reoviruses. In: Mandell GL, Bennett JE, Dolin R., editors. *Principles and Practice of Infectious Diseases*. 5th. Philadelphia, Pa, USA: Churchill Livingstone; 2000: 1696–1703. Farthing M, Linberg G, Dite P, Khalif I, Lindo ES, Ramakrishna BS, et al. Acute diarrhea. *WGO practice guidelines*; 2008. p. 1-28

hemophagocytic lymphohistiocytosis, hepatitis (in the immunodeficient child). In the severe forms of the disease the existence of viremia has been demonstrated.

Immediate complications of the disease, which indicate, in fact, and hospitalization are: dehydration, hydroelectrolytic disorders, metabolic acidosis, nutritional deficiency.

In rare cases, severe, life-threatening complications may occur: intestinal occlusion, gastric rupture, central pontine myelosis.

The death can occur both due to the complications that have arisen and due to the patient's pre-existing terrain (for example, immunocompromised with increased chances of sudden evolution and death).

The paraclinical diagnostic test, which accurately establishes the disease, is an antigen test, found in the faeces of the patients. Laboratory diagnostic kits based on agglutination latex or enzyme-like immunoabsorbent assays are used.

They are fast, reliable, with sensitivity and specificity 90%.

Blood tests (CBC test, serum ionogram), show hemoconcentration, hydroelectrolytic changes associated with ADS.

TREATMENT

The etiological diagnosis is important for the adoption of relevant therapeutic behavior. Viral infection contraindicates antibiotic therapy.

Hydration of the patient (oral or IV in severe forms), correction of hydrolytic electrolyte disorders (of hyponatremia, hypocalcemia, hypernatremia with convulsive potential) and correction of hypoglycemia are indicated. In case of metabolic acidosis, ORS with bicarbonate or citrate is supplemented (where possible). In severe forms iv molar solution of bicarbonate is administered. Oral hydration depends on many factors: age of the patient, oral tolerability, severity of the disease, individual association of symptoms (ex vomiting + diarrhea + fever). In infants it can be achieved with difficulty. As a general indication, in infants and young children, in children who do not have vomiting and ADS, it is recommended to continue the age-appropriate diet. Breastfeeding will not be discontinued and, in the case of those with frequent liquid stools and artificial feeding, delactose formulas are recommended, knowing the predilection of viral cantonation at the intestinal brush border, affecting lactase (an enzyme that aids lactose digestion)¹¹. Antidiarrheal cereals (rice), dietary preparations (carrots, redcurrants) are indicated. In order to prevent ADS in patients at high risk, the diet will be supplemented with oral rehydration solutions in the form of standardized preparations (Hipp ORS 200, Sun-lyte, Adrehyll etc) in amounts of 2 ml/kg for any stool emitted. In the first 4 hours, 50-100ml/kg of rehydration solutions are usually administered and, if the child's condition improves, the previous diet can be used.

Children with severe ADS (5%) cannot receive oral rehydration solutions due to incoercible vomiting, ileus, abdominal meteorism, lethargy, and is recommended hospitalization and IV administration of medication¹².

The stepping of the therapeutic gestures is the following:

- establishing the venous approach (even epicranial need)
- combating metabolic acidosis with 8.3% NaHCO₃ molar solution according to the ionogram or empirically 1-2 mEq / kg dissolved 1/2-1/3 in glucose solution.

¹¹ Hartling L, Bellemare S, Wiebe N, Russell K, Klassen TP, Craig W. Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. Cochrane Database Syst Rev. 2006;3:CD004390

¹² Hahn S, Kim S, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children. Cochrane Database Syst Rev. 2002;1:CD002847

- administration of infusion solutions (physiological serum, Ringer's lactate solution), thus $\frac{1}{2}$ of the amount needed in the first 4 hours and then $\frac{1}{2}$ in the remaining 20 hours, to which are added the subsequent losses.
- oral rehydration therapy after a maximum of 24 hours.
- diet

It is desirable, as in any diarrhea, it is the fastest realimentation and the current recommendations exclude transitional deficient diets (carrot, rice, soups, bananas) and it is recommended to return to the previous complete nutrition according to age, without restrictions¹³.

The use of antiemetics (metoclopramide) may cause secondary sedation of the child, preventing proper oral rehydration, due to the dopaminergic antagonist mechanism. Ondansetron can be indicated in cases with incoercible vomiting, being well tolerated. Antidiarrheal - racecadotril (Hidrasec) or diosmectite (Smecta) have a positive effect on AD. Probiotics modulate the immune response and compete competitively on viral attachment loci (*Lactobacillus reuteri* or *Sacharomyces boulardii*).

A statistic, compared over a period of 3 years for patients consulted in an outpatient department shows a decrease in rotavirus disease with the correct establishment of vaccine prevention¹⁴.

Good parent information through all possible sources will increase vaccination adherence. A serious impediment is the age at which vaccination is recommended (3-6 months) with 2 doses of oral vaccine.

The annual statistics for outpatient patients look like this:

- 2017-2022 of which AD = 521
- 2018-2328 of which AD = 501
- 2019-3018 of which AD = 511 (Fig 1)

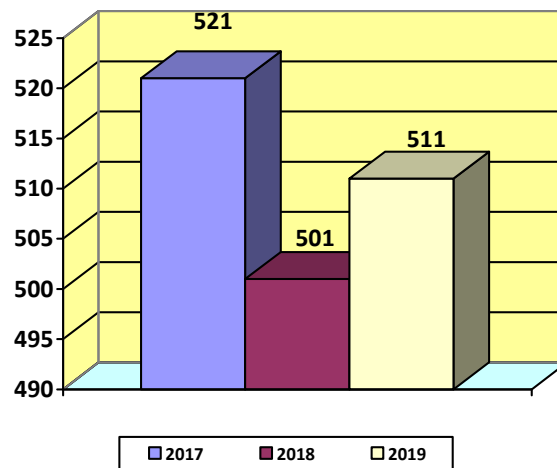


Fig 1 Annual outpatient number

¹³ Nelson EA, Ko WK, Kwan E, Leung SF, Poon KH, Chow CB, et al. Guidelines for the management of acute diarrhoea in young children. Hong Kong J Paediatr. 2003;8:203–36

¹⁴ do Carmo GM, Yen C, Cortes J, Siqueira AA, de Oliveira WK, Cortez-Escalante JJ, et al. Decline in diarrhea mortality and admissions after routine childhood rotavirus immunization in Brazil: a time-series analysis. PLoS Med 2011; 8:1001024; PMID:21526228; <http://dx.doi.org/10.1371/journal.pmed.1001024>; Richardson V, Hernandez-Pichardo J, Quintanar-SolaresM, et al. Effect of rotavirus vaccination on death from childhood diarrhea in Mexico. N Engl J Med. 2010;362(4):299-305. doi:10.1056/NEJMoa0905211

Virological tests and stool cultures were performed in all patients with AD and confirmed with rotavirus:

- 2017-203
- 2018-198
- 2019-171

The percentages are 38.96% (2017), 37.52 (2018), and 33.46 (2019). (Fig 2)

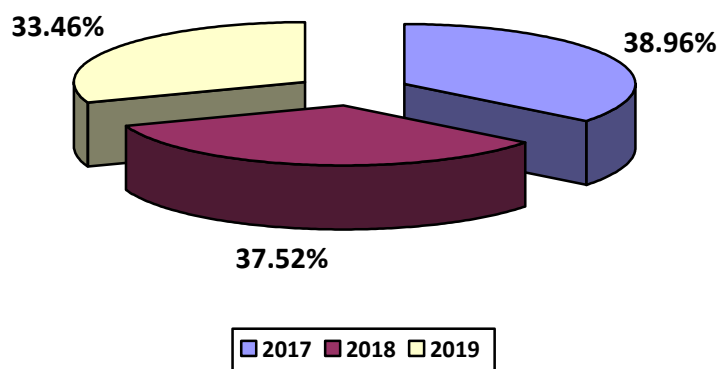


Fig 2. Cases confirmed by stool cultures

There were 71 children hospitalized in 2017 (34.97%), 62 in 2018 (32.97%) and 51 in 2019 (29.82%), which leads us to conclude that severe forms of disease have diminished.(Fig 3)

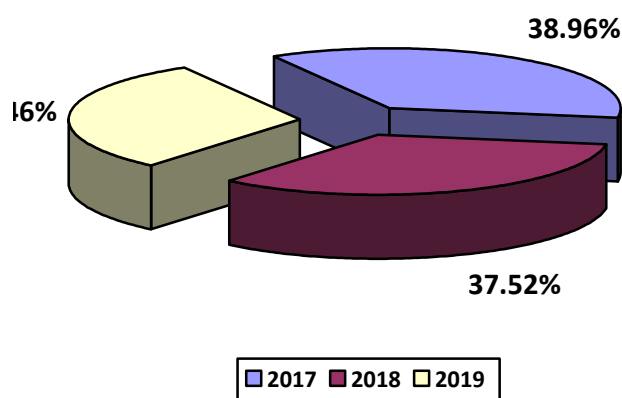


Fig 3 Hospitalized children (%)

Secondary lactose intolerance was noted in some cases, in 2018 - 15 cases and in 2019- 9 cases, requiring an extended diet with lactose milk. The mortality of cases with diarrhea during the 3 years was 0. (Fig 4)

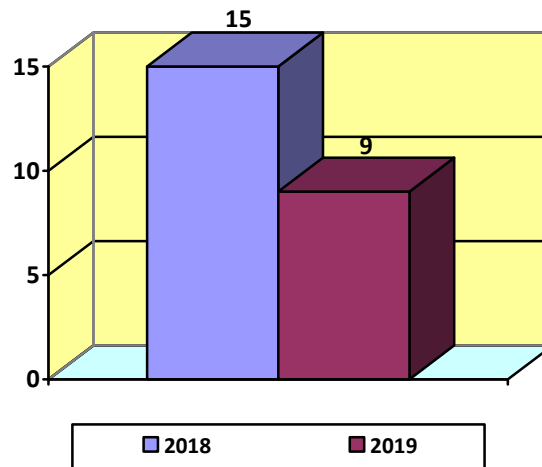


Fig 4 Patients with secondary lactose intolerance

All hospitalized patients were 3 months to 19 months of age.

IN CONCLUSION:

- rotavirus diarrhea is still a common condition in pediatrics
- it is even more severe as the younger age.
- there has been a decrease in the number of cases in the last 3 years
- there is a direct correlation between the severity of the disease, the young age and the need for hospitalization
- the reduction in the number of cases is due to the increased compliance with the specific vaccination
- lactose intolerance remains a possible complication
- oral rehydration gave results in the outpatient setting
- the specific diagnosis (virological tests) is absolutely necessary to avoid "traps" of therapy (eg antibiotics).

ACKNOWLEDGEMENTS

All authors equally contributed in the research and drafting of this paper.

All authors report no potential conflict of interest.

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SHAKEN BABY SYNDROME, A CONCRETE PRESENCE

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ABSTRACT:

A SHAKEN BABY IS A POSSIBLE MORE COMMON PEDIATRIC CONDITION THAN IS NORMALLY DIAGNOSED. IT IS NOT SO IMPORTANT TO ESTABLISH THE DIAGNOSIS, BECAUSE ONCE THE BRAIN DISORDERS ARE FORMED, THEY ARE IRREVERSIBLE, AS WELL AS HIGHLIGHTING POSSIBLE ALARM SIGNS THAT WOULD HELP PREVENT THE SYNDROME.

IN THIS SENSE, A SERIES OF QUESTIONNAIRES THAT COULD ASSESS THE FAMILY'S PREDISPOSITION TO APPLY SOME SUDDEN MOVEMENTS TO THE CHILD, WOULD PROVE TO BE LIFE SAVERS.

KEY WORDS: CHILD, SHAKEN, SYNDROME, BRAIN INJURY.

There have been several synonyms that describe the same entity as being practically a syndrome based on morphopathological changes following the shaken of a baby. It is also known as shaken, shaken or "shaken baby syndrome" (SBS).

It is not necessarily a recently diagnosed disease, the first descriptions dating back to 1970 when 2 doctors (a radiologist and a neurosurgeon) described a severe alteration of the brain, retina, ribs and limbs due to sudden movements exerted on or shaking their infants. The worldwide incidence is almost 10,000 cases, with mortality reaching 30%. The predilection age is 6-12 months, not being totally excluded until the age of 5-6 years⁶.

The explanations of the appearance of the pathophysiological and morphopathological changes (examined in the deceased) are various:

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⁶ Caffey, John (October 1974). "The Whiplash Shaken Infant Syndrome: Manual Shaking by the Extremities with Whiplash-Induced Intracranial and Intraocular Bleedings, Linked with Residual Permanent Brain Damage and Mental Retardation". *Pediatrics*. 54 (4): 396–403. PMID 4416579. Archived from the original on 2010-03-13. Retrieved 2011-04-30; Lure Al. Shaken infant syndrome. *Lancet* 2001; 357 (9263): 1207

- the baby's brain is immature (as all organ systems), it can move in the same time with the movements of the skull, it can undergo rapid acceleration and deceleration when encountering a resistance (recoil effect), by hitting the inner walls of the cranial box.
- the total head / length ratio in infants is $\frac{1}{4}$ (compared to $\frac{1}{10}$ in the big child) the neck musculature is insufficiently developed and may result in limitations of head movements during violence.
- In the same immature brain, the cerebral vessels, as well as the immature and the fragile ones, suffer easily ruptures, with the appearance of epidural or subdural hematomas that, by the strictly exercised mechanical effect, produce the compression of the brain tissue⁷.

The consequences of these changes of normal anatomical structure are: seizures, coma, loss of consciousness, cardiorespiratory arrest (by direct action on the brain centers). There may also be: bone fractures (ribs, upper limbs, usually, but also lower), retinal hemorrhages, loss of visual acuity. The shaken baby's syndrome is a form of abuse exerted on the baby and practitioners should be trained to recognize signs and symptoms such as: inability, drowsiness, irritability, vomiting, bruising, breathing difficulties (dyspnea sine materia) or abnormal respiratory rhythms (Küssmaul breathing), fractures of the ribs, limbs, paralysis, convulsions, retinal hemorrhages, blindness. If anamnestic is related to bad habits in the family (increased nervousness, other members' suddenness, noise intolerance, baby's sleep by swinging on his feet) the syndrome can be suspected relatively easily. Sometimes a child with a disability is seen by a doctor, and a diagnosis can be difficult to determine. If the changes in the structure and function of the child appear suddenly, the careful anamnestic investigation is required⁸. (Fig 1)

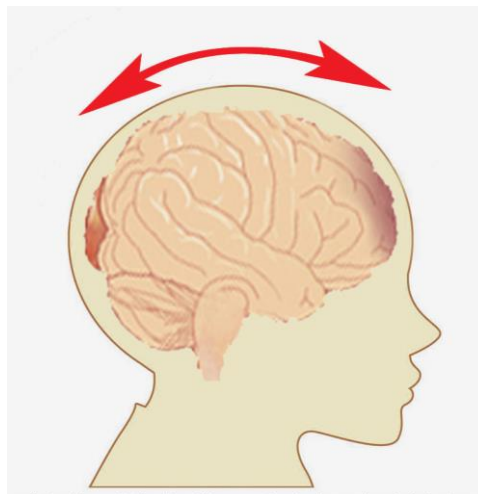


Fig 1 Shaken Baby Syndrome

⁷ Stewart TC, Polgar D, Gilliland J, et al. Shaken baby syndrome and a triple-dose strategy for its prevention. *J Trauma* 2011;71(6):1801–1807

⁸ David TJ. Shaken baby (shaken impact) syndrome: non-accidental head injury in infancy. *J R Soc Med* 1999;92(11):556–561

Complications are: seizures, paralysis, sight and hearing disorders (up to total loss), psychomotor retardation, behavioral disorders⁹.

The recognition of the syndrome requires compulsory hospitalization and emergency treatment through surgical techniques (stopping active cerebral hemorrhage), intubation and assisted ventilation. The magnitude of the changes made is determined by:

- X-ray (skull, spine, ribs, limbs)
- haematological examinations (eg post-hemorrhagic anemia)
- CT
- RMI
- ophthalmologic test
- audiometry

Not the treatment but the prevention of the syndrome will be defining for the evolution of the baby because a child who has survived the syndrome will no longer be normally developed but will have permanent sequelae¹⁰.

We recommend several measures for the family:

- hours of pre- and postnatal counseling, regarding the physiology of the baby, its handling, the necessary care
- parents should be informed about the syndrome
- the baby's crying should not be turned into a stress factor for the adults in the family, considering it to be a normal phenomenon.
- colic will have to be recognized and calmed correctly (position, massage, anti-alcoholic preparations, proper rhythm of meals)
- ventilation of the baby's room, outdoor walk, evening bath, quietly music, calms the child and relieves the anxieties of the surrounding adults.
- the mother does not have to neglect herself in order not to become nervous and frustrated.
- Tired or nervous adults should not be allowed to care for infants.

Starting from the description of the symptoms and the consequences of the syndrome, we tried to carry out questionnaires by interrogating for a period of 12 months all the parents of infants between 5-12 months to detect the possible risk that the respective child could ever suffer from SBS.

468 parents from all social backgrounds entered the study.

Regarding SBS, there are no noticeable differences between the environment of origin of the respective families. Moreover, it seems that the urban environment and the high socioeconomic level, together with the tendencies towards perfectionism of the parents, would increase the SBS risk.

The questions used are:

1. Is the child a stressor?
2. Has my mother experience postpartum mental changes?

⁹ Al-Saadoon M, Elnour IB, Ganesh A. Shaken baby syndrome as a form of abusive head trauma. Sultan Qaboos Univ Med J 2011;11(3):322–327

¹⁰ Oehmichen M, Schleiss D, Pedal I, et al. Shaken baby syndrome: re-examination of diffuse axonal injury as cause of death. Acta Neuropathol 2008;116(3):317–329; Balci E, Gun I, Mutlu Sarli S, et al. Still an unknown topic: child abuse and “shaken baby syndrome”. Ulus Travma Acil Cerrahi Derg 2011;17(5):430–434; Ettaro L, Berger RP, Songer T. Abusive head trauma in young children: characteristics and medical charges in a hospitalized population. Child Abuse Negl 2004;28(10):1099–1111

3. Is there alcohol in the family?
4. Is it a traditional family or another type of family structure?
5. What is the socio-cultural level of the parents?
6. Is the child permanently cared for by 1-2 people?
7. There are additional stressors (unemployment, divorce, family deaths, diseases of other family members)
8. Are parents informed about the baby's colic?
9. What measures of soothing do you use?
10. How does the baby sleep(swinging)?

A score above 5 on this questionnaire was associated with an increased risk of SBS onset.

Of the 468 infants studied, 254 were from urban areas and 214 were from rural areas.(Fig 2)

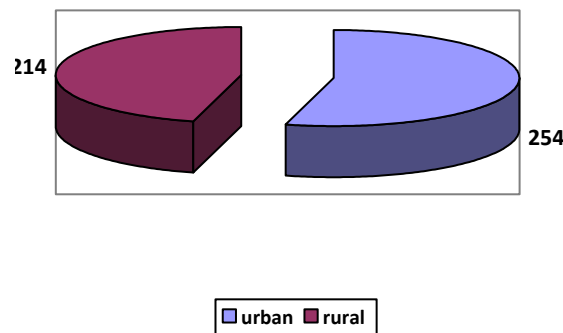


Fig 2 Residential areas

The distribution by series was in favor of the boys and in the rural area, and in the urban:187 (urban area) - 73.6% and 113 (rural area) - 52.8%.(Fig 3)

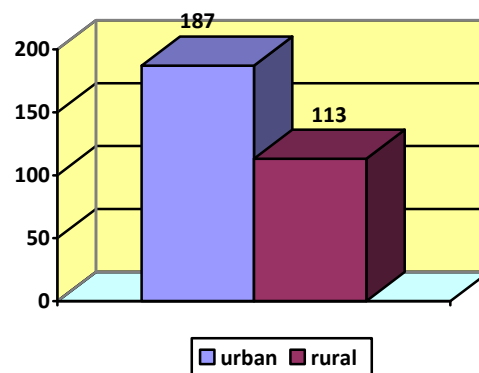


Fig 3 Boys distribution

Regarding the degree of education of the parents, they presented: higher education: 17 in rural and 93 in urban, high school 45 - in rural and 102 in urban, gymnasium 73 in rural

and 41 in urban, primary classes 52, rural and 11 urban the degree of illiteracy was 25 in the rural area and 7 in the urban area. (Fig 4)

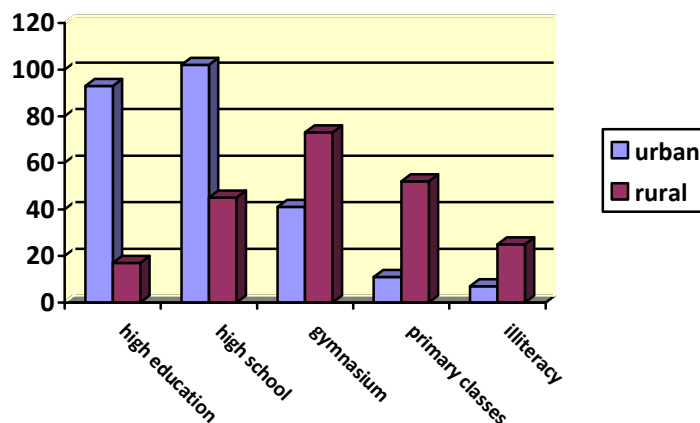


Fig 4 The degree of education of the parents

When applying questionnaires to parents' education groups, the results obtained were somewhat surprising.

The illiterate parents obtained predisposing data to SBS in 5 parents from rural (20%) and 2 from urban (28.5%).

In the group with higher studies, in 2 rural families (11.76%) a possible tendency was observed for the aggression of the child and in about 18 families in the urban area (19.3%) directly correlating with the stress and pressure level felt by parents.

For those with high school studies 5 out of 45 obtained a score of 6 in questionnaires (11.11%) and 21 in urban areas (20.58%). The almost double percentage in the urban environment was directly correlated with the social pressure felt, the frustration of the restriction of the activity with the appearance of the child, the service often in shifts of the second parent, the lack of communication and help, the big expenses, etc.

These things are not described or are of lesser importance in rural areas.

On the group with the graduated gymnasium, suggestive questionnaires were for 24 families from rural (32.8%) and 18 from urban (43.9%).

Lack of education, alcoholism, financial difficulties are better reflected in the city where the attractions are great, the ways to spend money are multiple, the comparisons work in the negative sense and the young families have no convenient help.

In the rural area, where the patriarchal society still thrives, with more families in the same area, even the same home, the degree of fatigue and frustration of the young parents is diluted, by the participation of other relatives in the child's upbringing.

In the case of those who graduated the primary classes, usually without jobs, and a precarious economic situation, the questionnaires were positive in 7 families from rural (13.46%) and 1 from urban (9.09%). In this case there are 2 interpretative possibilities: either the questions were not correctly understood and the answer is wrong, or, in large part, the children were neglected, deprived of the presence of the family, forgotten, so not physically traumatized at the age of infants, when it was realized the study.

IN CONCLUSION:

- SBS is a reality that we cannot deny, the possibility of occurrence in infants is significant.
- The environment and the education of the family can offer surprises: SBS seems to be correlated with the level of stress felt, rather than with the education, the educated families can escalate moments of anger, applied to the child.
- Information is very important due to the serious, irrecoverable consequences of SBS.
- The application of questionnaires showing the degree of risk for SBS could prevent the occurrence of consequences through the education of families, the using of psychological counseling and meetings, possibly doubled by the visualization of images with impact on the possible aggressors.
- There is the possibility of underdiagnosis of SBS in practice, often without making a clear parallelism between the possible sequelae (paralysis, blindness, deafness, psychomotor retardation) observed at an objective consultation of the baby and the existence of traumas which determine SBS.

ACKNOWLEDGEMENTS

All authors equally contributed in the research and drafting of this paper.
All authors report no potential conflict of interest.

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EARLY FLUID REPLACEMENT IN BOWEL OBSTRUCTION - EFFECTS ON MORTALITY

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ABSTRACT:

ACUTE INTESTINAL OBSTRUCTION OCCURS WHENEVER THERE IS ANY INTERRUPTION IN THE NORMAL FLOW OF INTESTINAL CONTENTS. MANAGEMENT OF INTESTINAL OBSTRUCTION IS AIMED TO PRIMARILY CORRECT THE PHYSIOPATHOLOGIC CHANGES CAUSED BY THE OBSTRUCTION ITSELF AND THEN, IF POSSIBLE, REMOVING THE SOURCE OF OBSTRUCTION. THE FORMER THERAPEUTIC ACTION IS ACCOMPLISHED BY INTRAVENOUS FLUID RESUSCITATION WITH INTRAVASCULAR ISOTONIC FLUIDS. EARLY FLUID REPLACEMENT PROVED AN IMPORTANT FACTOR TO REDUCE POSTOPERATIVE MORTALITY, ESPECIALLY IN THE ELDERLY. CRYSTALLOID SOLUTIONS SEEM TO BE THE BEST OPTION FOR VOLEMIC INITIAL RESUSCITATION.

KEY WORDS: FLUID REPLACEMENT, FLUID RESUSCITATION, BOWEL OBSTRUCTION

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INTRODUCTION

Acute intestinal obstruction occurs whenever there is any interruption in the normal flow of intestinal contents. Management of intestinal obstruction is aimed to primarily correct the physiopathologic changes caused by the obstruction itself and then, if possible, removing the source of obstruction. The former therapeutic action is accomplished by intravenous fluid resuscitation with intravascular isotonic fluids. We can easily evaluate the efficiency of resuscitation by a minimum gesture, the use of a bladder catheter to closely monitor urine output. Monitoring central venous pressure on the venous catheter has also proven to be very useful in the certification of vascular refill. Loss of fluid is directly proportional to the time of evolution of occlusion and with age. Decompensations from fluid extravasation are more important in the elderly. Several studies investigated the effects of rapid water re-balancing on mortality and found that it was significantly reduced to the elderly group.

MAIN TEXT

Refluxing of the vascular bed has an important and immediate effect on vascular perfusion in the mesenteric area. It rapidly improves circulation in this territory, and ischemic phenomena diminish. The effect is all the more important in a territory with preexisting mesenteric ischemia (in generalized atherosclerosis). It is known that the intestinal wall can undergo irreversible ischemic changes within a few hours, and the most sensitive layer is mucous. Thus, a quick corrective intervention can have major positive effects.

In some experimental studies in animals with intestinal occlusion, vascular bed replenishment improved blood pressure, increased blood flow to the mesenteric territory and thus limited ischemic bowel lesions, especially in the mucosa¹⁰.

Over time, the studies of the pathophysiology of intestinal occlusions has been attempted. All the results converge to the balance of fluids, which plays the most important role in this pathology. At the origin of the fluid losses in the intestinal occlusion is the inflammation that occurs in the small bowel wall. In this context, the liquids extravasate into the intestinal lumen and into the peritoneal cavity, leaving the vascular bed¹¹. Vomiting also contributes to worsening dehydration. Also, the absorptive function of the intestine is abolished if the intestinal transit is stopped.

Bowel obstructions are some of the most frequent emergencies in general surgery, commonly affecting elderly patients. Morbidity and mortality from bowel obstruction in elderly are very high¹². In fact, any emergency surgery has high mortality and morbidity in elderly¹³.

Most common causes of bowel obstruction are tumors, hernias and adhesions, which are present in more than 90% of cases¹⁴. Adhesions resulting from previous operations are

¹⁰ Fevang, J; Øvrebø, K; Grong, K; Svanes, K. *Fluid resuscitation improves intestinal blood flow and reduces the mucosal damage associated with strangulation obstruction in pigs*. J Surg Res. 2004 Apr; 117(2): 187-94

¹¹ Nellgård, P; Cassuto, J. *Inflammation as a major cause of fluid losses in small-bowel obstruction*. Scand J Gastroenterol. 1993 Dec; 28(12): 1035-41

¹² Ozturk, E; van Iersel, M; Stommel, MM; Schoon, Y; Ten Broek, RR; van Goor, H. *Small bowel obstruction in the elderly: a plea for comprehensive acute geriatric care*. World J Emerg Surg. 2018 Oct 20; 13:48

¹³ Scott, JW; Olufajo, OA; Brat, GA; Rose, JA; Zogg, CK; Haider, AH; et al. *Use of national burden to define operative emergency general surgery*. JAMA surgery. 2016; 151(6):e160480

¹⁴ Constantin, Vlad; Carâp, Alexandru; Bobic, Simona; Păun, Ion; Brătilă, Elvira; Socea, Bogdan; Moroşanu, Ana-Maria; Mirancea, Nicolae; *Accurate diagnosis of sigmoid colon endometriosis by immunohistochemistry and transmission electron microscopy - a case report*. Chirurgia, 2015, 110(5): 482-485; Bobic, Simona; Socea, Bogdan; Bratu, Ovidiu Gabriel; Stanescu, AMA; Baleanu, Vlad Dumitru; Davitoiu, Dragos Virgil; Dimitriu,

responsible for approximately two thirds of small bowel obstructions¹⁵. Some operations have higher risks of adhesion forming: appendectomies, colorectal surgery, gynecologic procedures, incisional hernia repair. Obstructions secondary to neoplasm is more common in large bowel occlusion in elderly patients. Other rare causes include: inflammatory bowel disease, intestinal intussusception, volvulus, gallstones¹⁶.

Considering the extravasation of the liquids from the vessels and the hemoconcentration, it explains the renal insufficiency of prerenal cause and the thromboembolic accidents. In this respect, prophylactic anticoagulant treatment measures are justifiable¹⁷. Thromboembolic risks are even higher at elderly patients, as age is an independent risk factor. Thus, rehydration becomes more important. Since the absorptive function of the small bowel is ceased and nil per os is recommended as therapeutic measures (not even liquids), the vascular refill should be made by intravenous lane.

The risk of venous thrombembolism is greater in patients with cancer¹⁸.

Some clinical trials demonstrated the benefits of esophageal Doppler-guided fluid management in colorectal surgery, focusing mainly on elective bowel resection¹⁹.

On the other hand, fluid overload could become dangerous, especially for patients with cardiac problems²⁰. This is the reason why the methods that assess hydration are also very important.

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¹⁵ Taylor, MR; Lalani, N. *Adult small bowel obstruction*. Acad Emerg Med. 2013; 20(6): 528-544

¹⁶ Socea, B; Nica, AA; Bratu, OG; Diaconu, CC; Smaranda, AC; Socea, LI; Bertesteanu, SVG; Dimitriu, M; Carap, AC; Constantin, VD. *Incidental finding of a sigmoid intussusception associated with rectal prolapse – a case report*. Arch Balk Med Union, 2018, 53(1): 143-6; Spinu, D; Bratu, O; Popescu, R; Marcu, D; Radulescu, A; Mischianu, D. *Clostridium difficile-an emerging plague*. Romanian Journal of Military Medicine, 2015, 118(3): 12-15; Bobic, Simona; Socea, Bogdan; Diaconu, Camelia; Bratu, Ovidiu; Marcu, Dragoș; Manea, Maria; Bertesteanu, Șerban; Tenea Cojan, Tiberiu Stefanita; Băleanu, Vlad-Dumitru; Constantin, Vlad Denis. *The therapeutic management in colonic diverticular disease - a review*. Research and Science Today, 2018, suppl 2: 66-80; Socea, Bogdan; Dumitrescu, Dan; Bratu, Ovidiu Gabriel; Carap, Alexandru Constantin; Badiu, Dumitru Cristinel; Bolocan, Alexandra; Paduraru, Dan Nicolae; Mischianu, Dan; Constantin, Vlad Denis. *Inflammatory bowel diseases: the surgical perspective*. Modern Medicine, 2019, 26(1): 13-16; Mihalache, Daniel I.; Socea, Bogdan; Smaranda, Alexandru C.; Nica, Anca A.; Carap, Alexandru C.; Bratu, Ovidiu G.; Stanescu, Ana Maria A.; Groseanu, Florin; Dimitriu, Mihai C.T.; Constantin, Vlad D. *Surgical approach of infected mesh with entero-atmospheric fistula – a case presentation*. Archives of the Balkan Medical Union, 2019, 54(3): 591-595.

¹⁷ Safta, Andreea Nicoleta; Constantin, Vlad Denis; Socea, Laura-Ileana; Socea, Bogdan; *The efficiency of low molecular weight heparins in the prophylaxis of venous thromboembolic complications in general surgery*. Farmacia, 2012, 60(1): 127-137; Laslo, Crista L; Pantea Stoian, Anca; Socea, Bogdan; Paduraru, Dan N; Bodean, Oana; Socea, Laura I; Neagu, Tiberiu P; Stanescu, Ana Maria Alexandra; Marcu, Dragoș; Diaconu, Camelia C. *New oral anticoagulants and their reversal agents*. J Mind Med Sci. 2018; 5(2): 195-201.

¹⁸ Iorga, RA; Bratu, OG; Marcu, RD; Constantin, T; Mischianu, DLD; Socea, B; Gaman, MA; Diaconu, CC. *Venous thromboembolism in cancer patients: Still looking for answers*. Exp Ther Med. 2019 Dec; 18(6): 5026-5032

¹⁹ Mowatt, G; Houston, G; Hernández, R; et al. *Systematic review of the clinical effectiveness and cost-effectiveness of oesophageal Doppler monitoring in critically ill and high-risk surgical patients*. Health Technol Assess. 2009; 13: 1-95; Roy, N; Maw, A; Stuart-Smith, K. *Fluid optimization guided by oesophageal Doppler significantly improves bowel perfusion*. Br J Anaesth. 2011 Dec; 107(6): 1012-3.

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Point-of-care ultrasound (POCUS) has become widely used as a tool to help clinicians prescribe fluid therapy, especially in Intensive Care Units. Common POCUS applications that serve as guides to fluid administration rely on assessments of the inferior vena cava to estimate preload and lung ultrasound to identify the early presence of extravascular lung water and avoid fluid over-resuscitation²¹. Pulmonary ultrasound reveal the presence of multiple B lines in cases of fluid overloading²².

Following a complex ileus, it also appears a circulation disturbance to the intestine or mesenterium. All the toxins and acidic metabolic products which emerge from the necrotic intestine are transferred through the systemic circulation to the whole body, being at the origin of systemic shock. Patients with small bowel obstruction with strangulation are at a higher risk for serious morbidity and mortality due to ischemic bowel. From the early beginning, a primary metabolic acidosis develops. With the progression of acidosis, hyperkalemia may also associate. A sanguin pH lower than 7.25 (severe acidosis) indicates a very poor prognosis.

The main goals of fluid resuscitation in bowel obstruction include volemic expansion, maintenance of adequate tissue perfusion and oxygenation. According to recently published studies, crystalloid solutions seem to be the most appropriate for initial fluid resuscitation²³. In a systematic study, resuscitation with colloids was associated with an increased absolute risk of mortality of 4%²⁴.

Another methanalysis concludes that there is no evidence from randomised controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. As colloids are not associated with an improvement in survival and are considerably more expensive than crystalloids, it is hard to see how their continued use in clinical practice can be justified²⁵.

About 60-80% of adhesive small bowel obstruction cases resolve without a surgical treatment²⁶. It is very important, but sometimes hard to identify which patients could undergo

²¹ Lee, CW; Kory, PD; Arntfield, RT. *Development of a fluid resuscitation protocol using inferior vena cava and lung ultrasound*. J Crit Care. 2016 Feb; 31(1): 96-100

²² Constantin, V; Carap, AC; Zaharia, L; Bobic, S; Ciudin, A; Brătîlă, E; Vlădăreanu, V; Socea, B. *High correlation of lung ultrasound and chest X-ray after tube drainage in patients with primary spontaneous pneumothorax: can we omit X-rays for tube management?* Eur Surg, 2015, 47(4): 175-180

²³ Corrêa, TD; Rocha, LL; Pessoa, CM; Silva, E; de Assuncao, MS. *Fluid therapy for septic shock resuscitation: which fluid should be used?* Einstein (Sao Paulo). 2015 Jul-Sep; 13(3): 462-8

²⁴ Schierhout, G; Roberts, I. *Fluid resuscitation with colloid or crystalloid solutions in critically ill patients: a systematic review of randomised trials*. BMJ. 1998 Mar 28; 316(7136): 961-4

²⁵ Perel, P; Roberts, I; Ker, K. *Colloids versus crystalloids for fluid resuscitation in critically ill patients*. Cochrane Database Syst Rev. 2013 Feb 28; (2): CD000567

²⁶ Assenza, M; De Gruttola, I; Rossi, D; Castaldi, S; Falaschi, F; Giuliano, G. *Adhesions small bowel obstruction in emergency setting: conservative or operative treatment?* G Chir. 2016 Jul-Aug; 37(4): 145-149; Socea, Bogdan; Smaranda, Cristian A.; Nica, Anca A.; Carâp, Alexandru C.; Dimitriu, Mihai; Socea, Laura I.; Bratu, Ovidiu G.; Dumitrescu, Dan; Berteşteanu, Şerban V.G.; Constantin, Vlad D.. *Rare small bowel obstruction due to phytobezoar – Case presentation*. Archives of the Balkan Medical Union, 2017, 52(4): 458-461; Socea, Bogdan; Bratu, Ovidiu; Diaconu, Camelia; Socea, Laura I.; Dimitriu, Mihai; Carâp, Alexandru C.; Nica, Anca A.; Smaranda, Alexandru; Moculescu, Cezar E.; Băleanu, Vlad D.; Daviţoiu, Dragoş; Constantin, Vlad D. *Does colostomy restoration increase the risk of developing a subsequent rectal cancer?* Archives of the Balkan Medical Union, 2018, 53(3): 369-372; Socea, Bogdan; Smaranda, Alexandru C.; Nica, Anca A.; Bratu, Ovidiu G.; Diaconu, Camelia C.; Băleanu, Vlad D.; Moculescu, Cezar E.; Dimitriu, Mihai; Carâp, Alexandru C.; Bobic, Simona; Constantin, Vlad D. *Non-operative management of the sigmoid volvulus – case presentation*. Archives of the Balkan Medical Union, 2018, 53(4): 619-622; Socea, Bogdan; Smaranda, Alexandru C.; Nica, Anca A.; Bratu, Ovidiu G.; Diaconu, Camelia C.; Băleanu, Vlad D.; Daviţoiu, Dragoş V.; Dimitriu, Mihai;

a conservative treatment to prevent an useless surgery, with high anesthetic and surgery risks, like in elderly patients. Adequate hydration, starvation and decompression by a naso-gastric tube could be the only required measures in selected cases, that could by avoid an unnecessary intervention.

In the pathophysiology of occlusion, the correction of volemia leads to the correction of peripheral tissue perfusion. Glomerular filtration rate increases, which prevents renal failure, and furthermore prevents hepatic failure also²⁷. Increased infusion in the affected bowel (mesenteric territory) leads to a decrease in ischemic and inflammatory phenomena, which decreases the discharge of toxic degradation products into circulation, decreasing ileus and abdominal pressure²⁸ and interrupting the vicious circle.

By ensuring proper peripheral perfusion, maintaining blood pressure and renal function, vascular replenishment contributes to decreased morbidity and mortality, especially in elderly patients. By combating hemoconcentration, hydration prevents thromboembolic accidents²⁹.

CONCLUSIONS

Bowel occlusion is a debilitating condition that often requires surgical treatment. It is an emergency condition with high morbidity and mortality, especially in elderly patients. A majority of cases of small bowel obstruction of adhesive cause can be solved without surgical intervention that higher the risks. Adequate hydration, starvation and decompression can be salutary.

Intravascular hydration is a simple, easily reproducible and cheap therapeutic measure, but its effects on morbidity and mortality are important. Crystalloids seem to be the best option.

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²⁹ Draghici, T; Negreanu, L; Bratu, OG; Stoian, AP; Socea, B; Neagu, TP; Stanescu, AMA; Manuc, D; Diaconu, CC. *Paraneoplastic syndromes in digestive tumors: a review*. Rom Biotechnol Lett. 2019; 24(5): 813-819

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MODERN MANAGEMENT IN THE TREATMENT OF RENO-URETERAL CALCULI

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ABSTRACT:

THE PRESENT ARTICLE IS A REVIEW IN THE MODERN MANAGEMENT OF THE RENO-URETERAL CALCULI. SEPARATE REVIEWS OF THE LITERATURE AND GUIDELINES WERE PERFORMED FOR EACH SEGMENT OF THE RENAL SYSTEM, REGARDING ONE OF THE MOST COMMON PATHOLOGY OF THIS SYSTEM: STONES. MOST IMPORTANT, ALL OF THE RECOMMENDATIONS REGARDING THE TREATMENT OF THIS DISEASE WERE BASED ON THE GUIDELINES AND ON EXPERT REVIEW OF THE LITERATURE. WE COMPARED THE TREATMENT OUTCOME AND THE DIFFERENT TYPES OF TREATMENT FOR RENAL AND URETERAL STONES.

KEY WORDS: RENO-URETERAL CALCULI, PERCUTANEOUS NEPHROLITHOTOMY, ESWL, URETEROSCOPY

INTRODUCTION

One of the most common medical problems is represented by urinary calculus, with a prevalence of 2-3% in the general population. Almost 80% of all urinary calculi are represented by kidney stones. The most important aspect is the high recurrence risk, usually associated with metabolic abnormalities, malnutrition, and even environmental and dietary

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factors. The effect of the renal stones is represented by pain- the most common effect, followed by blood in the urine, infection, impaired renal function, and if left untreated even kidney failure⁹.

There are many factors to consider regarding the best therapeutic approach regarding the patients with renal or ureteral stones. We can group them in 4 categories:

1. Stone factors – were we consider the size, location and the composition of the stone;
2. Clinical factors – were we consider all the factors regarding the patient (symptoms, associated infections, the particularities of the patient, etc);
3. Anatomical factors¹⁰;
4. Technical factors – the available equipment for the treatment¹¹.

The best type of treatment must consider these factors, and of course the surgeon experience¹². Regarding the ureteral calculi, the standard treatment is extracorporeal shock wave lithotripsy (ESWL) and semirigid ureteroscopy (URSR) lithotripsy¹³. When the stones are located in the kidney, depending of the size of the stone, we can use besides URSR, flexible ureteroscope, PCNL, mini PCNL, or in some cases open or laparoscopic surgery¹⁴.

⁹ Diaconu, C., Balaceanu, A., Morosan, E. Sepsis biomarkers: past, present and future. *Farmacia*. 2015;63(6):811-815; Tiglis, M., Neagu, T.P., Elfara, M., Diaconu, C.C., Bratu, O.G., Vacaroiu, I.A., Grintescu, I.M. Nefopam and its role in modulating acute and chronic pain. *Rev Chim (Bucharest)*. 2018;69(10):2877-2880; Iorga, L., Anghel, R., Marcu, D., Spinu, D., Pantea Stoian, A., Diaconu, C., Bratila, E., Socea, B., Neagu, T.P., Mischianu, D., Bratu, O.G. Renal sarcoma – a rare parenchymal tumor with a very poor prognosis. *Arch Balk Med Union*. 2018;53(3):434-438; Radulescu, D., Balcangiu Stroescu, A., Pricop, C., Geavlete, B., Negrei, C., Bratu, O., Ginghina, O., Vacaroiu, I. Vitamin K influence on cardiovascular mortality in chronic hemodialysed patients. *Rev Chim (Bucharest)*, 2017; 68(1): 52-54; Niculae, A., Peride, I., Marinescu-Paninopol, A., Vrabie, C.D., Ginghina, O., Jecan, C.R., Bratu, O.G. Renal artery bilateral arteriosclerosis cause of resistant hypertension in hemodialysed patients. *Rom J Morphol Embryol*. 2016; 57(2): 591-594; Nechita, A.M., Radulescu, D., Peride, I., Niculae, A., Bratu, O., Ferechide, D., Ciocalteu, A., Checherita, I.A., Mischianu, D. Determining factors of diuresis in chronic kidney disease patients initiating hemodialysis. *Journal of Medicine and Life*, 2015; 8(3): 371-377; Checherita, I.A., Smarandache, D., Radulescu, D., Peride, I., Bratu, O., Ciocalteu, A., Sebe, I., Lascar, I. Calcific uremic arteriolopathy in hemodialyzed patients. *Chirurgia (Bucur)*. 2013; 108(5):736-740; Peride, I., Radulescu, D., Niculae, A., Ene, V., Bratu, O.G., Checherita, I.A. Value of ultrasound elastography in the diagnosis of native kidney fibrosis. *Med Ultrason*. 2016; 18(3): 362-369; Niculae, A., Peride, I., Vinereanu, V., Radulescu, D., Bratu, O.G., Geavlete, B.F., Checherita, I.A. Nephrotic syndrome secondary to amyloidosis in a patient with monoclonal gammopathy with renal significance (MGRS). *Rom J Morphol Embryol*. 2017; 58(3): 1065-1068;

¹⁰ Marcu, R.D., Spinu, A.D., Socea, B., Bodean, O.M., Diaconu, C.C., Vasilescu, F., Neagu, T.P., Bratu, O.G. Castleman's disease – clinical, histological and therapeutic features. *Rev Chim (Bucharest)*. 2018;69(4):823-830; Bratu, O.G., Cherciu, A.I., Bumbu, A., Lupu, S., Marcu, D.R., Ionita Radu, F., Manea, M., Furau, C., Diaconu, C.C., Mischianu, D. Retroperitoneal tumors – treatment and prognosis of tumor recurrence. *Rev Chim (Bucharest)*. 2019;70(1):191-194.

¹¹ Ordon, M., Andonian, S., Blew, B., Schuler, T., Chew, B., Pace, K.T. CUA Guideline: Management of ureteral calculi. *Can Urol Assoc J*. 2015;9(11-12):E837-51

¹² Seitz, C., Tanovic, E., Kikic, Z., et al. Impact of stone size, location, composition, impaction, and hydronephrosis on the efficacy of holmium:YAG-laser ureterolithotripsy. *Eur Urol*. 2007;52:1751-1757

¹³ Chaussy, C., Brendel, W., Schmiedt, E. Extracorporeally induced destruction of kidney stones by shock waves. *Lancet*. 1980;2:1265-1268

¹⁴ Socea, B., Nica, A.A., Bratu, O.G., Diaconu, C.C., Smaranda, A., Socea, L., Bertesteanu, S., Dimitriu, M., Carap, A., Constantin, V. Incidental finding of a sigmoid intussusception associated with rectal prolapse – a case report. *Arch Balk Med Union*. 2018;53(1):143-146

NON-INVASIVE TREATMENT

There is also medical expulsive therapy using α -adrenoceptor antagonists (alpha-blockers), usually reserved for small distal ureteral stones that are non-obstructive or partial obstructive¹⁵. The conservative management is not recommended when there are infectious symptoms, or the patient presents intolerable pain, or the normal kidney function is threatened. Numerous studies have showed that 95% of ureteral stones from 2 to 4 mm in size will pass spontaneously, even without symptoms. When the size reaches 5 mm or more, the probability of elimination drops to 50%¹⁶. A study included in the EAU and AUA showed a stone passage rate of 68% decreasing to 47% for stones 5 to 10 mm in diameter¹⁷.

ESWL

This procedure remains a first – line treatment not only in renal calculi, but also in proximal ureteral calculi, due to its non-invasiveness, and high rate of effectiveness. Many studies indicated that a shock wave rate of 2 shocks/second can improve stone fragmentation, especially if the stone is larger than 1 cm. The optimal number of shocks applied in one session has not been exactly established. For ureteral stones, where the renal parenchyma is safe, treatment can safely be carried out up to 4000 or more shocks¹⁸. For upper stones it is recommended to use between 2000 and 3500 shocks (it has to be correlated with the intensity of the shocks).

URETEROSCOPY

There are a few types of lithotripsy commonly used with similar results: pneumatic, electro-hydraulic and Holmium:YAG laser. Studies demonstrated that holmium laser has the best results in lithotripsy (shortens the operation time and increases the effectiveness). A meta-analysis revealed that for calculi in the proximal ureter, the stone-free rates are the same between the URSR and the ESWL. Most of the ureteral stones are treated using the semi-rigid ureteroscope, because it provides an excellent flow of water and a good size regarding the working channel. Flexible ureteroscope is more reliable because of its mobility. Usually a dilatation and access sheath is necessary.

A study performed by Jia-Sheng Hu et al, on a lot of 81 patients with upper ureteral calculi who underwent ureteroscope lithotripsy assisted by a guide sheath showed a stone clearance rate of 100%. From all of the patients, 63 were successfully treated with semirigid ureteroscope lithotripsy assisted by a ureteral access sheath, and 18 patients were successfully treated with flexible ureteroscope lithotripsy assisted by a guide sheath¹⁹. The guide sheath was necessary due to the local complication that a ureteral stone can produce: edema in the

¹⁵ Spinu, D.A., Marcu, R.D., Socea, B., Diaconu, C.C., Scarneciu, C., Bodean, O.M., Dragomirescu, R.I.F., Stanescu, A.M.A., Mischianu, D.L.D., Bratu, O.G. Ureteral JJ stents: which one is better? Rev Chim (Bucharest). 2018;69(8):2061-2063

¹⁶ De Sio, M., Autorino, R., Di Lorenzo, G., et al. Medical expulsive treatment of distal ureteral stones using tamsulosin: a single-center experience. J Endourol. 2006;20:12-16

¹⁷ Miller, O.F., Kane, C.J. Time to stone passage for observed ureteral calculi: A guide for patient education. J Urol. 1999;162:688-691

¹⁸ Preminger, G.M., Tiselius, H.G., Assimos, D.G., et al. 2007 Guideline for the management of ureteral calculi. J Urol. 2007;52:1610-1631; Rassweiler, J.J., Knoll, T., Kohrmann, K.U., et al. Shock wave technology and application: An update. Eur Urol. 2011;59:784-796

¹⁹ Hu, J.S., Xie, G.H., Yuan, H.S., Liu, G.L., et al. Guide sheath-assisted ureteroscope lithotripsy for upper ureteral calculi: An observational study on 81 cases. Exp Ther Med. 2018;16(4):3459-3463

ureteric wall, chronic inflammatory diseases and inflammatory polyps and embedded stones²⁰.

There are some cases where the ESWL and the URSR has its limitations due to large impacted upper ureteral calculi. It is well known that laser based flexible ureteroscope can be used to treat most of the ureteral stones with a clearance rate up to 97%, there are very expensive instruments that may require multiple treatment sessions, so their global utilization is limited²¹.

Laparoscopic ureterolithotomy is an advanced method of treatment regarding large impacted ureteral calculi and can be used in some selected cases, where the endoscope methods failed due to large stones, anatomic anomalies, etc. The advantage of this therapeutic method is its nearly 100% stone-free rate²².

Jae Duck Choi et al performed a study on a batch of 100 patients with large upper ureteral calculi on which he compared the complications, success rate, patient characteristics, and the operation time between two groups: the first group of 48 patients received transperitoneal laparoscopic ureterolithotomy, and the second group of 52 patients received a combination of ureteroscopic lithotripsy with retrograde intrarenal surgery. The stone-free rate after a single procedure was 100% in the first group and 73.1% in the second group²³.

PERCUTANEOUS NEPHROLITHOTOMY

PCNL is a lithotripsy technique reserved for renal stones of 2 cm or more. It has been demonstrated that it is a very efficient for treatment of large or staghorn pyelo-calyceal stones. This procedure can be performed with the patient in 2 positions: prone or supine, each of them with its advantages and disadvantages. This procedure requires the use of 2 imaging devices: a fluoroscope and a ultrasound machine. The biggest disadvantage of this procedure is one of its complications which is hemorrhage, that sometimes can be severe and can lead to the loss of the kidney. Over the years, with the development of technology, other types of instruments were created, thus appearing mini PCNL, ultra-m-PCNL, super m-PCNL and micro PNL, where the instruments are getting smaller and smaller, so the complication rate is also smaller.

Brian R. Matlaga et al made a systematic review and meta-analysis regarding the treatment of ureteral and renal stones, comparing the outcome of the patients with renal stones, treated by different methods: URSR, ESWL and PCNL. The study concluded that semirigid ureteroscopy performed on a stone located in the distal ureter has a 55% more chances of stone-free, than the treatment with the shockwave lithotripsy. Also, the need for a reoperation in patients who underwent URSR is less than those treated with ESWL. The study also concluded that the risk of complications is almost the same in both procedures. Of

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²¹ Jeong, B.C., Park, H.K., Byeon, S.S., et al. Retroperitoneal laparoscopic ureterolithotomy for upper ureter stones. J Korean MedSci. 2006;21:441-444

²² Bodean, O., Bratu, O., Munteanu, O., Marcu, D., Spinu, D.A., Socea, B., Diaconu, C., Cirstoiu, M. Iatrogenic injury of the low urinary tract in women undergoing pelvic surgical interventions. Arch Balk Med Union. 2018;53(2):281-284

²³ Choi, J.D., Seo, S.I., Kwon, J., Kim, B.S. Laparoscopic ureterolithotomy vs ureteroscopic lithotripsy for large ureteral stones. JSLS. 2019; 23(2): e2019.00008

course, the best results in distal ureteral stones and renal stones of 1,5 cm or more was obtained with the flexible ureterscope²⁴.

DISCUSSION

Reno-ureteral calculi have many possible treatments, which makes comparative efficacy assessment particularly important. In the literature there are two main therapeutic options regarding the large ureteral distal stones: ESWL and URSR. Many studies compare the 2 treatment methods with various results²⁵, thus the first line of treatment is still a controversial issue. The success of both procedures is based on the size and the location of the stone, but also on comorbidities²⁶. Regarding the medium and distal ureteral stones, URSR is the preferred approach, with the highest stone-free rate. ESWL is recommended as first-line treatment regarding renal and proximal ureteral stones, which are less accessible using a semi-rigid ureteroscope. A study performed by Verze et al, on 273 patients which he divided in 2 groups: ESWL and URSR, showed a 92,7% stone-free success rate in the ESWL group, compared with a 94,85 stone free success rate in the URSR group²⁷. The difference between the studies are strongly correlated with the type of lithotripsy used in URSR but also with the surgeons experience with the ESWL/URSR. One of the drawbacks regarding the ESWL is that there is a relatively low stone clearance rate and that sometimes multiple procedures are necessary for complete stone fragmentation²⁸.

Percutaneous nephrolithotomy and flexible ureteroscopy have better results regarding large renal stones, but they are more invasive and have a significant morbidity rate²⁹. One of its advantage is that is feasible and has a high success rate in one single step. Also, the risk of complications associated with this procedure can be significantly reduced by careful intra operative planning and by choosing the correct position for the patient. The surgeon must adapt his technique to the patient not the patient to his technique. One of the limitations and disadvantages of PCNL is its fairly higher morbidity rate, associated with complications as significant hemorrhage, sepsis and viscera trauma³⁰. Also, to reduce the risk of major

²⁴ Matlaga, B.R., Jansen, J.P., Meckley, L.M., Byrne, T.W., Lingeman, J.E. Treatment of ureteral and renal stones: a systematic review and meta-analysis of randomized, controlled trials. *J Urol.* 2012;188(1):130-137.

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²⁹ Diaconescu, D., Pantea Stoian, A., Socea, L., Stanescu, A.M.A., Iancu, M.A., Socea, B., Pituru, S., Bratu, O., Diaconu, C. Hepato-renal syndrome: a review. *Arch Balk Med Union.* 2018;53(2):239-245

³⁰ Tica, O.A., Tica, O., Antal, L., Hatos, A., Popescu, M.I., Pantea Stoian, A., Bratu, O.G., Gaman, M.A., Pituru, S.M., Diaconu, C.C. Modern oral anticoagulant treatment in patients with atrial fibrillation and heart failure: insights from the clinical practice. *Farmacia.* 2018;66(6):972-976; Laslo, C., Pantea Stoian, A., Socea, B., Paduraru, D., Bodean, O., Socea, L., Neagu, T.P., Stanescu, A.M.A., Marcu, D., Diaconu, C. New oral

bleeding mini-PCNL can be solid option, but also by obtaining a perfect access for PCNL (from the skin to the collecting system) the risk decreases.

Usually most of the ureteral calculi can be managed well by URSR and ESWL, but a number of impacted ureteral stone, larger than 15 mm, may require the use of a more invasive method of treatment (open or laparoscopic ureterolithotomy)³¹. In fact, laparoscopic ureterolithotomy has the highest rate of stone free in a single session. Of course its indication is reserved for complicated cases associated with infection, technical difficulties and in cases where modern endoscopic treatment has its limitation. Often patients can prefer a single laparoscopic approach for a big ureteral stone, rather than 2 or more intervention using endoscopic procedures which also requires several more anesthetics and more days spent in hospital³².

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OPEN VS LAPAROSCOPIC RADICAL PROSTATECTOMY

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ABSTRACT:

THERE ARE A FEW STUDIES WHICH LOOKED INTO THE OVERALL BENEFIT AND LONG TERM OUTCOME OF RADICAL OPEN PROSTATECTOMY VERSUS LAPAROSCOPIC PROSTATECTOMY, THE SECOND PROCEDURE BEING MORE AND MORE POPULAR WITH THE PATIENT BUT ALSO WITH THE UROLOGIST. THE PURPOSE OF THIS ARTICLE IS TO COMPARE THE BENEFITS TO THE PATIENT, THE ADVANTAGES AND DISADVANTAGES BETWEEN THIS TWO PROCEDURES REGARDING THE PROSTATE CANCER. IN MAKING THIS ARTICLE PUBMED DATABASE WAS RESEARCHED AMONG SPECIALTY LITERATURE.

KEY WORDS: PROSTATE CANCER, RADICAL PROSTATECTOMY, OPEN APPROACH, LAPAROSCOPIC APPROACH

INTRODUCTION

In recent years laparoscopic prostatectomy has increased in popularity for prostate cancer as first line of treatment. In fact in most surgical centers it took the place of the open retropubic prostatectomy. Recent studies demonstrated that laparoscopic prostatectomy has a

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lower chance of positive margins than the open procedure¹⁰. Also the expectation for the outcome are higher. Laparoscopic procedure has also its limitation regarding the natural dexterity which is lower by the restricted manoeuvrability due to the instruments. Another disadvantage of this procedure is that the depth perception is compromised by the two-dimensional image. This problem is partially solved with the invention of the 3D monitor, but the costs of the equipment are higher thus not so available in every center. A different challenge regarding laparoscopic prostatectomy is represented by the rigidity and the length of the instruments resulting in an exaggeration in the transmitted movements which makes delicate fine procedures like the urethro-bladder anastomosis difficult. This type of surgery was introduced in 1992 by Schuessler et al in order to reduce the morbidity of the open procedure¹¹. Recent studies conducted by the National Institute for Health and Care Excellence, in England recommended radical prostatectomy to be performed to men with intermediate-risk and high-risk disease with a high long-term prospect of disease control¹². Despite the fact that there is no conclusive evidence that recognizes the superiority of the laparoscopic prostatectomy over the open procedure regarding the oncological benefit, many urological centers have invested a lot of money in laparoscopic tools, due to the low hospitalization time and the faster recovery time for the patient.

RESULTS

Ilic et al performed a Cochrane review that compared two studies on a lot of 446 randomised patients with prostate cancer. The mean PSA was 7,09 ng/ml and the prostate mean volume was 49,78 cm³. This study observed the difference between open, laparoscopic and robotic-assisted laparoscopic prostatectomy. The primary outcome showed no study regarding the prostate cancer-specific survival. The laparoscopic procedure had little to no difference regarding the urinary quality of life and the sexual quality of life. The main advantage of this procedure was the significant improvements regarding the duration of hospital stay and blood transfusion. Also the pain reported by the patient on the first day after the surgery was lower in the robotic and laparoscopic procedure than in open prostatectomy¹³.

SURGICAL TECHNIQUE

At the moment there are 3 ways to perform a radical prostatectomy: open, laparoscopic or robotic assisted. Among other type of treatment regarding prostate cancer we can mention external beam radiation therapy, brachytherapy, hormonal therapy and even active surveillance and watchful waiting. The main focus of this study is on the open and the laparoscopic approach for prostate cancer. The recommendation for the operation in prostate cancer is when there is a life expectancy over 10 years (EAU guideline). Bill-Axelsson A et al, concluded in his study that radical prostatectomy significantly reduces the mortality in

¹⁰ Antonelli, A., Sodano, M., Peroni, A., et al. Positive surgical margins and early oncological outcomes of robotic vs open radical prostatectomy at a medium case-load institution. *Minerva Urol Nefrol* 2016; 69: 63-68

¹¹ Schuessler, W.W., Schulam, P.G., Clayman, R.V., Kavoussi, L.R. Laparoscopic radical prostatectomy: initial short-term experience. *Urology*. 1997, 50: 854-857

¹² The National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management. NICE guidelines [CG175], 2014

¹³ Ilic, D., et al. Laparoscopic and robotic-assisted versus open radical prostatectomy for the treatment of localised prostate cancer. *Cochrane Database Syst Rev*, 2017; 9: CD009625

patients with prostate cancer, over watchful waiting¹⁴. Experience and careful attention to any surgical details have showed to have lower rates of positive surgical margins. Despite the fact that there is a considerable methodological uncertainty, laparoscopic prostatectomy has a reduced risk regarding the positive margins and a lower morbidity¹⁵.

In late 1997 Schuessler et al. researched this new type of approach for the treatment of prostate cancer, where he described it as feasible, but he did not observe any difference with the open procedure, regarding the erectile function, continence, and the degree of tumor removal¹⁶.

Regarding the pelvic lymph node dissection, Fossati, N., et al published a study where he systematically reviewed specialty literature regarding the benefits and harms of pelvic lymph node dissection and the oncological and no-oncological outcomes for the patients that underwent radical prostatectomy. He evaluated studies that considered the limited, standard, super- extended lymph node dissection and no lymph node dissections. The only main benefit for this procedure was that it provides important information regarding the prognosis and staging, information that can't be obtained by other investigations. Besides that, there is no improvement to the oncological outcome. On the contrary super-extended lymph node dissections is associated with worse intraoperative and perioperative outcome¹⁷. To correctly stage the prostate cancer after radical prostatectomy, an extended lymph node dissection must be performed, including the lymphatic nodes in the obturator fossa over and under the obturator nerve, the nodes medial and lateral to the internal iliac artery and external iliac artery¹⁸. This procedure can't be performed in the classic extraperitoneal laparoscopy, but can be performed in transperitoneal laparoscopic prostatectomy and the open prostatectomy.

EAU guidelines suggested the concept of sentinel node biopsy based on the point that the sentinel node is the first station where the migrating tumor cells can reach, therefore a biopsy on this level can predict the need of lymph node dissection. However there a few studies on this biopsy, therefore it is still consider as an experiment.

Nerve-sparing surgery can be successfully performed in patients with localized prostate cancer both through the classic open prostatectomy and by laparoscopic procedure. The nerve sparing prostatectomy is more difficult laparoscopic if you don't have a 3D monitor, that allows you a better view on the nerve fibers attached to the prostate. Although it preserves the erectile function to the patient, the nerve sparing surgery must not be perform if

¹⁴ Bill-Axelson, A., Holmberg, L., Garmo, H., Rider, J., Taari, K., Busch, C., et al. Radical prostatectomy or watchful waiting in early prostate cancer. *New England Journal of Medicine* 2014; 370: 932–42

¹⁵ Ramsay, C., et al. Systematic review and economic modelling of the relative clinical benefit and cost-effectiveness of laparoscopic surgery and robotic surgery for removal of the prostate in men with localised prostate cancer. *Health Technol Assess*, 2012. 16: 1

¹⁶ Schuessler, W., Schulam, P., Clayman, R., Kavoussi, L. Laparoscopic radical prostatectomy: initial short-term experience. *Urology* 1997;50:854-857

¹⁷ Fossati, N., Willemse, P.M., van den Bergh, R.C.N., et al. The Benefits and Harms of Different Extents of Lymph Node Dissection During Radical Prostatectomy for Prostate Cancer: A Systematic Review. *Eur Urol*. 2017;72(1):84-109; Tigliş, M., Neagu, T.P., Elfara, M., Diaconu, C.C., Bratu, O.G., Vacariu, I.A., Grintescu, I.M. Nefopam and its role in modulating acute and chronic pain. *Rev Chim*. 2018;69(10):2877-2880; Bratu, O.G., Cherciu, A.I., Bumbu, A., Lupu, S., Marcu, D.R., Ionita Radu, F., Manea, M., Furau, C., Diaconu, C.C., Mischianu, D. Retroperitoneal tumors – treatment and prognosis of tumor recurrence. *Rev Chim*. 2019;70(1):191-194

¹⁸ Mattei, A., et al. The template of the primary lymphatic landing sites of the prostate should be revisited: results of a multimodality mapping study. *Eur Urol*, 2008; 53: 118; Marcu, R.D., Spinu, A.D., Socea, B., Bodean, O.M., Diaconu, C.C., Vasilescu, F., Neagu, T.P., Bratu, O.G. Castleman's disease – clinical, histological and therapeutic features. *Rev Chim*. 2018;69(4):823-830

there is any doubt that there can be residual tumor, or the tumor invades the neurovascular bundle¹⁹.

COMPLICATIONS RELATED TO RADICAL PROSTATECTOMY

Among the most common and frequent complication in radical prostatectomy we can name the post-operative incontinence, post-operative urinary retention and erectile dysfunction²⁰. This complication usually occurs after open radical prostatectomy. Because the technology evolved thus laparoscopic and robotic assisted laparoscopy being more and more used, studies on this subject demonstrated a rate between 89% an 100% regarding the continence rate for patients that underwent this. The mean rate of continence among patients with open retropubic prostatectomy was 80% to 97%²¹. There is a lack of data regarding the potency of patients that underwent radical prostatectomy open or laparoscopic. All the studies regarding this complications showed little difference between the two types of surgery. A study performed by Haglind E et al. demonstrated that the erectile dysfunction was observed in 70.4% after robotic assisted prostatectomy and 74.7% after open retropubic prostatectomy²².

Sinan Khadhoury et al conducted a study by using the database of The British Association of Urological Surgeons that described contemporary radical prostatectomy from all the urological centers in England over a period of 2 years. The surgical approach was robot-assisted laparoscopic in 65%, laparoscopic in 23%, and open retropubic prostatectomy in 12%. The nerve sparing procedure was performed in 57.3% of cases²³.

One of the main disadvantage in laparoscopic or robotic assisted laparoscopy is represented by the learning curve. Murat Ucar et al performed a study in Turkey where they analyzed the effect of the learning curve on the oncological outcome and complications in patients that underwent robotic-assisted laparoscopic prostatectomy. The study was conducted on a lot of 132 patients that war divided in 2 groups: the first 45 cases and the rest of the cases. The main difference in the two groups was regarding the operation time which was 250 minutes in the first group and 235 minutes in the second group which shows the importance of practice when you start to use this type of surgery. There was no notable difference between the two groups regarding potency and continence rates at 3 months and 12 months, postoperatively. Also the recovery, blood loss and hospitalization time was equal

¹⁹ Iorga, L., Anghel, R., Marcu, D., Spinu, D., Pantea Stoian, A., Diaconu, C., Bratila, E., Socea, B., Neagu, T.P., Mischianu, D., Bratu, O.G. Renal sarcoma – a rare parenchymal tumor with a very poor prognosis. Arch Balk Med Union. 2018;53(3):434-438; Socea, B., Nica, A.A., Bratu, O.G., Diaconu, C.C., Smaranda, A., Socea, L., Bertesteanu, S., Dimitriu, M., Carap, A., Constantin, V. Incidental finding of a sigmoid intussusception associated with rectal prolapse – a case report. Arch Balk Med Union. 2018;53(1):143-146

²⁰ Spinu, D.A., Marcu, R.D., Socea, B., Diaconu, C.C., Scarneciu, C., Bodean, O.M., Dragomirescu, R.I.F., Stanescu, A.M.A., Mischianu, D.L.D., Bratu, O.G. Ureteral JJ stents: which one is better? Rev Chim. 2018;69(8):2061-2063

²¹ Maffezzini, M., Seveso, M., Taverna, G., Giusti, G., Benetti, A., Graziotti, P. Evaluation of complications and results in a contemporary series of 300 consecutive radical retropubic prostatectomies with the anatomic approach at a single institution. Urology, 2003; 61: 982

²² Haglind, E., et al. Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial. Eur Urol, 2015; 68: 216

²³ Khadhoury, S., Miller, C., Fowler, S., Hounsborne, L., Adshead, A.M.J., McGrath, J.S. The British Association of Urological Surgeons (BAUS) radical prostatectomy audit 2014/2015 –an update on current practice and outcomes bycentre and surgeon case-volume. BJU Int. 2018;121(6):886-892

between the two groups. And after 12 month after the operation the continence rate was 90%²⁴.

DISCUSSION

Radical prostatectomy is the first line of treatment in patients diagnosed with localized prostate cancer, with a life expectancy over 10 years²⁵. The main goal of the surgery even if it's performed classic open retropubic or laparoscopic and robotic assisted is to leave the patient cancer free. Surgical technique is very important regarding the oncological and functional outcome as well as the surgeons experience. With the advance of technology and the spreading of the laparoscopic approach on this type of cancer, the expectation of the patient is high regarding his quality of life (continence and erectile function)²⁶. However, as any new surgical technique it has a learning curve. The laparoscopic technique permitted a more accurate precision in lymph node dissection, anastomosis and in the preservation of the neurovascular bundle²⁷. To determine the learning curve for robotic assisted prostatectomy, Islamaglu et al published a study where he concluded that a number of 50 operations are required, even if the surgeon is experienced in laparoscopy²⁸. Moreover, the complication rates of laparoscopic radical prostatectomy is between 1.6% and 6.2% and they are dependent

²⁴ Ucar, M., Varol, A.T., Gulkesen, K.H., et al. Does The Learning Curve Affect the Surgical, Functional, and Oncologic Outcomes in Bilateral Nerve-Sparing Robot Assisted Laparoscopic Prostatectomy? *Cureus*. 2019; 11(7): e5274

²⁵ Heidenreich, A., Bellmunt, J., Bolla, M., et al. European Association of Urology (2011) EAU guidelines on prostate cancer: part 1. Screening, diagnosis, and treatment of clinically localized disease. *Eur Urol*. 2011; 59:61-71; Marcu, D., Spinu, D., Mischianu, D., Socea, B., Oprea, I., Bratu, O. Oncological follow-up after radical prostatectomy. *Rom J Mil Med*. 2017; 120(3): 39-42; Bratu, O.G., Diaconu, C.C., Mischianu, D.L.D., Constantin, T., et al. Therapeutic options in patients with biochemical recurrence after radical prostatectomy (Review). *Experimental And Therapeutic Medicine*. 2019; 18: 5021-5025; Ciuca, G.A., Bratu, O., Spinu, D., Dinu, M., Farcas, C., et al. The importance of life quality questionnaire in patients with prostate cancer, pre- and post-radical prostatectomy. *Rom J Mil Med*. 2016; 119(2): 12-16; Bratu, O., Spinu, D., Oprea, I., Popescu, R., et al. Complications of radical retropubic prostatectomy-our experience. *Rom J Mil Med*. 2015; 118(3): 23-25; Popescu, R., Bratu, O., Spinu, D., Marcu, D., et al. Neuroendocrine differentiation in prostate cancer -a review. *Rom J Mil Med*. 2015; 118(3): 16-19; Spinu, D., Bratu, O., Marcu, D., Mischianu, D., et al. The use of ELISA and PCR in identifying correlations between viral infections and benign prostatic hypertrophy. *Rev Chim*. 2018; 69(3): 645-649.

²⁶ Socea, B., Smaranda, A.C., Nica, A.A., Bratu, O.G., Diaconu, C., Baleanu, V.D., Davitoiu, D.V., Dimitriu, M., Carap, A.C., Bobic, S., Constantin, V.D. Postcolonoscopy acute appendicitis - our case series and review of literature. *Arch Balk Med Union*. 2018;53(4):599-602; Diaconescu, D., Pantea Stoian, A., Socea, L., Stanescu, A.M.A., Iancu, M.A., Socea, B., Pituru, S., Bratu, O., Diaconu, C. Hepato-renal syndrome: a review. *Arch Balk Med Union*. 2018;53(2):239-245.

²⁷ Belinski, C., Aungurenci, A., Marcu, D., Spinu, D., Bratu, O., Mischianu, D. Current therapeutic strategies for erectile function recovery after radical prostatectomy – literature review and meta-analysis. *Rom J Mil Med*. 2019; 122(3): 9-17; Marcu, D., Bratu, O., Spinu, D., Radulescu, A., Farcas, C., Mischianu, D. Penile prosthesis-a viable solution for erectile dysfunction refractory to conservatory therapy. *Rom J Mil Med*. 2015; 118(3): 33-39; Cherciu, A., Spinu, D., Sandru, F., Marcu, D., Iorga, L., Anghel, R., Bratu, O., Mischianu, D. Erectile dysfunction after radical prostatectomy. *Annals of Academy of Romanian Scientists Series of Medicine*. 2020; 1(1):29-34; Bratu, O., Oprea, I., Marcu, D., Spinu, D., et al. Erectile dysfunction post-radical prostatectomy – a challenge for both patient and physician. *Journal of Medicine and Life*. 2017; 10(1): 13-18; Bratu, O., Mischianu, D., Constantinoiu, S. Transobturator urethral suspension surgical treatment of urinary incontinence in men. *Chirurgia (Bucur)*. 2013; 108(2):250-255; Scarneciu, I., Andrei, C., Scarneciu, C., Lupu, A.M., Bratu, O.G., Lupu, S. Voluminous urethral stone-a very rare complication after male suburethral sling surgery as a result of sling erosion into proximal urethra. *Urology Journal*. 2018;15(5): 297-299.

²⁸ Islamoglu, E., Karamik, K., Ozsoy, C., Tokgoz, H., Ates, M., Savas, M. The learning curve does not affect positive surgical margin status in robot-assisted laparoscopic prostatectomy. *Urol J*. 2018; 15:333-338

on this learning curve²⁹. It is very important that a surgeon is well familiar with the open procedure, because sometimes conversion is required, mainly because the complication appeared during the surgery. Among them the most frequent are bleeding, access injury and rectum injury³⁰. Rectum injury is one of the most feared complication that can appear, and the literature describe this complication in 1%-2% of cases. The reason for this complication is mainly because of the prostate cancer underdiagnosed on the RM and or the adhesions after antiandrogen therapy.

The main advantage observed in many studies in using the laparoscopic approach over the open prostatectomy is the erectile function which is better preserved. The risk of injuring the neurovascular bundle is lower in laparoscopic prostatectomy. The continence rate is also a little higher in laparoscopic prostatectomy over the open procedure³¹. However there are some studies that showed there is no difference regarding the post-operative outcome between the two procedures. A study performed by Barry et al. in 2012 showed that there is no difference in continence and erectile function between the two groups in 14 months follow up³². In opposition with this study, Hu et al, reported that the continence and erectile function are much better after a classic open prostatectomy than a laparoscopic prostatectomy³³.

CONCLUSIONS

Both surgery techniques have its own advantage and disadvantages regarding the continence and erectile functions. Also regarding the oncological outcome all studies showed that there is no difference between the two techniques. The laparoscopic approach has the advantage of a theoretical better erectile function outcome, and the advantage that the duration of hospitalization is lower.

²⁹ Gregori, A., Simonato, A., Lissiani, A., Bozzola, A., Galli, S., Gaboardi, F. Laparoscopic radical prostatectomy: perioperative complications in an initial and consecutive series of 80 cases. *Eur Urol* 2003;44:190-194; Diaconu, C., Balaceanu, A., Morosan, E. Sepsis biomarkers: past, present and future. *Farmacia*. 2015;63(6):811-815

³⁰ Guillonueau, B., Rozet, F., Cathelineau, X., Lay, F., Barret, E., Doublet, J.D., et al. Perioperative complications of laparoscopic radical prostatectomy: the Montsouris 3-year experience. *J Urol* 2002;167:51-56; Tica, O.A., Tica, O., Antal, L., Hatos, A., Popescu, M.I., Pantea Stoian, A., Bratu, O.G., Gaman, M.A., Pituru, S.M., Diaconu, C.C. Modern oral anticoagulant treatment in patients with atrial fibrillation and heart failure: insights from the clinical practice. *Farmacia*. 2018;66(6):972-976; Laslo, C., Pantea Stoian, A., Socea, B., Paduraru, D., Bodean, O., Socea, L., Neagu, T.P., Stanescu, A.M.A., Marcu, D., Diaconu, C. New oral anticoagulants and their reversal agents. *Journal of Mind and Medical Sciences*. 2018;5(2):195-201

³¹ Radavoi, G.D., Pricop, C., Jinga, V., Mates, D., Radoi, V.E., Jinga, M., Ursu, R.I., Bratu, O.G., Mischianu, D.L., Iordache, P. A comprehensive analysis of genome-wide association studies to identify prostate cancer susceptibility loci for the Romanian population. *Rom J Morphol Embryol*. 2016;57(2):467-475; Radulescu, A., Madan, V., Aungurenci, A., Bratu, O., Farcas, C., Dinu, M., Mischianu, D. Antibiotic resistant urinary tract infections in an urology ward. *Rom J Med*. 2015; 118(3): 20-22.

³² Barry, M.J., Gallagher, P.M., Skinner, J.S., Fowler, F.J. Adverse effects of robotic-assisted laparoscopic versus open retropubic radical prostatectomy among a nationwide random sample of medicare-age men. *J Clin Oncol* 2012;30:513-518

³³ Hu, J.C., Gu, X., Lipsitz, S.R., et al. Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA* 2009;302:1557-1564

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VITAMIN D AND ITS RELATIONSHIP WITH CARDIOVASCULAR DISEASES

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ABSTRACT:

VITAMIN D DEFICIENCY HAS BEEN ASSOCIATED WITH DISEASES SUCH AS RICKETS, OSTEOMALACIA, OSTEOPOROSIS, SKIN DISEASES AND CARDIOVASCULAR DISEASE. VITAMIN D DEFICIENCY IS ASSOCIATED WITH INCREASED INFLAMMATION, INCREASED EXPRESSION OF INFLAMMATORY CYTOKINES, ENDOTHELIAL CELLS AND DYSFUNCTION OF VASCULAR SMOOTH MUSCLE CELLS AND DECREASED VDR EXPRESSION AND ACTIVITY, WHICH MAY LEAD TO THE DEVELOPMENT OF VASCULAR DISEASES, SUCH AS ATHEROSCLEROSIS, ANEURYSMS, VASCULAR CALCIFICATIONS, AND ARTERIAL HYPERTENSION. ALTHOUGH THERE IS EVIDENCE THAT VITAMIN D DEFICIENCY IS ASSOCIATED WITH CARDIOVASCULAR DISEASE, A CAUSAL RELATIONSHIP HAS NOT BEEN IDENTIFIED YET.

KEY WORDS: VITAMIN D DEFICIENCY, ATHEROSCLEROSIS, CARDIOVASCULAR DISEASE.

INTRODUCTION

Vitamin D is a fat-soluble vitamin found in some food sources, produced non-enzymatically under the skin, following sun exposure, and metabolized in the liver and kidneys by involving cytochrome P450 enzymes⁷. Vitamin D plays a crucial role in mineral

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⁷ Holick, M.F. Vitamin D deficiency. N Engl J Med. 2007;357(3): 266–281

homeostasis and skeletal health and, as a steroid and immunomodulatory hormone, vitamin D regulates the body's immune response⁸.

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. In 2015, the World Health Organization (WHO) estimated that CVD were responsible for over 17.7 million deaths, representing a total of 31% of global deaths⁹. One of the most important ethiological factors for CVD is atherosclerosis, characterized by lipid deposition and subsequent accumulation of T cells and macrophages, as a result of the response to endothelial injury¹⁰. In these processes, reactive oxygen species play a pivotal role, as they can cause lipid oxidation, such as low density lipoprotein (LDL) and polyunsaturated fatty acids, which are deposited in the vascular wall, directly damage cellular components and further promote inflammation by activating several pro-atherogenic transcription factors¹¹.

Vitamin D deficiency has been associated with diseases such as rickets, osteomalacia, osteoporosis, skin diseases and cardiovascular diseases¹². Some studies have demonstrated the presence of vitamin D receptors in many tissues and have suggested plausible vitamin D pathways that may be linked to cardiovascular disease. Associations between low levels of serum 25-hydroxy vitamin D [25 (OH) D] and increased risk of cardiovascular disease have been shown by several observational studies¹³.

THE LINK BETWEEN VITAMIN D AND CARDIOVASCULAR DISEASE

Vitamin D deficiency leads to increased inflammation, increased expression of inflammatory cytokines, and decreased expression and activity of VDR (vitamin D receptor). This leads to increased signaling of the downstream inflammatory signaling cascades, with loss of collagen, fibrosis, increased oxidative stress, increased inflammation, increased

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⁹ Roth, G.A., Johnson, C., Abajobir, A., et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. *J Am Coll Cardiol.* 2017;70: 1–25

¹⁰ Tousoulis, D., Psarros, C., Demosthenous, M., et al. Innate and adaptive inflammation as a therapeutic target in vascular disease: the emerging role of statins. *J Am Coll Cardiol.* 2014;63: 2491–2502; Bejan, G.C., Stanescu, A.M.A., Ghilencea, N.L., Matei, D. Analiza actuala a aspectelor terapeutice moderne in tratamentul HTA si al comorbiditatilor asociate. *Revista Medicala Romana* 2018;LXV(2):102-107

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¹³ Manson, J.E., Bassuk, S.S., Lee, I.M., et al. The VITamin D and Omega-3 Trial (VITAL): Rationale and design of a large randomized controlled trial of vitamin D and marine omega-3 fatty acid supplements for the primary prevention of cancer and cardiovascular disease. *Contemp Clin Trials.* 2012;33: 159–171; Zhang, R., Li, B., Gao, X., et al. Serum 25-hydroxyvitamin D and the risk of cardiovascular disease: dose-response meta-analysis of prospective studies. *Am J Clin Nutr.* 2017;105: 810–819.

sensitivity to infections and decreased protective mechanisms¹⁴. Finally, all these processes induce various cardiovascular diseases, such as cardiomyopathy, ventricular hypertrophy, myocardial infarction, heart failure, cardiac fibrosis and rhythm abnormalities¹⁵. Therefore, vitamin D supplementation may decrease these mediators and slow down cardiovascular disease progression and development¹⁶.

In rats, diets low in vitamin D resulted in higher systolic pressure and lower calcium concentration, after which supplementation with vitamin D analogues led to the reversal of these effects¹⁷.

There has also been evidence that vitamin D can regulate matrix homeostasis, which may lead to a critical situation in inflammatory diseases and aneurysms, where matrix destabilization is significant¹⁸.

Vitamin D deficiency may lead to the development of vascular diseases, such as atherosclerosis, aneurysms, calcification, and hypertension¹⁹. Because vitamin D deficiency is associated with the pathogenesis of vascular disease development and progression, vitamin D supplementation may be useful for prevention of CVD and their complications²⁰.

Although there is evidence that vitamin D deficiency is associated with more cardiovascular disease, a causal relationship has not yet been identified.

MYOCARDIAL INFARCTION, CARDIAC HYPERTROPHY AND CARDIOMYOPATHY

Myocardial infarction has been associated with vitamin D deficiency, regardless of season²¹. Low plasma vitamin D levels are independently associated with poor in-hospital outcomes and at one year in patients with acute myocardial infarction²².

¹⁴ Chen, S., Law, C.S., Grigsby, C.L., et al. Cardiomyocyte-specific deletion of the vitamin D receptor gene results in cardiac hypertrophy. *Circulation*. 2011;124:1838–1847; Socea, B., Nica, A.A., Smaranda, C.A., Carap, A.C., Socea, L.I., Dimitriu, M., Bratu, O.G., Moculescu, C.E., Bertesteanu, S.V.G., Constantin, V.D. Solitary cecum diverticulitis – a surprising diagnosis. *Archives of the Balkan Medical Union*. 2017;52(4): 467-470

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¹⁹ Stanescu, A.M.A., Grajdeanu, I.V., Totan, A., et al. The complex context of the involvement of vitamin D deficiency in obesity. *Rev Chim (Bucharest)* 2019;70(10): 3654-3656

²⁰ Iancu, M.A., Bejan, C.G., Stanescu, A.M.A., et al. Deficitul de vitamina D in asistenta medicala primara. *Revista Medicala Romana*, 2018;LXV(1): 37-40; Stanescu, A.M.A., Matei, A., Grajdeanu, I.V., et al. Sindromul metabolic in raport cu nivelul seric al vitaminei D corelat cu afectarea cutanată. *Revista Medicala Romana*. 2017;LXIV(4): 300-304

²¹ Martinesi, M., Bruni, S., Stio, M., Treves, C. 1,25-Dihydroxy-vitamin D3 inhibits tumor necrosis factor- α -induced adhesion molecule expression in endothelial cells. *Cell Biol Int*. 2006;30: 365–375

²² Aleksova, A., Belfiore, R., Carriere, C., et al. Vitamin D deficiency in patients with acute myocardial infarction: an Italian single-center study. *Int J Vitam Nutr Res*. 2015; 85(1–2): 23–30

Hyperlipidemia is a risk factor for CVD, and serum vitamin D has an inverse association with total cholesterol levels, low density lipoprotein (LDL), homocysteine, triglycerides, and a positive association with high density lipoprotein (HDL). Vitamin D supplementation may be protective against CVD²³.

Vitamin D deficiency is associated with increased inflammation, pro-inflammatory cytokines and atherosclerosis, and supplementation with vitamin D can reduce these factors. Hence the idea of the implication of vitamin D deficiency in the appearance of myocardial infarction, but the role of vitamin D in both the pathogenesis of myocardial infarction and the pathogenesis of atherosclerosis needs to be further studied²⁴.

VDR gene polymorphisms or genetic variations could be a positive predictor for myocardial infarction²⁵. The cardioprotective effect of VDR activation is attributed to the inhibited endoplasmic reticulum, attenuated mitochondrial insufficiency, decreased autophagy dysfunction and reduced cardiomyocyte apoptosis²⁶.

Cardiac hypertrophy of the left ventricle (LVH) and myocardial performance are associated with low levels of vitamin D²⁷. Diabetes is a risk factor for LVH²⁸. LVH reversal in diabetic rats treated with vitamin D and attenuation of TNF- α expression by inhibiting nuclear factor-kappa beta signaling suggest the role of vitamin D in LVH reversal²⁹.

Cardiomyopathy. The pathogenesis of dilated cardiomyopathy (DCM) is usually idiopathic. Various studies have reported vitamin D deficiency-induced hypocalcemia in infants and hypoparathyroidism-induced hypocalcemia in adults as the cause of DCM and

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HF³⁰. Low levels of maternal vitamin D have been suggested as a cause for childhood hypocalcemia. Improvement of clinical symptoms after supplementation with vitamin D and calcium for the treatment of hypovitaminosis and hypocalcemia highlights the importance and protective role of vitamin D in cardiomyopathy³¹.

Low circulating levels of vitamin D have been correlated with cardiac steatosis. Furthermore, complete deletion of the animal VDR gene, as well as deletion of the myocyte-specific VDR gene, are associated with impaired cardiac structure and function³².

Obesity is a chronic inflammatory disease associated with low levels of vitamin D. Low levels of vitamin D associated with obesity may be due to increased total clearance of vitamin D and increased consumption of vitamin D in the fight against inflammation associated with obesity³³. Chronic inflammation of obesity is a risk factor for diabetes and together they are risk factors for heart disease, such as cardiomyopathy, coronary artery disease, myocardial infarction, fibrosis, arrhythmias and HF³⁴.

HEART FAILURE, RHYTHM ABNORMALITIES AND CARDIAC FIBROSIS

Heart failure. Vitamin D deficiency is associated with increased inflammation and inflammatory cytokines, such as TNF- α , interleukin (IL)-6 and interleukin-1 β , involved in mediating heart disease and heart failure³⁵. Vitamin D supplementation reduces these cytokines in chronic heart failure³⁶.

Low levels of vitamin D and hypoparathyroidism are associated with remodeling of cardiomyopathy and worsening of heart failure³⁷. Improvement and beneficial effects of vitamin D on the structure and function of LV in the VINDICATE study (Vitamin D treatment with patients with chronic heart failure), in patients with heart failure and decreased renin activity with short-term supplementation of vitamin D, suggest the therapeutic role of vitamin D³⁸.

³⁰ Fan, Y., Zhang, S.X., Ren, M., Hong, L.F., Yan, X.N. Impact of 1,25-(OH)₂D₃ on left ventricular hypertrophy in type 2 diabetic rats. Chin Med Sci J. 2015;30(2):114–20

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Rhythm anomalies. Vitamin D deficiency is associated with cardiac fibrosis, which is a hallmark of arrhythmias. Low levels of vitamin D are associated with heart failure and atrial fibrillation in patients with heart failure³⁹. Low levels of vitamin D are significantly associated with increased left atrial fibrosis in patients with paroxysmal rhythm abnormalities, as well as with the recurrence of rhythm abnormalities after cryoablation and post-coronary artery bypass graft surgery⁴⁰.

Cardiac fibrosis and remodeling. Negative regulation of the activity of TGF- β 1, SMAD3, CTGF and PARP1 / SIRT1 / mTOR pathways with vitamin D suggests the protective role of vitamin D against fibrosis⁴¹. Inflammation plays a major role in post-infarction remodeling, and vitamin D, as an anti-inflammatory agent, can play a crucial role⁴². Because vitamin D deficiency is associated with the development of hypertrophy and cardiac fibrosis, VDR genomics may play a role in the development of cardiac fibrosis. The cardioprotective effects of VDR activators and modulators suggest the potential therapeutic role of vitamin D⁴³.

CONCLUSIONS

Vitamin D deficiency is associated with cardiovascular disease, including coronary heart disease, myocardial infarction, heart failure and cardiac fibrosis, cardiomyopathy. Increased inflammation in diabetes and/ or obesity lowers the circulating levels of vitamin D, thus increasing the risk of cardiovascular disease. Vitamin D supplementation alleviates inflammation and pro-inflammatory cytokines and thus may play a therapeutic role in the treatment of cardiovascular disease.

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EFFECT OF ESCITALOPRAM ALONE OR COMBINATION WITH SORAFENIB ON HEPG2 HEPATOCELLULAR CELL LINE PROLIFERATION

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ABSTRACT:

HEPATOCELLULAR CARCINOMA IS ONE OF THE MOST COMMON CANCERS. THE MAIN TREATMENT FOR HEPATOCELLULAR CANCERS IS SURGERY. DRUG TREATMENT CAN BE PERFORMED IN ADVANCED CASES AFTER SURGICAL TREATMENT OR RELAPSE THERAPY. SORAFENIB IS A DRUG THAT IS USED PRIMARILY IN THE TREATMENT OF HEPATOCELLULAR CANCER. ESCITALOPRAM IS A DRUG IN THE SEROTONIN REUPTAKE INHIBITOR GROUP USED TO TREAT DEPRESSION. THERE ARE STUDIES SHOWING THE EFFECT OF ESCITALOPRAM ON PROLIFERATION. THE PURPOSE OF THIS STUDY IS TO EVALUATE THE USE OF ESCITALOPRAM ALONE AND IN COMBINATION WITH SORAFENIB IN LIVER CANCER. THE EFFECT OF ESCITALOPRAM AND IN COMBINATION ON PROLIFERATION OF HEPATOCELLULAR CELL LINES WAS ASSESSED BY XTT PROLIFERATION ASSAY. THE HALF INHIBITING CONCENTRATION (IC 50) WAS CALCULATED BY REGRESSION ANALYSIS, PHOTOGRAPHED UNDER AN INVERTED MICROSCOPE. THE SYNERGISTIC EFFECT HAS BEEN EVALUATED. THE EFFECT ON MORPHOLOGICAL CHANGES WAS VISUALIZED UNDER THE INVERTED MICROSCOPE. THE RESULTS OF OUR STUDY CONFIRM THE SYNERGISTIC EFFECT OF USE OF ESCITALOPRAM IN COMBINATION WITH SORAFENIB IN LIVER CANCER. PROSPECTIVE RANDOMIZED TRIALS ARE NEEDED TO EVALUATE ITS CLINICAL USE.

KEY WORDS: ESCITALOPRAM, HEPG2, PROLIFERATION, SORAFENIB, CANCER

INTRODUCTION

Le carcinome hépatocellulaire (CHC) est le cinquième cancer le plus répandu dans le monde.

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⁴ Maltepe University, Faculty of Medicine, *Histology and Embryology Department*; Maltepe University, Faculty of Medicine, Cancer and stem cell research center, (MUKKAM)

C'est la troisième cause de décès de cancer dans le monde ⁵. Chez les femmes, il occupe le 9ème rang mondial. Le traitement systémique à la doxorubicine s'est révélé partiellement bénéfique sans augmentation de la survie. D'autres traitements tels que l'immunothérapie, les radiations internes et le tamoxifène n'ont pas montré d'effet antitumoral ou n'ont pas affecté la survie du CHC ⁶. Le sorafénib montre son effet en inhibant de nombreuses kinases efficaces dans la prolifération des tumeurs et l'angiogenèse ⁷. Il a été démontré que le sorafénib prolongeait la survie des patients atteints d'un carcinome hépatocellulaire avancé ⁸. Il a été approuvé par la FDA en 2007 pour les patients atteints d'un CHC avancé et est maintenant devenu le traitement de référence pour ces patients ⁹. Le repositionnement d'un médicament est l'évaluation de l'utilisation de médicaments à l'efficacité clinique et à l'innocuité démontrées dans une nouvelle indication ¹⁰. C'est l'une des méthodes permettant de réduire les coûts et d'accélérer la transmission du médicament à la clinique pendant le processus de développement du médicament. Dans cette étude, l'effet de l'escitalopram sur la prolifération cellulaire et la morphologie du cancer du foie sera évalué. L'escitalopram est l'énantiomère (S) du citalopram, un inhibiteur de la recapture de la sérotonine (ISRS) sélectif racémique. Lorsqu'il est administré par voie orale, il est rapidement absorbé et atteint sa concentration plasmatique maximale en environ de 3-4 heures. La concentration à l'état d'équilibre est atteinte dans les 7 à 10 jours. Sa demi-vie est de 27 à 30 heures¹¹. La sélectivité de l'escitalopram s'est avérée supérieure à celle de certains autres ISRS. L'efficacité de l'escitalopram s'est avérée supérieure ou égale à celle d'autres médicaments ISRS et inhibiteurs sélectifs de la recapture de la noradrénaline (IRSN). Les effets indésirables causés par l'escitalopram sont légers, transitoires et donc tolérables ¹². En outre, l'effet inhibiteur de l'escitalopram sur les enzymes du CYP et la glycoprotéine P étant inférieur à celui des autres médicaments, le risque d'interaction médicamenteuse est donc inférieur à celui des autres ISRS fréquemment prescrits ¹³. Le but de cette étude était d'évaluer l'utilisation de l'escitalopram seul et en association avec le sorafénib dans le cancer du foie.

MATÉRIEL ET METHODES

Culture de cellules

Des cellules HepG2 isolées chez un malade chez lequel un carcinome hépatocellulaire a été diagnostiqué (American Type Culture Collection, États-Unis) ont été utilisées dans notre étude.

⁵ Raza A, Sood GK. Hepatocellular carcinoma review: current treatment, and evidence-based medicine. *World J Gastroenterol* 2014; 20: p. 4115-27.

⁶ Llovet JM. Updated treatment approach to hepatocellular carcinoma. *J Gastroenterol* 2005; 40: p. 225-35.

⁷ Llovet JM, Ricci S, Mazzaferro V, Hilgard P, et al. Sorafenib in advanced hepatocellular carcinoma 2008; *N Engl J Med* 359: p. 378-90.

⁸ Bruix J, Raoul JL, Sherman M, Mazzaferro V, et al. Efficacy and safety of sorafenib in patients with advanced hepatocellular carcinoma: subanalyses of a phase III trial. *J Hepatol* 2012;57: p. 821-829

⁹ Villanueva A, Llovet JM. Targeted therapies for hepatocellular carcinoma. *Gastroenterology*. 2011; 140:1410-26. doi: 10.1053/j.gastro.2011.03.006. Epub 2011 Mar 13.

¹⁰ Li YY, Jones SJ. Drug repositioning for personalized medicine. *Genome Med* 2012; 4: 27.

¹¹ Rao N. The clinical pharmacokinetics of escitalopram. *Clin Pharmacokinet* 2007; 46: 281-90.

¹² Kirino E. Escitalopram for the management of major depressive disorder: a review of its efficacy, safety, and patient acceptability. *Patient Prefer Adherence* 2012; 6: 853.

¹³ Sanchez C, Reines EH, Montgomery SA. A comparative review of escitalopram, paroxetine, and sertraline: Are they all alike? *Int Clin Psychopharmacol*. 2014; 29:185-96. doi:10.1097/YIC.000000000000023.

Les cellules ont été cultivées dans du milieu DMEM (Dulbecco Modified Eagle Medium) de contenant 10% de sérum de veau foetal (FBS) et 1% d'antibiotique (Streptomycine 10 mg / ml et Pénicilline 10 000 U / ml). Les cellules ont été stockées dans un incubateur humidifié avec 5% de CO₂ à 37 ° C. Lorsque les cellules ont atteint une densité de 70-80%, elles ont été passées par trypsination dans des conditions stériles.

Evaluation de la prolifération cellulaire

Le kit de prolifération cellulaire XTT (Biological Industries, USA) a été utilisé pour mesurer la prolifération cellulaire. Le test est une méthode colorimétrique à base de sel de tétrazolum.

La procédure biochimique est basée sur une activité des enzymes mitochondriales, qui deviennent inefficaces peu de temps après la mort cellulaire. La densité mesurée est proportionnelle au nombre de cellules métaboliquement actives. Les cellules ont été colorées avec du bleu trypan, comptées avec une lame de thoma et étalées à 10 000 cellules / puits dans une plaque à 96 puits. Le lendemain, de l'escitalopram seul ou associé au sorafénib a été ajouté aux cellules du milieu et incubé pendant 24 heures.

La concentration maximale d'escitalopram appliquée aux cellules était de 300 µM et la concentration maximale de sorafénib était de 50 µM. Le taux de dilution concerne les deux médicaments. Après incubation, du réactif XTT a été ajouté et après 4 heures d'incubation, la densité optique du produit soluble dans chaque puits a été mesurée à 500 nm avec le lecteur de plaques à 96 puits Synergy Lecteurs de microplaques par absorbance.

La concentration en inhibiteur (CI 50) a été déterminée pour escitalopram avec cette méthode.

La CI 50 a été définie comme la concentration du médicament qui a réduit la prolifération cellulaire à 50% des cellules témoins non traitées. La valeur de CI50 a été calculée par analyse de régression non linéaire

SynergyFinder (<https://synergyfinder.fimm.fi>), une application Web développée pour analyser les données de la matrice de réponse à la dose du médicament, a été utilisée pour déterminer l'effet combiné de l'escitalopram - sorafénib. Le degré d'effet d'une combinaison de médicaments peut être visualisé sous la forme d'une carte de synergie sur la matrice de dose ¹⁴. Le modèle d'indépendance de Bliss accepte un processus stochastique dans lequel les effets des deux médicaments se produisent indépendamment et l'effet de combinaison attendu peut être calculé en fonction de la probabilité d'événements indépendants. Cette étude est basée sur le modèle de référence d'indépendance de Bliss ¹⁵.

Évaluation de la morphologie cellulaire

Les groupes de traitement et le groupe témoin ont été évalués pour la morphologie cellulaire par microscopie à contraste de phase (PrimoVert Invert, Zeiss).

RÉSULTATS

Effet antiprolifératif de l'escitalopram

L'effet antiprolifératif de l'escitalopram sur les cellules HepG2 a été déterminé par le test de prolifération cellulaire XTT. La dose maximale est de 300 µM et la dose minimale de 23 µM.

¹⁴ Ianevski A, He L, Aittokallio T, Tang J. SynergyFinder: a web application for analyzing drug combination dose-response matrix data. *Bioinformatics* 2017; 33:2413-15. doi:10.1093/bioinformatics/btx162.

¹⁵ Bliss CI. The toxicity of poisons applied jointly. *Ann App Biol* 1939; 26: 585-615

Des concentrations décroissantes de médicament avec un taux de dilution de $\frac{3}{4}$ ont été appliquées aux cellules. La relation entre les différentes concentrations d'escitalopram et la réponse antiproliférative des cellules est illustrée à la figure 1a. Le graphique montre une diminution progressive de la prolifération cellulaire avec l'augmentation des concentrations d'escitalopram. La valeur $P=100$ - viabilité% (Figure 1)

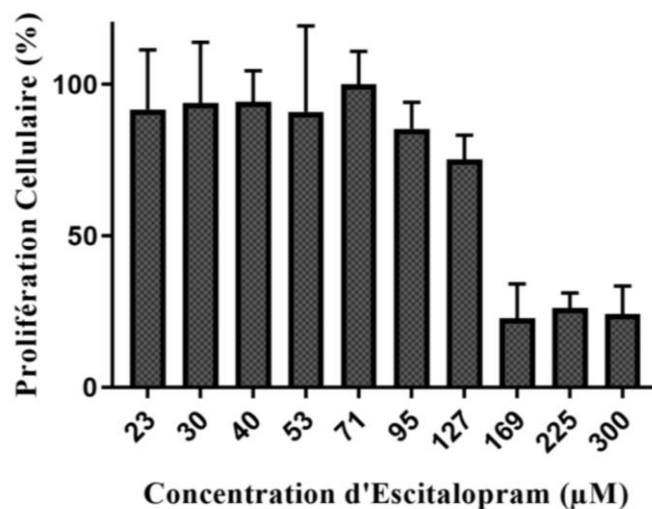


Figure 1: Effet antiprolifératif de l'escitalopram sur les cellules HepG2. Les données représentent 3 expériences et sont exprimées en moyenne \pm erreur type

Effet antiprolifératif de la combinaison d'escitalopram et sorafénib sur la morphologie cellulaire

Dans le cas de l'administration combinée de médicaments, si A et B ont chacun un effet, ils peuvent alors produire un effet synergique, additif ou antagoniste en combinaison. Par définition, effet synergique; L'effet combiné des médicaments A et B a considérablement augmenté par rapport à l'effet de chaque médicament seul. Par conséquent, il y a une interaction positive. À effet antagoniste; L'effet combiné des médicaments A et B était significativement réduit par rapport à l'effet de chaque médicament seul; il existait donc une interaction négative. L'effet additif est défini comme la somme des effets individuels de l'effet obtenu par la combinaison de médicaments¹⁶. Définir l'effet additif est le critère le plus important pour définir l'effet synergique et antagoniste¹⁷. L'application SynergyFinder met en évidence les régions de dose des synergistes et des antagonistes en rouge et vert, respectivement, sur la carte de synergie 2D. Le score de synergie d'une combinaison de médicaments est moyenné sur toutes les cellules à combinaison de doses (Figure 2). Le valeur de CI50 pour l'escitalopram dans les applications il a été de 130 µM (Figures 1). Lorsque ces deux médicaments ont été administrés ensemble, l'escitalopram à 71,2 µM et le sorafénib à 8,9 µM ont réduit la prolifération cellulaire jusqu'à 50% des cellules témoins. Ceci indique un effet synergique pour les deux médicaments, comme le montrent les figures 2A et 2B. Le score de synergie moyen est de 22, 3. La zone avec l'effet le plus synergique est

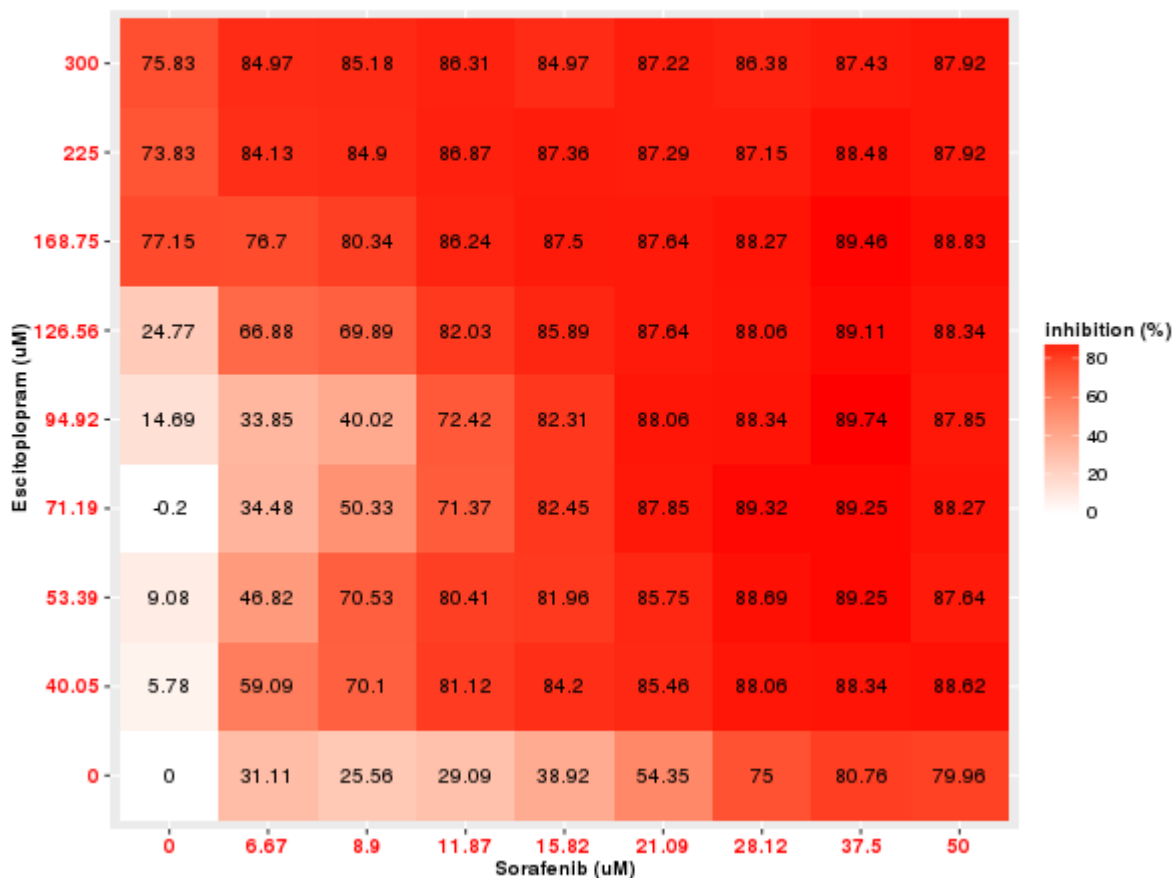
¹⁶ Aktaş G. Antibiotic Combinations and Synergistic Interactions. *Türk Mikrobiyol Cem Derg* 2015; 44: 47-55.

¹⁷ Chou TC. Theoretical basis, experimental design, and computerized simulation of synergism and antagonism in drug combination studies. *Pharmacol Rev* 2006; 58: 621-81.

marquée par des lignes en pointillés sur la figure 2. Cette zone couvre les plages de doses de 40,1 μM et de 71,2 μM pour l'escitalopram, ainsi que de 8,9 et 8,8 et 15,8 μM de sorafénib.

Sorafenib & Escitalopram

Dose-response matrix (inhibition)



Bliss synergy score: 21.291

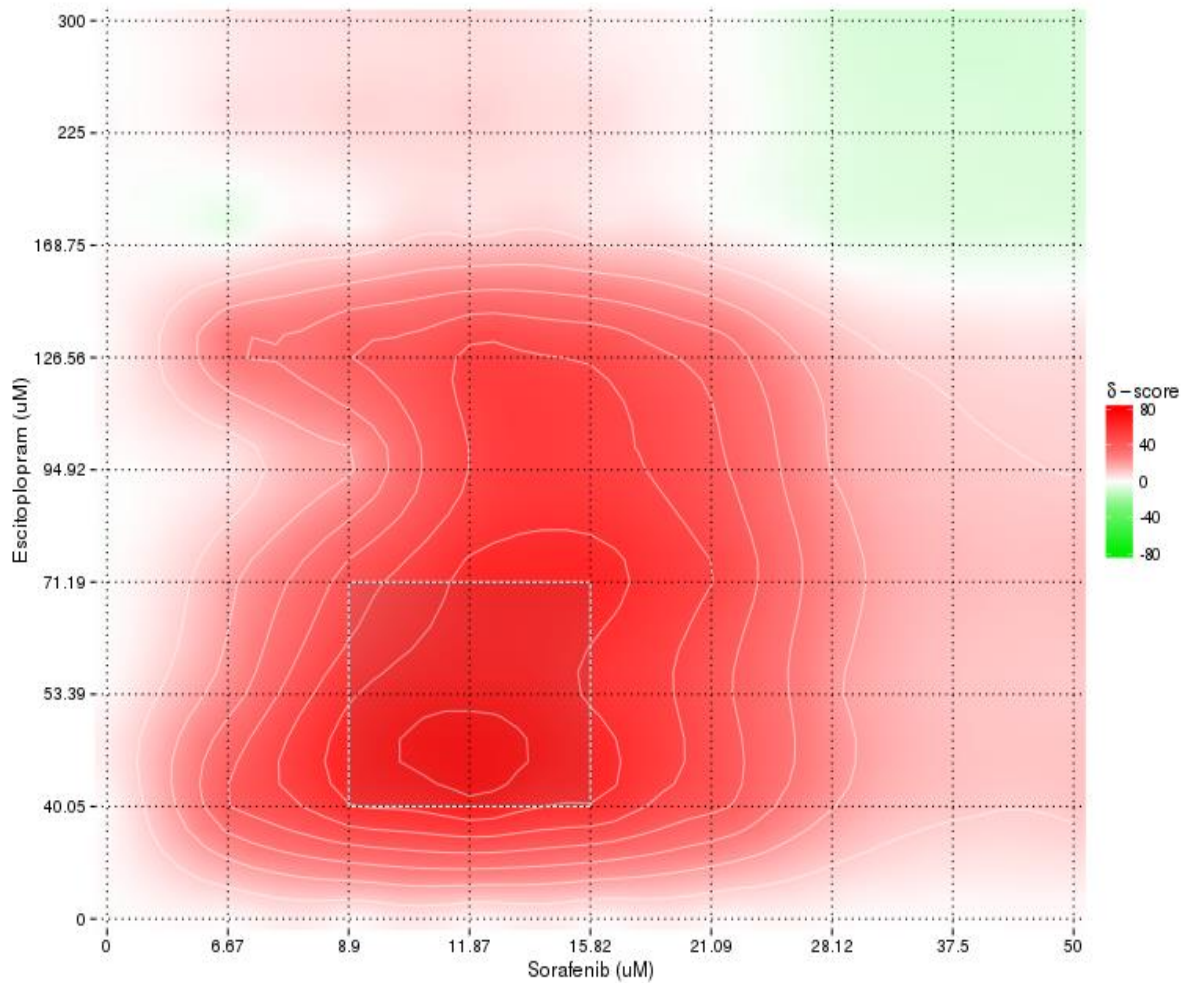


Figure 2: a) % de valeurs d'inhibition calculées par l'application de SynergyFinder. Il montre la relation entre différentes concentrations d'escitalopram et de sorafénib dans différentes combinaisons et réponse antiproliférative. b) Carte de synergie 2D et score de synergie moyen. La zone avec l'effet le plus synergique est indiquée par des lignes pointillées.

L'effet de la combinaison d'escitalopram et sorafénib sur la morphologie cellulaire

La morphologie des cellules traitées avec le médicament a été évaluée par microscopie à contraste de phase avec le groupe témoin. Seules les cellules traitées à l'escitalopram ou au sorafénib sont rétrécies et plus petites que les cellules saines témoins (figures 3A, B et C). De plus, des cellules se développant sur les cellules (bulles) et les vacuoles dans le cytoplasme des cellules sont observées.

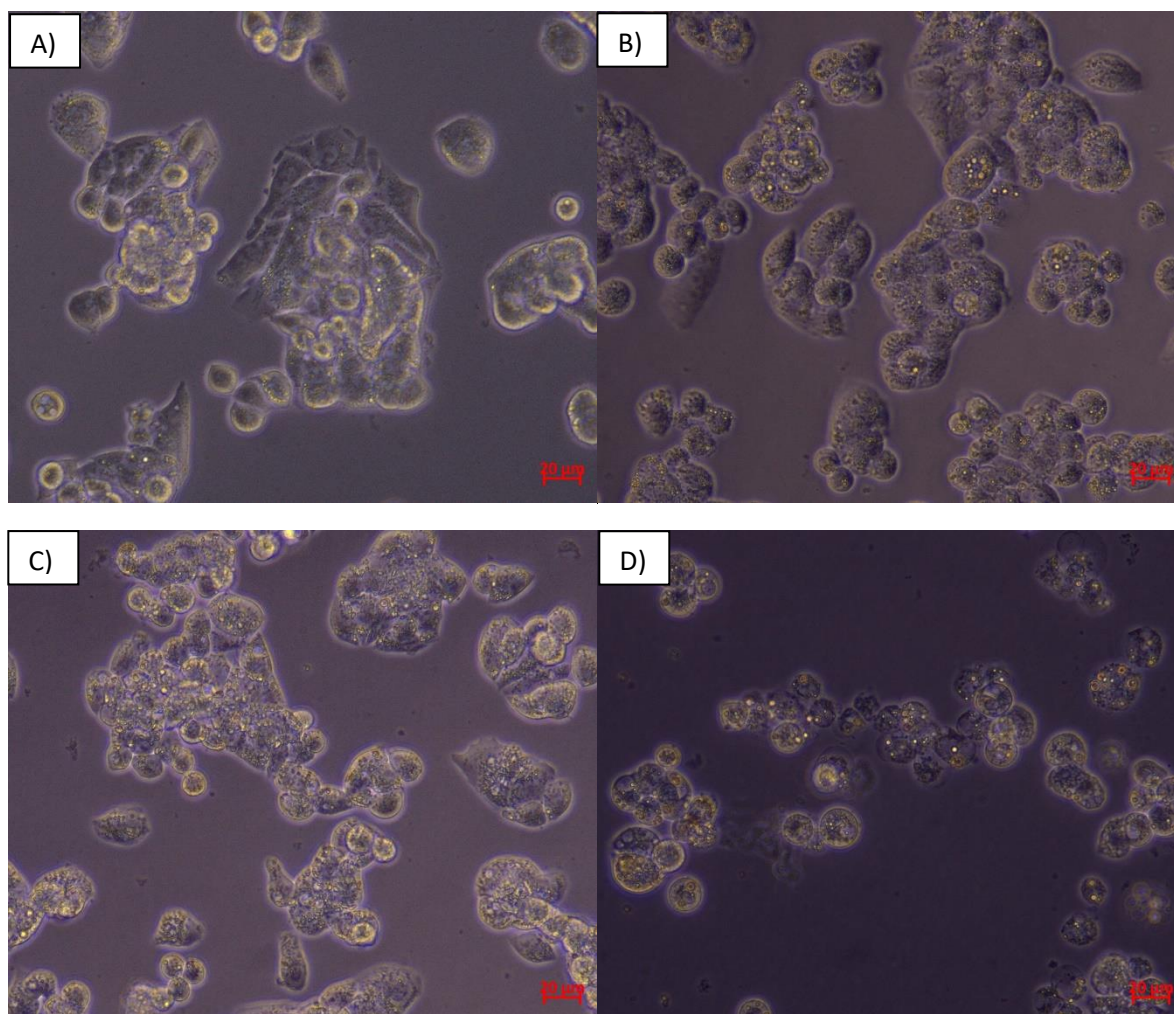


Figure 3: Les cellules traitées avec le groupe control (A), le sorafénib uniquement (B), l'escitalopram uniquement (C) La combinaison d'escitalopram et de sorafénib (D) ont été évaluées pour leur morphologie par microscopie à contraste de phase

DISCUSSION

Retour de vieux médicaments, repositionnement d'eux est devenu une découverte de médicaments attrayante. Le repositionnement des médicaments a représenté environ 30% des médicaments et vaccins approuvés par la Food and Drug Administration (FDA) au cours des dernières années¹⁸. La pharmacothérapie pour la dépression s'est développée au cours des 30 dernières années. Les antidépresseurs les plus couramment utilisés, notamment les inhibiteurs sélectifs du recaptage de la sérotonine (ISRS) et les inhibiteurs du recaptage de la sérotonine et de la noradrénaline (IRSNA), ont été approuvés pour une utilisation de la fin des années 1980 à la fin des années 2000. L'escitalopram, l'énantiomère S du citalopram, a été introduit en 2002 et constitue le plus récent ISRS⁹. Dans une récente méta-analyse

¹⁸ Jin G, Wong ST. Toward better drug repositioning: prioritizing and integrating existing methods into efficient pipelines. *Drug Discov Today* 2014;19:637-44. doi:10.1016/j.drudis.2013.11.005. Epub 2013 Nov 14.

comparant l'efficacité et l'acceptabilité de antidépresseurs dans le traitement aigu de l'adulte présentant un trouble dépressif majeur, l'escitalopram s'est révélé très efficace et acceptable¹⁹. Le sorafénib est un inhibiteur oral de la multikinase en qui s'est révélé efficace dans les essais cliniques de phase III chez des patients atteints d'un carcinome hépatocellulaire avancé (HCC)⁴. Après le sorafénib, l'utilisation clinique a été approuvée pour l'indication pertinente. La dépression est une comorbidité fréquente dans les cas de cancer et affecte plus de 10% des patients²⁰. Différents antidépresseurs sont utilisés pour traiter la dépression chez ces patients. L'escitalopram est un inhibiteur faible ou négligeable du CYP2D6 et il est peu probable qu'il interagisse avec les médicaments anticancéreux²¹. Des études récentes ont montré que l'escitalopram induit l'apoptose dans la culture cellulaire et réduit la prolifération^{22, 23, 24}. Un effet antiprolifératif similaire a été démontré dans l'expérimentation animale²⁰. Pour ces raisons, l'escitalopram peut être administré en association avec d'autres agents anticancéreux pour le traitement clinique du cancer. Dans cette étude, l'escitalopram administré seul ou ensemble avec sorafénib à des cellules HepG2 dans une large gamme de doses. La valeur IC₅₀ de l'escitalopram était de 130 μ M par le test de prolifération cellulaire XTT. Kuwahara et ses collaborateurs ont précédemment rapporté cette valeur à 94,8 μ M dans une étude portant sur des cellules HepG2. En revanche, la cytotoxicité a été évaluée avec le sel monosodique de 2- (2-méthoxy-4-nitrophényl) -3- (4-nitrophényl) -5- (2,4-disulfophényl) -2H-tétrazolium (WST-8)¹⁹. Dans les cellules de glioblastome, la valeur de CI₅₀ de l'escitalopram a été calculée à 107 μ M après 48 heures par le test de prolifération des cellules MTT¹⁸. La combinaison d'escitalopram et de sorafénib a un effet synergique. La plage de doses de 40,1 μ M et 71,2 μ M pour l'escitalopram et les gammes de doses de 8,9 μ M et 15,8 μ M pour le sorafénib sont considérées comme l'effet le plus synergique. Par rapport aux effets d'un médicament seul, des concentrations plus faibles de sorafénib et d'escitalopram se sont avérées efficaces pour inhiber la prolifération cellulaire dans les applications combinées. Comme on le sait, il s'agit de la première étude dans laquelle une combinaison d'inhibiteur de multikinase, le sorafénib et d'antidépresseur ISRS, l'escitalopram, a été administrée. Le sorafénib montre que son effet antiprolifératif est renforcé de manière synergique avec l'escitalopram. On pense que cette découverte est à la base des études évaluant l'efficacité de la co-administration de sorafénib et d'escitalopram dans le traitement du CHC.

CONCLUSIONS

L'administration d'une association d'escitalopram et de sorafénib ont diminué la prolifération. Les cellules se contractent, se contractent et flottent dans le milieu en se

¹⁹ Cipriani A, Furukawa TA, Salanti G, Chaimani A et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet* 2018;391:1357-66.

²⁰ Smith, HR. Depression in cancer patients: Pathogenesis, implications and treatment. *Oncol Lett* 2015; 9: 1509-14.

²¹ Caraci F, Crupi R, Drago F, Spina E. Metabolic drug interactions between antidepressants and anticancer drugs: focus on selective serotonin reuptake inhibitors and hypericum extract. *Curr Drug Metab* 2011;12: 570-7.

²² Dikmen M, Cantürk Z, Oztürk Y. Escitalopram oxalate, a selective serotonin reuptake inhibitor, exhibits cytotoxic and apoptotic effects in glioma C6 cells. *Acta Neuropsychiatr* 2011; 23: 173-8.

²³ Kuwahara J, Yamada T, Egashira N, Ueda M, et al. Comparison of the Anti-tumor Effects of Selective Serotonin Reuptake Inhibitors as Well as Serotonin and Norepinephrine Reuptake Inhibitors in Human Hepatocellular Carcinoma Cells. *Biol Pharm Bull* 2015; 38:1410-4. doi: 10.1248/bpb.b15-00128.21)

²⁴ Chen VC, Hsieh YH, Chen LJ, Hsu TC, Tzang BS. Escitalopram oxalate induces apoptosis in U-87MG cells and autophagy in GBM8401 cells. *J Cell Mol Med* 2018; 22:1167-78. doi: 10.1111/jcmm.13372.

séparant de la surface à laquelle elles adhèrent. Ces caractéristiques morphologiques sont compatibles avec l'apoptose de mort cellulaire programmée.

Déclaration de liens d'intérêts

Les auteurs n'ont aucun conflit d'intérêts à déclarer.

Remerciements

Nous remercions İrem Özbey et Professeur agrégé Gülbüz Sezgin pour vérifier l'orthographe et la grammaire; Hatice Mardin pour assistance technique. Le projet est soutenu par le conseil de recherche de l'Université de Maltepe.

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