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THROMBOPROPHYLAXIS IN SURGICAL PATIENTS

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ABSTRACT:
SURGICAL PATIENTS HAVE AN INCREASED RISK FOR VENOUS THROMBOEMBOLISM, THE MOST COMMON PREVENTABLE CAUSE OF DEATH IN THIS CATEGORY OF PATIENTS. THROMBOPROPHYLAXIS WITH MECHANICAL METHODS, SUCH AS INTERMITENT PNEUMATIC LEG COMPRESSION AND GRADUATED COMPRESSION STOCKS, AND ANTICOAGULANT AGENTS, SUCH AS UNFRACTIONED HEPARIN AND LOW MOLECULAR WEIGHT HEPARIN ARE COMMONLY USED TO PREVENT THROMBOSIS,THUS REDUCING MORBIDITY AND MORTALITY IN THESE PATIENTS.

KEY WORDS: VENOUS THROMBOEMBOLISM, ANTICOAGULANTS, THROMBOPROPHYLAXIS

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INTRODUCTION

Venous thromboembolism (VTE) refers to the formation of blood clots in one of the large veins of the body, especially in the veins from lower limbs[8]. VTE encompasses two other conditions: deep vein thrombosis (DVT) of the leg or pelvis and pulmonary embolism (PE)[9].

VTE is associated with high morbidity and mortality in hospitalized patients. Therefore, thromboprophylaxis is the most adequate strategy in surgical patients in order to decrease morbidity and mortality from VTE[10].

MAIN TEXT

Epidemiology

Thrombosis in the surgical patientis a major cause of death in the United States. Each year, 2 milion of individuals die because of VTE[11].

VTE is the third cause of morbidity, after myocardial infarction and stroke. The incidence for VTE in the European population is 104 - 183 per 100.000 persons/year[12]. The frequency of VTE is from 15 to 40% for thegeneral surgery patients and from 40 to 60% in patients who undergo orthopaedic surgery. Also, 15% of patients hospitalized for an acute medical pathology will develop VTE[13].

VTE is especially a pathology associated with older age. Also, the incidence rates of VTE are higher for men (130 per 100.000 persons) than for women (110 per 100.000 persons)[14].

Surgical patients and risk factors for VTE

Numerous studies have shown that surgical patients are at high risk for developing VTE. Data from literature noticed that without thromboprophylaxis, fatal PE have a frecquency from 0,1% to 0,8% in general surgical procedures, 3% in patients with surgical hip replacement and 7% in patients undergoing orthopedic surgery for a fractured hip[15].

The risk for VTE is higher in patients who undergo major general surgery or orthopedic surgery, such as surgery of the lower limb, hip or knee arthroplasty or surgery for hip fracture[16]. The risk factors for VTE are represented by[17]:

- lower extremity paralysis due to spinal cord injury,
-fracture of the pelvis, hip or long bones,
-multiple trauma,

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[8] Geerts W, Heit JA, Clagett GP et al. *Prevention of venous thromboembolism*. Chest. 2001;119:132S-175S

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-obesity,
-cancer,
-previous VTE,
-prolonged immobilization,
-use of hormonal therapy,
-central venous catheters,
-increased age,
-comorbidities, such as stroke, congestive heart failure, myocardial infarction in the last 6 months.

Also, there are blood clotting abnormalities that predispose to VTE, such as hereditary or acquired thrombophilia, deficiencies of antithrombin, protein C or protein S, factor V mutation (Leiden) and antiphospholipid antibody syndrome[18].

VTE risk stratification[19]

Low risk patients:

- minor surgical procedures
- patients <40 years, without risk factors for VTE
- no need for specific thrombopropylactic methods

Moderate risk patients:

- minor surgical procedures in patients with risk factors for VTE
- minor surgery for patients between 40-60 years without risk factors
- major surgery for patients < 40 years or without risk factors
- needs thromboprophylaxy with UFH, LMWH, IPC or GCS. The use of IPC or GCS are less effective than anticoagulants in these cases

High risk patients:

- minor surgery in patients > 60 years
- major surgery in patients > 40 years or with risk factors for VTE

Highest risk patients:

- major surgery in patients > 60 years
- major orthopedic surgery
- spinal cord injury
- trauma
- needs HNF, LMWH or warfarin, associated with IPC or GCS

[18] Bick RL. *Management of venous thrombosis and thromboembolism: prevention and treatment.* Surg Technol Int. 2002. 10: 226

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Thromboprophylactic methods

Thromboprofylactic methods are classified in mechanical and pharmacological agents[20]. Mechanical agents are represented by intermitent pneumatic leg compression and graduated compression stocks.

Intermitent pneumatic leg compression (IPC) is used for the prevention of VTE in surgical patients with moderate risk and in patients who undergo neurosurgery and cardiac surgery.

Graduated compression stocks (GCS) is used for low risk surgical patients[21].

Pharmacological agents commonly used are anticoagulants, such as low dose or adjusted dose of unfractioned heparin (UFH), low-molecular-weight heparin (LMWH), fondaparinux and oral anticoagulants[22].

UFH and LMWH binds reversibly to antithrombin III and accelerate the inhibition of thrombin and activated factor X.

UFH will initially be administred in a dose of 5000 units and then will be given in a continued endovenous infusion in a dose of 16 - 20 IU per body weight, while maintaining an activated partial thromboplastin time (aPTT) twice more than normal.

UFH has an increased risk for hematomas. Also, the platelet count should be monitored every day, because UFH can induce thrombocytopenia[23]. Postoperatory, if oral anticoagulant is recommended, it will be administred concomitant with UFH, starting on the sixth day of treatment with heparin.

UFH will be given in a single bolus of 5000 units at every 8 hours for prophylaxy of VTE. In cases of treatment of VTE or in patients with history of thrombosis, UFH will be administred in a initial dose of 5000 units and then in continuous infusion.

LMWH (Enoxaparin, Dalteparin), administred once or twice daily, is as effective as UFH in prevention of thrombosis. The side effects, such as bleeding or hematomas, are lower for LMWH than for UFH. LMWH is administred subcutaneous. For prophylaxy of VTE, Enoxaparin is given 1 mg per kilogram body weight per 24 hours. Dalteparin is administred 100 IU per kilogram body weight, one dosefor 24 hours[24].

Oral anticoagulants, such as antagonists of vitamin K, can be initiated postoperatory if is recommended. Oral anticoagulants will not prevent the occurence of the small venous thrombi, but can prevent their extension[25].

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Fondaparinux is administred in a single dose per 24 hours, being adjusted according to body weight: 5 mg per 24 hours at body weight over 50 kg, 7,5 mg at body weight between 50 and 100 kg and 10 mg at over 100 kg[26].

Principles of achieving thromboprophylaxis

Guidelines notice that in cases of low risk for VTE, in patients without risk factors, there is no need for anticoagulants[27].

Studies on this issue notice that in patients with moderate risk, a dose of LMWH will be administred with 2 hours before the surgical procedure[6]. Also, LMWH will be continued postoperatory in a single dose/24 hours.

Data from literature shows that in cases of patients with high risk for developing VTE, LMWH will be initiated with 12 hours before the surgery and will be continued postoperatory in a single dose/24 hours[28].

Also,guidelines notice that patients with highest risk for VTE or with multiple risk factors will receive high dose of LMWH with 2 hours before the surgery and another dose at 12 hours postoperatory. LMWH will be continued with one dose for 24 hours[29].

Guidelines recommend that if UFH is used in patients with moderate risk for developing VTE, it will be administred in doses of 5000 units at every 12 hours. For the patients with high risk, UFH will be given in bolus of 5000 units at every 8 hours.

As a general rule, tromboprophylaxis is realised until the risk factors for which it was indicated are minimized or until the patient is in a lower risk class.

Thromboprophylaxis in clinical settings

Patients undergoing *general surgery*, with low risk for VTE, do not need specific methods of thromboprophylaxis, in these cases adequate hidration being essential. Patients in other category of risk, need prophylaxis with low dose UFH or LMWH[30]. Large trials which compared UFH with LMWH observed that these two agents have the same efficiency[7]. Mechanical methods are used for the patients with high risk of bleeding. Also, for the patients with high risk for VTE, mechanical methods can be combined with anticoagulants. Heparin or oral anticoagulants should be

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administred for at least 10 days. Patients with risk factors for VTE, such as cancer, previous VTE, hormonal therapy, need thromboprophylaxis with anticoagulants for at least 30 days[31].

In patients undergoing *vascular or cardiothoracic surgery*, should be administred UFH or LMWH. The incidence of VTE for these patients is for 25-30%. Antiplatelet drugs should be administred 1 year in patients with coronary artery bypass grafting or peripheral vascular reconstructive surgery[32].

In *neurosurgical patients*, mechanical methods of thromboprophylaxis are recommended. Also, in high risk patients, mechanical methods will be associated with anticoagulants[33]. On the other hand, studies noticed an incidence of 24-33% of DVT for mechanical agents as a unique method of thromboprophylaxis[34]. In several studies, it was shown that the combination of LMWH with mechanical methods reduced VTE from 33% to 13% [35].

In cases of *acute spinal cord injury*, LMWH is recommended. Studies on this issue noticed that for spinal cord injury, UFH is less effective than LMWH[36]. Also, LMWH or oral anticoagulants will be administred for extended thromboprophylaxis[37]. Mechanical methods will be used in cases of high risk of bleeding.

In cases of *trauma*, patients will receive anticoagulants. A randomized trial which compared UFH with LMWH, rates of DVT were reduced from 44% to 15% with UFH and from 31% to 6% with LMWH[38]. Based on this trial, patients with trauma should receive thromboprophylaxis with

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LMWH. Mechanical methods will be used in case of contraindicationfor anticoagulants. Also, inferior vena cava filters are used in situations that anticoagulants are contraindicated. UFH or oral anticoagulants are used in cases of hip fracture or hip replacement therapy. A cohort study conducted on patients with multiple trauma shown a rate of ultrasound detected DVT of 58%.[39] Thromboprophylaxis with anticoagulants in these case should be continued longer if patients remain immobilized.

Patients undergoing *major orthopedic surgery*, including hip or knee arthroplasty, need primary profilaxy with anticoagulants. In these patients, extended tromboprophylaxis is needed[40]. However, two trials noticed an incidence of 27% of DVT in patients undergoing surgery for hip fracture receving UFH[41].

CONCLUSION

VTE is the most severe complication in surgical patients, being associated with high rates of mortality and morbidity. The risk for VTE is determined by the type of surgery and the patient characteristics. Thromboprophylaxis with optimal mechanical or pharmacological agents is the most effective strategy to reduce mortality and morbidity for the patients undergoing different types of surgical procedures.

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