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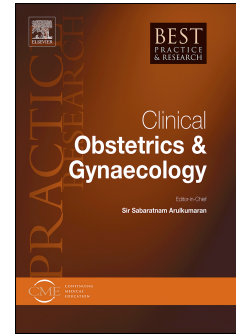
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**Endometriosis classification for pain: can the ASRM classification be improved?**

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**Abstract**

Endometriosis is a chronic prevalent disease that affects 5-15% of women in reproductive age. Different classifications systems have been proposed to categorize endometriosis. In 1979, the American Fertility society proposed a new classification to correlate surgical findings of endometriosis with fertility and was revised in 1996 (rASRM). Despite the rASRM classification system is widely used and accepted around the world, it has limitations. The objective of this study was to critically access and discuss the current classification for endometriosis.

Keywords: endometriosis; classification; rASRM score; Enzian classification; endometriosis Fertility Index.

## Introduction

Endometriosis is a chronic prevalent disease that affects 5-15% of women in reproductive age that significantly impairs the quality of life of patients (1). It can manifest as three main phenotypes: superficial, ovarian and deep lesions: (i) superficial endometriosis, characterized by small peritoneal lesions, usually located in the pelvis; (ii) ovarian endometrioma (OMA), a cyst with that contains a chocolate colored fluid derived from repeated hemorrhages of the endometriotic foci in the cyst during menses related to the presence of adhesions to the posterior leaf of the broad ligament or the pelvic wall; and (iii) deep endometriosis (DE), defined by the invasion of the peritoneum deeper than 5 mm (2). Histological analysis of DE often shows undifferentiated glandular and/or stromal cells surrounded by a significant fibrotic tissue (3). The disease is noted to be multifocal in many cases just as the three phenotypes may be co-exist within the same patient.

DE may represent 48% of all endometriosis cases and is related to more severe symptoms compared to superficial endometriosis, including severe dysmenorrhea and infertility (4, 5). DE can involve multiple sites in the pelvis including the bladder, bowel, retrocervical region, vagina and ureter (6). Surgical excision of DE that includes complete resection of all nodules can be challenging, often requiring a multidisciplinary team, and can involve high rates of complications (7).

### *An Ideal Classification for Endometriosis*

An ideal classification system for endometriosis should have the following features: 1. provide information on the severity and type of endometriosis, 2. correlate with severity and type of symptom including pain and infertility, 3. Accessible, reproducible and easy to perform, and 4. provide information regarding prognosis of the disease (8).

Different classifications systems have been proposed to categorize endometriosis. In 1921, Sampson proposed a classification for ovarian cysts. Wicks and Larson, in 1949, developed a classification system based on histological findings for endometriosis and later, Acosta, in 1973, developed a classification based on surgical findings (9, 10). Chapron, in 2003 (11), having noted the anatomical distribution of the disease proposed a classification for deep infiltrative endometriosis (DIE) that divided DIE into anterior (A1) and posterior compartment (P1-3). For example, lesions are categorized as A1 for endometriosis lesions affecting the

bladder, P1 for uterosacral ligaments, P2 for vagina, and P3 for intestinal involvement. However, up to the present time, none of the previously mentioned classification systems were widely accepted or implemented.

#### *Revised American Society for Reproductive Medicine Classification (rASRM)*

In 1979, the American Fertility society proposed a new classification to correlate surgical findings of endometriosis with fertility and was revised in 1996 (rASRM) (12, 13). The original system was based on an arbitrary score system that divided women to different stages: I (1-5 points), II (6-15 points), III (16-40 points), and IV (>40 points) (Figure 1). Higher points in this system are given in the presence of greater than 3 cm ovarian endometrioma (20 points each side), complete cul-of-sac blockage (40 points), and presence of ovarian (16 points) or tubal adhesions (16 points). The main advantages of rASRM classification system includes the fact that it is widely used and accepted around the world, it is easy to classify and it is easily understood by patients (8).

The rASRM system has limitations. The rASRM system does not take into consideration the presence of the deep disease in different sites like uterosacral ligaments, bladder, vagina and the bowel. But as most of the patients with deep endometriosis compromising the posterior compartment present cul de sac obliteration, giving 40 points to this commitment, indirectly the 40 points represent the advanced disease. In addition to this observation, the rASRM system doesn't describe properly the sites of the disease.

The objective of this study is to critically access and discuss the current classification for endometriosis.

#### *The rASRM stage and the histologic findings*

Multiple recent studies have pointed out the limitations to the current widely accepted rASRM system. In 2008 Kazanegra et al. evaluated the pathologic findings of 104 patients, submitted to laparoscopy. The rASRM stage I-IV were concordant in only 66.1%, 78.0%, 92.0%, and 81.1%, respectively (14). Fernando et al. (15), in 2013, also find a poor correlation between rASRM stage I and histological analysis (49.7%). Laparoscopy accuracy and staging of endometriosis depends on the surgeon experience and systematic inspection of pelvic cavity for lesions. Also, DE in retroperitoneum and vagina can be not visualized without adequate dissection (1).

*Does the rASRM stage correlate with symptoms?*

Some studies have been published in order to correlate the rASRM classification with the severity of the symptoms. Patients with endometriosis typically presents with dysmenorrhea, acyclic pelvic pain, deep dyspareunia, cyclic intestinal or urinary symptoms, and infertility (6). In 1996, Vercellini et al. (16) evaluated 244 patients, looking for the correlation between pain symptoms measured by visual analogic scale (VAS) and rASRM stage. No correlation was found between stages I-II and III-IV in acyclic pelvic pain (VAS 5 vs. VAS 4;  $p>0.05$ ), deep dyspareunia (VAS 5 vs. VAS 1;  $p>0.05$ ) and dysmenorrhea (VAS 8 vs VAS 8;  $p>0.05$ ). In 2006, the same group observed 1054 patients (17), when no association of dysmenorrhea and deep dyspareunia was found between stages I-IV. In the subgroups of acyclic pelvic pain a significant association was observed with severe stage (OR 8.68, CI = 1.23-61.23;  $p=0.03$ ).

In 1997, Guzick et al. performed a study with 469 patients with endometriosis. No difference in pregnancy rates were observed between rASRM stages (stage I 35.5%, stage II 34.7%, stage III 33.3%, and stage IV 29.5%). Also, no difference was observed in cumulative pregnancy rate after 36 months (18). Many studies evaluated the correlation of pain symptoms and infertility with the classification of the disease, however no consistent association was observed (19).

*Does the rASRM stage predict the actual amount of disease?*

The rASRM classification does not consider the involvement of posterior compartment and retroperitoneal structures in its scoring. As cul-of-sac blockage is often found in women with DE involving the rectosigmoid, this automatically classify the patient as stage 4, conferring a certain correlation between the stage and the most severe lesion (8). However, as this system does not take into consideration the location of the disease, which is a critical factor for the surgical planning and difficulty, patients with bowel involvement with no cul-of-sack blockage, for example, can be classified as stage II, while a patient with bilateral endometrioma with no deep lesion can be classified as stage III (1, 5).

In 2007, Vercellini et al. (19) conducted a study with 1054 patients with endometriosis, being classified as stage I in 319 patients, stage II in 139, stage III in 292, and stage IV in 304. Deep endometriosis was observed in 169 patients, being classified as stage II, III and IV in 43,

55 and 69 cases, respectively. No correlation was observed between location and stage of endometriosis.

*Are there complementary classifications to rASRM that can improve it?*

Some complementary classifications have already been proposed. The endometriosis fertility index (EFI) is a prognostic score published in 2010, approached in a relevant manner the issue related to infertility, as a complement to the rASRM classification to register the fertility status (20). Its take into consideration the function of the ovaries, tubes, and fimbrias, patient's age, years of infertility, and previous pregnancies (Figure 3). Despite EFI have good correlation with spontaneous pregnancy rate, it also requires a surgical staging, does not consider uterine abnormalities, and does not correlate with pain symptoms (21).

In order to improve and supplement one of the weaknesses of rASRM system, which is the location and severity of the DE, as well as its correlation with pain, the German Foundation for Endometriosis Research and the endometriosis work group from Villach, Austria, published in 2005, a proposal to classify the DE – the Enzian classification system (22), (figure 2).

The revised Enzian classification had removed, in 2011, the option of classifying superficial disease in the uterosacral ligaments and the pouch of Douglas, the problem of duplicate classification was solved as shown by Haas et al. (23). Accordingly, the revised Enzian classification can be considered a great complement to the rASRM score for describing DE (23), even after the revised version in 2011 intended to facilitate its interpretation. Although this new system complements the rASRM scoring system regarding the extent and location of DE, including retroperitoneal structures, it still has currently a poor level of international acceptance and it is mainly used in the German-speaking countries (8). The Enzian system is not a score like the rASRM score, but a morphological characterization of lesions and it appears to be more complex to be used by clinicians than the rASRM score; this classification is complex for the patients to understand as well (24).

To confirm if the revised Enzian classification correlates with clinical symptoms, especially with pain, Haas et al. published a prospective study in 2013 including 194 women surgically treated for DE (24). After they have been classified by both systems – rASRM and Enzian – at the end of the procedure, authors correlated with the clinical symptoms, which have been recorded preoperatively. Regarding the locations in the Enzian classification, authors

found that they correlate partially with clinical symptoms, especially lesions in compartment A with general abdominal pain ( $p=0.012$ ) and lesions in compartment C with bowel symptoms ( $p=0.011$ ). Moreover, a strong correlation was seen between general abdominal pain ( $p=0.002$ ) and dysmenorrhea ( $p<0.001$ ) with the severity grade in the Enzian classification (23). However, although the Enzian system might correlate well with pain and dysmenorrhea as suggested, it does not include the level of pain within its classification system.

### **Conclusion**

The biggest challenge of classifying endometriosis is to correlate the staging of disease to the two most relevant clinical features, infertility and pain. This information is crucial for a complete endometriosis classification system, as mentioned in a consensus from World Endometriosis Society (WES) recently published (25). As already pointed out, rASRM scoring system lack on those two issues (8).

Definitely, grading pain through scores is relevant when we are dealing with endometriosis. Fact is that none endometriosis classification system currently in use includes this information. Either to improve the available systems such as rASRM and Enzian to include the level of pain within endometriosis classification or to develop a new system that would complement the existent systems, surely, efforts should be made within related societies to achieve the ideal classification for endometriosis.

### **Conflicts of interest statement**

Dr Abrão MS is consultant for Abbvie and Olympus. The other authors have no conflicts of interests to declare.



**Practice points**

- American Society for Reproductive Medicine (1996) classification scores endometriosis into stages I-IV.
- In rASRM classification, the higher points in this system are scored in the presence of ovarian endometrioma greater than 3 cm, complete cul-of-sac blockage, and presence of ovarian or tubal adhesions.
- rASRM classification advantages includes the fact that it is widely used and accepted around the world, it is easy to classify and it is easily understood by patients. However, it does not correlate well with symptoms, does not take in consideration the location and type of the disease, and shows a variability inter and intra-observer.

**Research agenda**

- To improving the current or develop new classification systems to better correlate with symptoms.
- To evaluate the natural progression of lesions according to rASRM stages.

**Figure 1. Revised ASRM classification of endometriosis, 1996**

**Figure 2. Revised ENZIAN score, 2011**

**Figure 3. Endometriosis Fertility Index, 2013**

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REVISED AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE CLASSIFICATION OF  
ENDOMETRIOSIS 1985

Patient's Name \_\_\_\_\_ Date: \_\_\_\_\_

Stage I (Minimal) 1-5 Laparoscopy \_\_\_\_\_ Laparotomy \_\_\_\_\_ Photography \_\_\_\_\_  
 Stage II (Mild) 6-15 Recommended Treatment \_\_\_\_\_  
 Stage III (Moderate) 16-40 \_\_\_\_\_  
 Stage IV (Severe) >40 \_\_\_\_\_  
 Total \_\_\_\_\_ Prognosis \_\_\_\_\_

Peritoneum	ENDOMETRIOSIS	< 1 cm	1 – 3 cm	> 3 cm
		Superficial	1	2
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
POSTERIOR CULDESAC OBLITERATION		Partial		Complete
		4		40
Ovary	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
	Tube	R Filmy	1	2
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4*	8*	16

\*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Additional Endometriosis: \_\_\_\_\_

Associated Pathology: \_\_\_\_\_

\_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

\_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

To Be Used with Normal  
Tubes and Ovaries

L



R

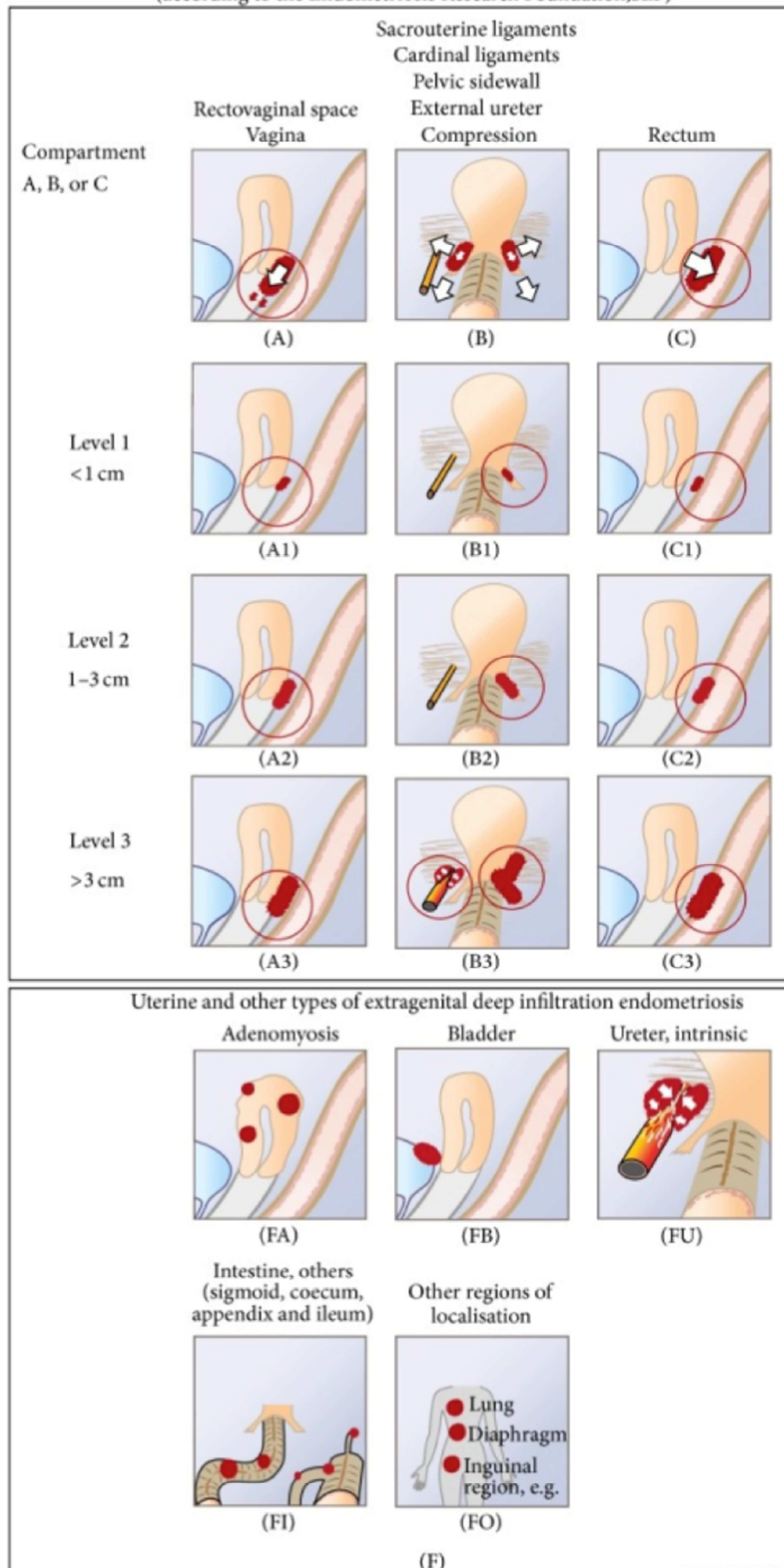
To Be Used with Abnormal  
Tubes and/or Ovaries

L



R

Enzian 2012  
 Classification of deeply infiltrating endometriosis  
 (according to the Endometriosis Research Foundation,SEF)



SCRIPT

## Endometriosis Fertility Index (EFI) Surgery form

Least function (LF) score at conclusion of surgery

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

Fallopian Tube	<input type="text"/>	<input type="text"/>
Fimbria	<input type="text"/>	<input type="text"/>
Ovary	<input type="text"/>	<input type="text"/>
Lowest Score	<input type="text"/>	+ <input type="text"/>
	Left	Right
		= <input type="text"/>
		LF Score

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.

## Endometriosis Fertility Index (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age	If age is < 35 years	2	LF Score	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	If years infertile is ≤ 3	2		AFS Endometriosis Score	If AFS Endometriosis Lesion Score is < 16
	If years infertile is > 3	0	If AFS Endometriosis Lesion Score is ≥ 16		0
Prior Pregnancy	If there is a history of a prior pregnancy	1	AFS Total Score	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:			<input type="text"/>	+	<input type="text"/>
			Historical		Surgical
					= <input type="text"/>
					EFI Score

Estimated percent pregnant by EFI score

