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STAGING ENDOMETRIOSIS – A CONTINUOUS CHALLENGE

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ABSTRACT:
ENDOMETRIOSIS IS SUCH A COMPLEX DISEASE, WITH VARIOUS CLINICAL MANIFESTATIONS AND MORPHOPATHOLOGICAL PRESENTATIONS, THAT MOST OF THE TIME, THE INTRAOPERATORY FINDINGS DON'T MATCH THE PATIENT'S SYMPTOMATOLOGY. IN THAT REGARD, FOR MANY YEARS, GYNECOLOGISTS AROUND THE WORLD STRUGGELED TO CONCEIVE MULTIPLE CLASSIFICATION AND STAGING SYSTEMS IN ORDER TO CONSIDERATE AND TO INCLUDE ALL THE ASPECTS OF ENDOMETRIOSIS FROM QUALITY OF LIFE, PAIN, INFERTILITY, TO BETTER RESEARCH APPLICATIONS AND BETTER MANAGEMENT OF THE DISEASE.

KEYWORDS: CLASSIFICATION SYSTEMS, STAGING SYSTEMS, ENDOMETRIOSIS

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INTRODUCTION

Endometriosis is an enigmatic disease with many facets. The endometrial-like tissue has the ability to proliferate outside the uterine cavity and create great disturbances not only at the *site of implantation, but also at the eutopic endometrium, partially on behalf of its functional capacity to respond to hormonal stimuli (exogenous, endogenous or local)*[8].

The pelvic or extrapelvic endometriosic implants produce the well known "endometriosis effects". Excessive vaginal bleeding, pain (with different grades of intensity), infertility, intestinal occlusion, urinary symptoms, malignancies or, in rare cases, thoracic or neurologic symptoms are only some of the complications associated with endometriosis.

This pathology is an important economic burden in society and a continuous source for frustration among clinicians due to the difficulty in alleviating pain, reducing and preventing the infertility rates or improving the quality of life unaffected women[9].

Endometriosis has a prevalence of 8 – 10% among women of reproductive age, up to 30% of patients having primary or secondary infertility issues related to endometriosis [1]. Its prevalence is higher among women with subfertility (up to 50%) than fertile women (5–10%)[10].

The first historical reference of endometriosis dates back since 1500 BC from a discovery of an ancient Egyptian papyrus which described a treatment for a "painful disorder of menstruation". More than 3000 years later, Daniel Shroen described in his 1690 book titled *"Disputatio Inauguralis Medica de Ulceribus Ulceri"*, a more detailed presentation of the peritoneal endometriosis describing the adhesions and endometriomas as complications of the disease.

Since then, until the early 20th century, scientists from Germany, Holland, England or Scotland provided extensive studies on endometriosis, introducing in the medical dictionary terms like "chocolate cyst" or endometriomas[11]. At that point, the main concern shifted towards the pathogenesis of endometriosis, thus emerging theories[12] like the lymphatic dissemination of the endometrial tissue, the persistence of Wolffian rests on retrograde menstruation and implantation theory[13].

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Giving that, gynecologists from around the world deal with such a chameleonic disease (with no pathognomonic signs or symptoms[14]), the diagnosis of endometriosis can be delayed many years[15], ranging from 7 to 12[16].

One of the biggest challenges consists in establishing the best way to treat the disease and to find the perfect validated staging systems for helping the doctors manage the disease accurately[17].

Staging systems are important in order to create a common use, to evaluate the prognosis, the therapy response or the risk of recurrence, to evaluate the quality of life in women with endometriosis and to facilitate research applications[18].

Despite the struggle in developing staging systems, the classification of endometriosis has remained controversial, due to the many forms of the disease, the focusing on the anatomy and histology for 'surgical staging' and recently, on the prognostic value[19].

In 1921, Sampson elaborated the first classification of endometriosis, followed by similar attempts from Albrecht et al. in 1955, Acosta et al. in 1973 (fig. 1)[20], Kistner in 1977 (fig. 2) and Buttram in 1978 (fig. 3) [10,13].Their systems were criticized for many reasons, *including their inability to predict clinical outcomes*[21]*, especially the pregnancy rates in infertile patients*[22].

The American Society for Reproductive Medicine was founded in 1944 in Chicago with the name of American Society for the Study of Sterility and later renamed as American Fertility Society and includes today members from over 100 countries worldwide[23]. In 1979, the society published the AFS score which, following its multiple revisions from 1985 (rAFS score) and finally 1996 (rASRM) (fig. 4), became the most used classification worldwide[24].

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[19] Johnson, NP; Hummelshoj, L; Adamson, GD; Keckstein, J; Taylor, HS; Abrao, MS; Bush, D; Kiesel, L; Tamimi, R; Sharpe-Timms, KL; Rombauts, L; Giudice, LC; for the World Endometriosis Society Sao Paulo Consortium. *World Endometriosis Society consensus on the classification of endometriosis.* Hum Reprod, 2017, 32(2): 315-324.

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[23] https://en.wikipedia.org/wiki/American_Society_for_Reproductive_Medicine

[24] Johnson, NP; Hummelshoj, L; Adamson, GD; Keckstein, J; Taylor, HS; Abrao, MS; Bush, D; Kiesel, L; Tamimi, R; Sharpe-Timms, KL; Rombauts, L; Giudice, LC; for the World Endometriosis Society Sao Paulo Consortium. *World*

In order to understand why additional systems for endometriosis staging were created, a brief presentation of the rASRM Classification is required. Although the rASRM score meets the requirements only partially, for an endometriosis classification, it has the advantages of being relatively easy to be used by the clinicians and to be understood by the patients[25]. Its disadvantages include the lack of information about the retroperitoneal structures with deep infiltrating endometriosis (DIE) and a poor correlation with pain[26] and sterility, this criteria not being included in the scoring system[27].

Mild

1. Scattered, fresh lesions lie, implants not associated with scarring or retraction of the peritoneum) in the anterior or posterior cul-de-sac or pelvic peritoneum.
2. Rare surface implant on ovary, with no endometrioma, without surface scarring and retraction, or small endometrioma.
3. No peritubular adhesions.

Moderate

1. Endometriosis involving one or both ovaries, with several surface lesions, with scarring and retraction, or small endometrioma.
2. Minimal periovarian adhesions associated with ovarian lesions described.
3. Minimal peritubular adhesions associated with ovarian lesions described.
4. Superficial implants in the anterior and/or posterior cul-de-sac with scarring and retraction. Some adhesions, but not sigmoid invasion.

Severe

1. Endometriosis involving one or both ovaries with endometrioma > 2 x 2 cm (usually both).
2. One or both ovaries bound down by adhesions associated with endometriosis, with or without tubal adhesions to ovaries.
3. One or both tubes bound down or obstructed by endometriosis; associated adhesions or lesions.
4. Obliteration of the cul-de-sac from adhesions or lesions associated with endometriosis.

Endometriosis Society consensus on the classification of endometriosis. Hum Reprod, 2017, 32(2): 315-324; Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026; Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

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5. Thickening of the uterosacral ligaments and cul-de-sac lesions from invasive endometriosis with obliteration of the cul-de-sac.
6. Significant bowel or urinary tract involvement[28].

The rASRM score represents the sum of the values assigned when evaluating the size of the endometriosic lesions which involves the peritoneum and the ovaries, the adhesions that affect the ovaries and the Fallopian tubes and the degree (partial or complete) of posterior cul-de-sac obliteration. The resulting number classifies endometriosis into four grades of severity, as it follows: minimal (stage I - 1 to 5 points), mild (stage II - 6 to 15 points), moderate (stage III– 16 to 40 points) and severe (stage IV > 40 points)[29].

The deficiencies in the rASRM score regarding fertility are covered by Adamson and Pasta's 2010 Endometriosis Fertility Index (EFI score), while the lack of description of retroperitoneal structures affected by DIE is surpassed by the Enzian score[30] and pain is described by the American Association of Gynecological Laparoscopists (AAGL) classification[31].

Stage I

Areas of endometriosis are present on the posterior pelvic peritoneum (cul-de-sac, uterosacral ligaments} or on the surface of the broad ligaments but do not exceed 5 mm in diameter. Avascular adhesions may involve the tubes, but the fimbriae are free. The ovaries may show a few avascular adhesions, but there is no ovarian fixation. The surfaces of the bowel and the appendix are normal.

Stage II

A. Areas of endometriosis are present on the posterior pelvic peritoneum (cul-de-sac, uterosacral ligaments; and the broad ligaments but do not exceed 5 mm in diameter. Avascular adhesions may involve the tubes, but the fimbriae are free. Ovarian involvement by endometriosis has been subclassified as follow:

IIA-1: Endometrial cyst or surface is 5 cm or less
IIA-2: Endometrial cyst or surface is over 5 cm.
IIA-3: Ruptured endometrioma; the bowel and the appendix are normal.

[28] Roberts, CP; Rock, JA; *The current staging system for endometriosis: does it help?* Obstet Gynecol Clin North Am. 2003 Mar; 30(1):115-32.
[29] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026.
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[31] Johnson, NP; Hummelshoj, L; Adamson, GD; Keckstein, J; Taylor, HS; Abrao, MS; Bush, D; Kiesel, L; Tamimi, R; Sharpe-Timms, KL; Rombauts, L; Giudice, LC; for the World Endometriosis Society Sao Paulo Consortium. *World Endometriosis Society consensus on the classification of endometriosis.* Hum Reprod, 2017, 32(2): 315-324.

Stage IIB

The posterior leaf of the broad ligament is covered by adherent ovarian tissue. The tubes present adhesions not removable by endoscopic procedures. The fimbriae are free. The ovaries are fixed to the broad ligament and show areas of endometriosis over 5 mm in diameter. The cul-de-sac presents multiple implants, but there is no adherent bowel nor is the uterus in fixed position. The bowel and the appendix are normal.

Stage III

The posterior leaf of the broad ligament may be covered by adherent tube or ovary. The tubal fimbriae are covered by adhesions. The ovaries are adherent to the broad ligament, and tube may or may not show surface endometriosis or endometriomas. The cul-de-sac shows multiple areas of endometriosis, but there is no evidence of adherent bowel or uterine fixation. The bowel and the appendix are normal.

Stage IV

Endometriosis involves the bladder serosa, and the uterus is in fixed, third-decree retroversion. The cul-de-sac is covered by adherent bowel or is obliterated by the fixed uterus. The bowel is adherent to the cul-de-sac, uterosacral ligaments, or uterine corpus. The appendix may be involved by the endometriotic process[32].

THE REVISED ENZIAN CLASSIFICATION

The Enzian staging system was developed in 2005[33]. It was designed with the purpose to complete the rASRM score and to fulfil the classification of DIE lesions with the involvement of retroperitoneal structures and other organs[34]. It also correlates the clinical symptoms (pain and dysmenorrhea) with the severity grades of the disease[35]. Because of some overlaps with the rASRM score, the Enzian classification was revised (2010 and 2011) in order to optimize the system and to create a separate classification for DIE[36]. Despite of being simplified, this scoring system has

[32] Roberts, CP; Rock, JA; *The current staging system for endometriosis: does it help?* Obstet Gynecol Clin North Am. 2003 Mar; 30(1):115-32.

[33] Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1; Adamson, GD; *Endometriosis Fertility Index: is it better than the present staging systems?* Curr Opin Obstet Gynecol 2013, 25: 186–192. doi:10.1097/GCO.0b013e32836091da.

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[35] Adamson, GD; *Endometriosis Fertility Index: is it better than the present staging systems?* Curr Opin Obstet Gynecol 2013, 25: 186–192. doi:10.1097/GCO.0b013e32836091da.

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still a low acceptance at the international level and is currently used almost exclusively in German-speaking countries. It is more complicated than rASRM Classification and it is more difficult to be understood by the patients. Also, there is currently no data available about the correlation of the Enzian classification with sterility and infertility[37].

Stage I (Peritoneum)

A. No peritoneal involvement.

B. Scattered superficial surface endometrial implants on the pelvic peritoneum (anterior or posterior cul-de-sac, uterosacral ligaments, or the broad ligaments), which do not *exceed* 5 mm in diameter. Neither tubal nor ovarian involvement.

C. Same as for B, but invasive endometriosis or plaques or endometrial implants > 5 mm in diameter. Fine, filmy adhesion may be present that may be lysed without great danger of resultant adhesions.

Stage II (Ovarian): 1. Right; 2. Left; 3. Bilateral

A. No ovarian involvement.

B. Superficial surface endometrial implants of ovary of < 5 mm in diameter, which can be removed by scraping or f taiga ration without great danger of resultant adhesions. Fine, filmy adhesions may be present and lysed without great danger of resultant adhesions.

C. Invasive endometriosis (plaques or endometrioma) > 5 mm but < 2 cm that require surgical removal. Fine, filmy adhesion may be present, which may be lysed without great danger of resultant adhesions.

D. Invasive endometriosis > 2 cm that requires surgical removal or a ruptured endometrioma of any size. Fine, filmy adhesion may be present, which may be lysed without great danger of resultant adhesions.

E. B, C, or D with sufficient dense adhesions to fix ovary to adjacent tissue (usually posterior leaf of broad ligament).

Stage III (Tuba): 1. Right; 2. Left; 3. Bilateral

A. No tubal involvement.

B. Superficial endometrial implants on tube that do not *exceed* 5 mm in diameter and can be removed by scraping or fulgaration without great danger of resultant adhesions. Fine, filmy adhesion may be present, which may be lysed without great danger of resultant adhesions.

C. Invasive endometriosis (plaques or endometrioma > 5 mm but < 2 cm that require surgical removal. Fine, filmy adhesion may be present, which may be lysed without great danger of resultant adhesions.

D. Tube involved with adhesions that distort tuba I anatomy and\or limit tubal movement. Fimbriae are free and tube is patent. C may be present.

[37] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026.

E. Fimbriae are covered by adhesions or distal end of tube is occluded. B, C, or D may be present.

Stage IV (Cul-de-sac)

A. Neither B nor C is present.

B. Invasive endometriosis of bladder or colon.

C. Posterior cul-de-sac obliterated and for uterus fixed and retroverted. Bowel or adnexa may be adherent to cul-de-sac area. B is usually present[38].

After excluding from the original classification, the minor peritoneal lesions, the revised Enzian classification includes three degrees of severity (grade 1: invasion <1 cm, grade 2: invasion 1–3 cm, grade 3: invasion > 3 cm)[39].

The severity is rated after evaluating the lesions from each compartment[40], giving that retroperitoneal structures are divided into three compartments (Compartment A: rectovaginal septum, vagina; Compartment B: Sacro uterine ligament to the pelvic wall; Compartment C: rectum, sigmoid colon).

Deep invasion beyond the lesser pelvis and invasion of the organs are registered separately as it follows: FA = adenomyosis, FB = involvement of the bladder, FU = intrinsec involvement of the ureter, FI = bowel disease cranially to the rectosigmoid junction, and FO ("others") = other locations - for example abdominal wall endometriosis[41].

[38] Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[39] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026; Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[40] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026; Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[41] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026; Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

The Enzian classification is not a scoring system (like the rASRM score), but more a morphological description of the endometriosic lesions, with size included (fig. 5)[42]. It has the advantage that it can also be used as a clinical classification, similarly to the TNM classification[43].

The number that follows represents the size of the lesion and the following lowercase letter indicates the location or the involved compartment, while two letters indicate bilateral disease[44]. For example, when the clinical evaluation suspects rectovaginal septum involvement, the lesion is referred to as Enzian: A1 B0 C0 ("c" for "clinical"). If the suspicion is histologically confirmed, the lesion is graded Enzian: A1 B0 C0. Thus, this nomenclature allows a more accurate surgical planning and a suspicion over the involvement of retroperitoneal structures before the postoperative histological confirmation[45]. The prefix „E" indicates the presence of an endometriosic tumor[46].

THE EFI SCORE

Laparoscopic surgery is considered the first choice for diagnosis and treatment of infertility related to endometriosis[47].

Adamson and Pasta developed in 2010 the EFI score, in order to predict the probability of pregnancy following the surgical staging and treatment of endometriosis in patients who attempt spontaneous non-IVF conception[48].

The EFI score emerged due to the need of filling the gap of rASF score when predicting postoperative pregnancy rates in women with endometriosis[49]. One factor identified to be correlated with pregnancy rate, but not included in the EFI is uterine abnormality, this simply because uterine abnormality is very uncommon in infertile patients with endometriosis[50]. However,

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[42] Adamson, GD; *Endometriosis classification: an update*. Curr Opin Obstet Gynecol. 2011 Aug; 23(4): 213-20. doi: 10.1097/GCO.0b013e328348a3ba; Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[43] Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[44] Adamson, GD; *Endometriosis classification: an update*. Curr Opin Obstet Gynecol. 2011 Aug; 23(4): 213-20. doi: 10.1097/GCO.0b013e328348a3ba.

[45] Haas, D; Wurm, P; Shamiyeh, A; Shebl, O; Chvatal, R; Oppelt, P; *Efficacy of the revised Enzian classification: a retrospective analysis. Does the revised Enzian classification solve the problem of duplicate classification in rASRM and Enzian?* Arch Gynecol Obstet. 2013 May; 287(5): 941-5. doi: 10.1007/s00404-012-2647-1.

[46] Adamson, GD; *Endometriosis classification: an update*. Curr Opin Obstet Gynecol. 2011 Aug; 23(4): 213-20. doi: 10.1097/GCO.0b013e328348a3ba.

[47] Zeng, C; Xu, JN; Zhou, Y; Zhou, YF; Zhu, SN; Xue, Q; *Reproductive performance after surgery for endometriosis: predictive value of the revised american fertility society classification and the Endometriosis Fertility Index.* Gynecol Obstet Invest. 2014; 77(3): 180-5. doi: 10.1159/000358390.

[48] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

[49] Zeng, C; Xu, JN; Zhou, Y; Zhou, YF; Zhu, SN; Xue, Q; *Reproductive performance after surgery for endometriosis: predictive value of the revised american fertility society classification and the Endometriosis Fertility Index.* Gynecol Obstet Invest. 2014; 77(3): 180-5. doi: 10.1159/000358390.

[50] Nada, Elena-Silvia; Brinduse, Lacramioara; Bratu, Ovidiu; Marcu, Dragos; Bratila, Elvira; *Endometriosis-associated infertility*, Modern Medicine, 2018, 25 (3): 132.

when this condition is discovered, it needs to be taken into consideration in predicting pregnancy rates. Defective reproductive function of the uterus or gametes will clearly affect prognosis and need to be taken into consideration as fertility factors, just as they would with any patient with any other pathology[51].

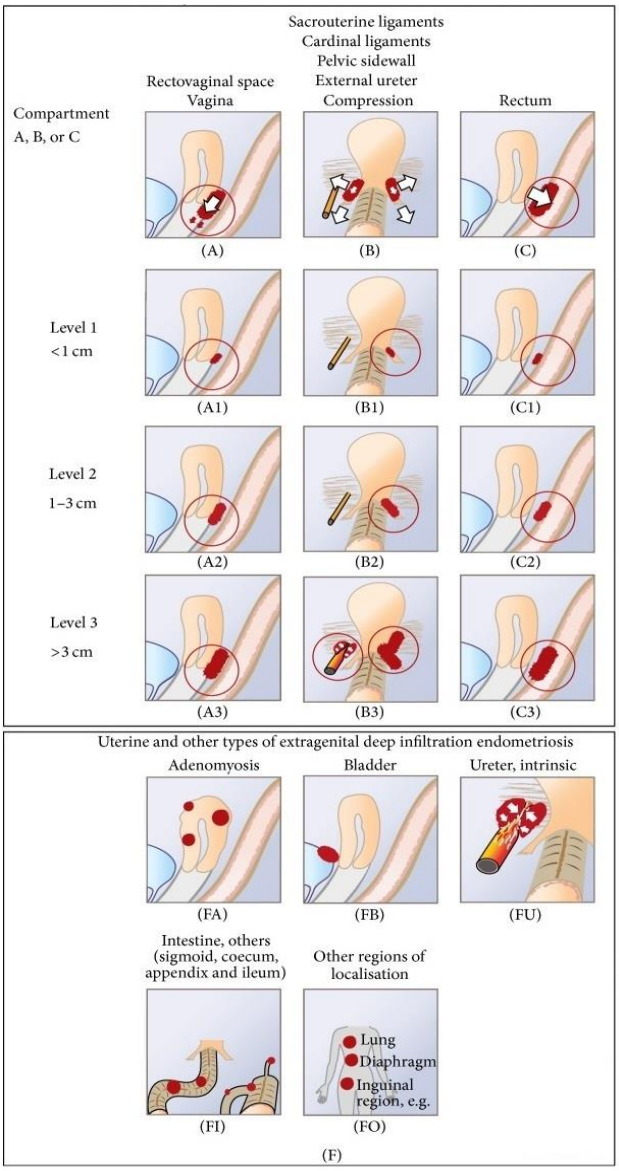

Fig. 5 – The Enzian Classification 2012 of deep infiltrating endometriosis (according to the Endometriosis Research Foundation, SEF)[52]

[51] Haas, D; Shebl, O; Shamiyeh, A; Oppelt, P; *The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses.* Acta Obstet Gynecol Scand. 2013 Jan; 92(1): 3-7. doi: 10.1111/aogs.12026; https://en.wikipedia.org/wiki/American_Society_for_Reproductive_Medicine

[52] Klugsberger, B; Shamiyeh, A; Oppelt, P; Jabkowski, C; Schimetta, W; Haas, D; *Clinical outcome after colonic resection in women with endometriosis.* Biomed Res Int. 2015; 2015:514383. doi: 10.1155/2015/514383.

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The ovarian reserve, quantified either by the plasmatic levels of antimullerian hormone (AMH), or by the ultrasonographic count of ovarian antral follicles[53] also, was not included in the EFI score[54]. *Alongside the ovarian reserve, others factors responsible for infertility in patients with endometriosis are omitted, including adenomiosis and digestive or urinary lesions not treated during laparoscopy for adnexal endometriosis involvement*[55].

EFI score can be useful in deciding the type, the duration and the costs of treatment following endometriosis surgery, anterior to recurring to assisted reproductive technologies in patients with good prognosis. It also allows clinicians to avoid wasting time and treatment in patients with poor prognosis[56].

When calculating EFI score the following factors are to be considered: historical factors (age, duration of infertility, previous pregnancy) and surgical factors (least function score, AFS score for endometriosis, total AFS score)[57].

Surgical findings that predict pregnancy rates were identified and used to develop the "Least Function Score", that, combined with elements of the AFS endometriosis score and historical factors statistically identified to predict pregnancy rates, was used to create the Endometriosis Fertility Index[58]. The least function score evaluates anatomical and functional

[53] Bruja, Alexandra; Brinduse, Lacramioara; Bratu, Ovidiu; Diaconu, Camelia; Bratila, Elvira; *Methods of transvaginal ultrasound examination in endometriosis*. Modern Medicine. 2018, 25 (3): 111-116.

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[56] Adamson, GD; *Endometriosis classification: an update*. Curr Opin Obstet Gynecol. 2011 Aug; 23(4): 213-20. doi: 10.1097/GCO.0b013e328348a3ba; Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

[57] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035; Boujenah, J; Poncelet, C; Madelenat, P; *The Endometriosis Fertility Index (EFI) is simple to use.* Gynecol Obstet Fertil. 2016 May; 44(5): 259-62. doi: 10.1016/j.gyobfe.2016.03.013.

[58] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

features of the tubes and ovaries[59], thus becoming a significant predictor of fertility[60]. The functional score is determined by the surgeon bilaterally for the tube, fimbria and ovary, where 0 = absent or non-functional; 1, 2 and 3 = severe, moderate, and mild dysfunction, respectively; and 4 = normal with respect to the reproductive functionality of the organ/structure (fig. 6).

Structure	Dysfunction	Description
Tube	Mild	Slight injury to serosa of the fallopian tube
	Moderate	Moderate injury to serosa or muscularis of the fallopian tube; moderate limitation in mobility
	Severe	Fallopian tube fibrosis or mild/moderate salpingitis isthmica nodosa; severe limitation in mobility
	Nonfunctional	Complete tubal obstruction, extensive fibrosis or salpingitis isthmica nodosa
Fimbria	Mild	Slight injury to fimbria with minimal scarring
	Moderate	Moderate injury to fimbria, with moderate scarring, moderate loss of fimbrial architecture and minimal intrafimbrial fibrosis
	Severe	Severe injury to fimbria, with severe scarring, severe loss of fimbrial architecture and moderate intrafimbrial fibrosis
	Nonfunctional	Severe injury to fimbria, with extensive scarring, complete loss of fimbrial architecture, complete tubal occlusion or hydrosalpinx
Ovary	Mild	Normal or almost normal ovarian size; minimal or mild injury to ovarian serosa
	Moderate	Ovarian size reduced by one-third or more; moderate injury to ovarian surface
	Severe	Ovarian size reduced by two-thirds or more; severe injury to ovarian surface
	Nonfunctional	Ovary absent or completely encased in adhesions

Fig. 6 - Description of least function terms[61].

[59] Boujenah, J; Hugues, JN; Sifer, C; Bricou, A; Cédrin-Durnerin, I; Sonigo, C; Monforte, M; Poncelet, C; *Endometriosis Fertility Index ou classification de l'American Society of Reproductive Medicine pour les patientes infertiles endométriosiques operées. Lequel est le plus pertinent?* Gynecol Obstet Fertil. 2015 Dec; 43(12): 806-9. doi: 10.1016/j.gyobfe.2015.10.006.

[60] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

[61] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system*. Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

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ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score		Description
4	=	Normal
3	=	Mild Dysfunction
2	=	Moderate Dysfunction
1	=	Severe Dysfunction
0	=	Absent or Nonfunctional

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

	Left	Right	
Fallopian Tube			
Fimbria			
Ovary			
Lowest Score		+	=
	Left	Right	LF Score

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age			LF Score		
	If age is ≤ 35 years	2		If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile			AFS Endometriosis Score		
	If years infertile is ≤ 3	2		If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy			AFS Total Score		
	If there is a history of a prior pregnancy	1		If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: Historical + Surgical = EFI Score

ESTIMATED PERCENT PREGNANT BY EFI SCORE

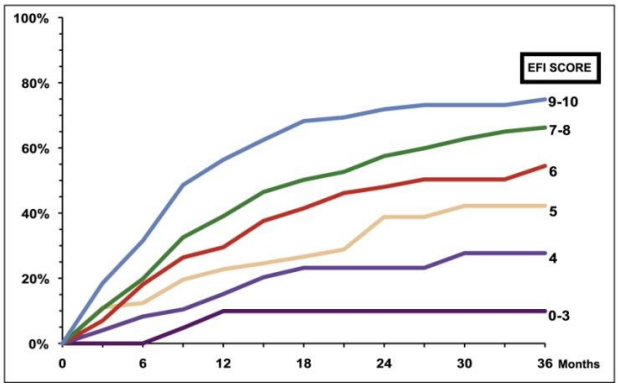

Fig. 7 – Endometriosis fertility index[62]

[62] Brătilă, Elvira; Ionescu, Oana-Maria; Badiu, Dumitru-Cristinel; Berceanu, Costin; Vlădăreanu, Simona; Pop, Doina Mihaela; Mehedinţu, Claudia; *Umbilical hernia masking primary umbilical endometriosis.* Rom J Morphol Embryol, 2016, 57(2): 825-829.

The total least function score is obtained by adding the lowest score from each side to give a combined total of potential for reproductive function of the adnexa. A completely normal pelvis would have a score of 4 + 4 = 8 and corresponding to an excellent reproductive potential. *A completely non-functional pelvis with no reproductive potential would have a score of 0 + 0 = 0.* Because pregnancy requires the functioning of all three segments (tube, fimbria and ovary) the lowest score of those three structures determines the ability of that side to function.

The EFI score ranges from 0 to 10, with 0 representing the poorest prognosis and 10 the best prognosis (Fig. 7). The estimated cumulative percentage of pregnant patients according to the value of the EFI score is presented in the graphic[63].

EFI EXTERNAL VALIDATION

Yacoub et al. in France studied whether EFI is a good pregnancy predictive tool in patients with surgically documented endometriosis followed by intrauterine insemination (IUI) or in vitro fertilization (IVF). The authors concluded that their study showed that the AFS score is not a good tool *of predicting the potential of obtaining pregnancies*, in contrast with the simple and reliable EFI score in patients with surgically documented endometriosis followed by IUI or IVF management[64]. These findings were also supported by Wang et al.[65] in 2013 and Garavaglia et al. in 2015[66] who acknowledged in their studies the superiority of EFI over rASF score in IVF outcomes in patients with endometriosis.

Three other studies that validated the EFI score are available online: Wei et al. in 2011[67], Tomasetti et al. in 2013[68] and Boujenah et al. in 2015[69].

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[63] Adamson, GD; Pasta, DJ; *Endometriosis fertility index: the new, validated endometriosis staging system.* Fertil Steril. 2010 Oct; 94(5): 1609-15. doi: 10.1016/j.fertnstert.2009.09.035.

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[69] Boujenah, J; Hugues, JN; Sifer, C; Bricou, A; Cédrin-Durnerin, I; Sonigo, C; Monforte, M; Poncelet, C; *Endometriosis Fertility Index ou classification de l'American Society of Reproductive Medicine pour les patientes infertiles endométriosiques operées. Lequel est le plus pertinent?* Gynecol Obstet Fertil. 2015 Dec; 43(12): 806-9. doi: 10.1016/j.gyobfe.2015.10.006.

THE AMERICAN ASSOCIATION OF GYNECOLOGICAL LAPAROSCOPISTS (AAGL) CLASSIFICATION[70]

In 2007, the AAGL initiated a project to develop an endometriosis scoring system to document the morphology of endometriosis seen during surgery. The aim was to obtain a clinically useful classification system developed from analysis of the descriptions. After developing the tabulation format, AAGL continued with a research in which 30 endometriosis experts gave a weighted score to different anatomical features considered to be important with respect to pain and infertility.

The AAGL special interest group (SIG) is now about to propose a new classification system in which surgical difficulties are categorized in four levels:

Level 1: Excision or desiccation of superficial implants, and simple thin avascular adhesions.

Level 2: Stripping of ovarian endometriomas; appendectomy; DIE not involving vagina, bladder (not requiring suture), bowel or ureter; dense adhesions not involving the bowel and/or the ureter.

Level 3: Dense adhesions involving the bowel and/or the ureter; bladder surgery requiring suture; ureterolysis; bowel surgery without resection (shaving).

Level 4: Bowel resection with end-to-end anastomosis; ureteral reimplantation or anastomosis.

The AAGL-SIG reported that preliminary results correlate well with pain, infertility and surgical difficulty. AAGL results show that this new classification appears to be better than the existing staging systems in correlating stage of disease to pain intensity and level of surgical difficulties. To date no studies shown that this classification is able to predict pregnancy rates in endometriosis patients with infertility[71].

CONCLUSIONS

Even though many efforts were made during the last decades, the perfect classification for endometriosis still eludes medical professionals while the disease itself remains a challenge prone to generate frustration among clinicians. Efforts should continue to be made in order to develop a classification worldwide accepted that also offers information regarding fertility and quality of life of affected patients.

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All authors report no potential conflict of interest.

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