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Anatomic distribution of endometriosis: a reappraisal based on series of 1101 patients.

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Conflict of interest

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ABSTRACT

Objective: To reappraise the anatomic distribution of endometriosis lesions in cases with Superficial Implants (SI), Ovarian Endometrioma (OMA) and Deep Infiltrating Endometriosis (DIE).

Materials and Methods: A prospective observational study was operated between January 1989 to June 2009. A total of 1333 consecutive patients with a laparoscopic diagnosis of endometriosis, were extracted from our database. Due to missing data or repeated operations, 232 patients were excluded from the study. Finally, 1101 patients who met the selected criteria were included in the present analysis.. Primary outcome of study was the anatomic location of endometriotic lesions. Secondary outcomes were laterality of lesions as well as location of adhesions.

Results: Mean age of patients was 33.06 years (range 15-63 years) while the mean BMI was 21.5. The ovary was the most frequent site of endometriotic lesions (737 patients, 66.94%) followed by the utero-sacral ligaments (USL) (45.51%), the ovarian fossa (32.15%), the pouch of Douglas (29.52%) and the bladder (21.25%). Deep Infiltrating Endometriosis (DIE) was diagnosed in 159 patients (14.4%) with an increasing rate starting from the mid-nineties. The left side was predominant for all locations except fromr ovarian SI and fallopian tube, but for this latter location the number of cases was limited. 600 (54.4%) patients had adhesions wjth the adnexa being the most frequent site of location (47.4%).

Conclusions: Ovary was the main site of endometriotic lesions followed by the utero sacral ligaments. Left side was predominant for all locations except for ovarian SI and fallopian tube. The diagnosis of DIE has constantly being increased since mid-nineties. The large cohort of patients included in the study has strengthened previous reported data.

Key-words: endometriosis;anatomic distribution;ovary;deep infiltrating;laterality

Introduction

Endometriosis is a frequent gynecologic disease affecting 8-10% of reproductive-aged women and is defined by the presence of endometrial glandular epithelium and stroma implants in extra-uterine location.[1] Although aitiopathogenesis is still controversial, retrograde menstruation appears to be the prevalent mechanism facilitating the extra-uterine implantation of endometriosis implants.[2,3]

Mainly located in the pelvic cavity, endometriosis lesions appear as Superficial Implants (IS), Ovarian Endometriomas (OMA) and deep infiltrating endometriosis (DIE). New forms of Superficial implants (SI), the most frequent encountered endometriosis lesions, were described in the eighties (non-pigmented or subtle appearance of endometriosis)[4-6] while in the nineties the term DIE was introduced in order to describe all kind of infiltrating endometriosis including digestive and urinary endometriosis.[7,8] Finally, it was proposed and agreed that the laparoscopic diagnosis of endometriosis, especially when facing non pigmented lesions, should be confirmed by histopathology.[9,10]

The anatomic distribution of endometriosis is an issue of high clinical and scientific interest. Previous publications have managed to define the stage of the disease and the adequate treatment, providing new insights in the pathogenesis of endometriosis.[11,12] However, it is still of great interest to reassess the anatomic distribution of endometriosis in larger cohort of patients, especially as the diagnostic criteria for endometriosis have changed since 1989.

The aim of this study was to reassess the anatomic distribution and location of endometriosis implants in patients with laparoscopically confirmed endometriosis and the evolution of the disease throughout the interval 1989-2009.

Materials and methods

A retrospective study of prospectively collected data was performed in a private setting at Bordeaux France. Institutional review board approval was not required for this study according to French regulations when the study was initiated. Informed consent was obtained from all women.

A total of 1333 consecutive cases diagnosed with endometriosis through laparoscopy procedure were extracted from our database for this study. Due to iterative procedures (116 patients performed by one of the authors (AA)) as well as missing information (116 patients, mainly the histological report), 232 cases were excluded from the study. Finally, 1101 patients who met the selected criteria were included. All women were preoperatively informed about this new operative approach (laparoscopic surgery) and gave their consent for an eventual further analysis.

Medical history data as well as age, BMI, fertility status, symptoms and clinical were extracted from the files and used for this retrospective analysis. All consecutive patients were operated by the same surgeon (AA) under general anesthesia and tracheal intubation. Video laparoscopy available since mid 1988 was used for all patients and relevant findings were occasionally recorded (Storz GBM, Germany). In case of endometriosis' presence, a careful and detailed assessment was conducted and lesions were scored according to the AFS classification (AFS 1985) and reported in the operative record.[13]

For study purposes, 28 sites of the peritoneal cavity with potential endometriosis lesions (implants, nodes or cysts) were arbitrary selected and coded : bladder (median, left, right and bilateral), round ligament (right, left and bilateral), fallopian tube (right left, and bilateral), ovarian superficial implants (SI), nodes and cyst less than 3 cm in diameter (right, left, and bilateral), ovarian endometrioma (right, left and bilateral), ovarian fossa (right, left and bilateral), utero sacral ligaments (right, left and bilateral), uterus, pouch of Douglas, digestive superficial implants, pelvic lateral wall (right end left). Ovarian endometriomas of > 3cm diameter were coded as OMA. Deep infiltrating endometriosis (DIE) was defined as the presence of lesions in the recto-vaginal septum and parametrium, invading the urinary and digestive tracts and utero-sacral nodes

affecting the ureter. For the fallopian tube, only SI and occluding corneal nodes, with a microsurgical repair, were coded. Sub-mesocolic lesions (including diaphragm) were also coded in only one item in regards to the small number of cases expected. Adhesions were separately coded at 4 sites (adnexa, uterus, sigmoid and pouch of Douglas).

Subtle endometriosis lesions were gingerly searched and a biopsy was performed in all cases. [4,6,13] Surgical procedures followed the biopsies if needed. Outcomes and complications of the surgical procedures are not reported in this work because part of those patients were lost postoperatively and was not our purpose to have follow up data for them.

Primary and secondary outcomes

Primary outcome of the present study was the exact anatomic location of lesions.. Secondary outcomes were the rate of deep infiltrating endometriosis during the various study periods, laterality of endometriosis, pelvic adhesions' anatomic distribution and prevalence according to past history.

Statistical analysis

Continuous variables were expressed as mean (range) while frequencies of categorical data as n (%). Statistical analysis was performed with Statistical Package for Social Science 17.0. Staistical significance was defined at $P<.05$

Results

The mean age of the 1101 patients who met the criteria was 33.06 years (range 15-63 years) with 20 adolescents aged less than 20 years old and 19 post menopausal women. The mean BMI was 21.5 while 263 patients (23.89%) had a history of previous laparoscopy or laparotomy for endometriosis. Additionally, 64 patients (5.81%) had a documented history of pelvic infection and 129 cases (11.71%) had a previous pelvic surgical procedure not related to endometriosis.

Pain, infertility or both were the most frequent complains leading to perform laparoscopy. 405 (36.78%) patients had pain (group I), 376 (34.15%) pain and infertility (group II), 247 (22.43%) infertility without pain (Group III) and 76 (6.90%) neither pain nor infertility. Other reasons for laparoscopy were identification of asymptomatic adnexal mass during a routine ultrasound exam or reasons not related to endometriosis (24 cases). Only 17 patients (1.54%) reported acute pelvic pain and in 5 of them this was related to cyst rupture. Indication for laparoscopy and correlation with endometriois stage AFS (1985) is reported in **Table 1**.

Primary outcomes

Anatomic distribution of lesions

A total of 3416 site specific lesions (excluding adhesions) were coded for the 1101 patients according to our system (mean number of lesions per patient 3.10).

The ovary was the most frequent site of endometriosis, identified in 737 patients (66.94%) Of these patients, 485 presented both OMA and SI, 227 presented only OMA, while SI exclusively were observed only in 25 patients.

Other frequent locations were the utero-sacral ligaments (USL), the ovarian fossa, the pouch of Douglas and the bladder. The most rare location of endometriosis was sub-mesocolic compartment (n=14 patients), enrolling 3 cases located in Caecum, 2 in appendix, 3 in diaphragm, 5 in lateral wall and 1 in umbilical.

The anatomic distribution and rates per patient or per lesion are detailed on **Table 2**.

Secondary outcomes

Deep Infiltrating Endometriosis

DIE (excluding USL lesions except when involving the ureter) was diagnosed in 159 patients (14.4%). Rate of DIE increased progressively with a marked shift in 1995 and 2001 (P<.001). Reported rates are based on laparoscopic diagnosis and histopathologic confirmation and not just in the clinical suspicion and/or examination.(**Table 3.)** 148 patients with DIE had associated pain (93.1%), of which 132 reported infertility as well (89.2%). 143 cases (89.94%) had lesions located in the rectovaginal septum combined with or without other locations. The sigmoid was involved in 11 cases, the bladder in 9 cases and the ureter in 6 cases. 123 patients (77.36%) had associated adhesions and 86 associated OMA (69.9%). All DIE cases had other associated endometriotic lesions and all those combined with OMA had adhesions.

Laterality of endometriosis

The laterality of lesions was evaluated in cases of unilateral locations. The left side was predominant for all locations evaluated except for ovarian SI and the fallopian tube. Left laterality was significantly higher for fossa ovarica vs. fallopian tube and ovarian SI (p<.001). Laterality of endometriosis is indicated in **Table 4**.

Prevalence and locations of adhesion in relation to past history

There were overall 600 patients diagnosed with adhesions. Patients were divided into 4 groups based on their past history: group I no reported history, group II history of endometriosis, group III history of pelvic infection and group IV previous pelvic surgery. The prevalence of adhesions was significantly higher in patients with recurrent endometriosis (76.4%) compared to other groups (P<.001) while the group of patients with a past history of pelvic infection presented the lowest rate of adhesions (40.63%).Prevalence of adhesions according to past history is presented in **Table 5**.

The most frequent anatomic location of adhesions was adnexa (47.4%), followed by sigmoid, pouch of Douglas and uterus. Anatomic distribution of adhesions in relative diagnosed cases is presented in **Table 6**.

Discussion

This large retrospective study of electronic health records has strengthened previous reports regarding anatomic distribution of endometriosis and has shown a significant progressive increase of Deep Infiltrating Endometriosis diagnosis in the last twenty years. The risk for pelvic adhesions in patients with history of pelvic infection is similar to patients without any history.

Anatomic distribution of endometriosis has been also published by previous studies, however, results have not been so clearly interpreted as ours. Specifically, Jenkins et al have evaluated the importance of anatomic distribution of endometriosis in a series of 182 consecutive patients with infertility and endometriosis undergoing laparoscopy during 1980-1984.[11] However, authors were not yet aware of the so called subtle or non pigmented lesions at that time [5,8] while video laparoscopy permitting image magnification and histopathological confirmation was not yet available, which leads to a profound bias in their results. Furthermore, relative studies performed in the last twenty years, reporting on endometriosis localization have focused on special types of endometriosis such as SI , OMA or DIE and not in overall diagnosed forms.[15-19] Moreover, a recent study of anatomic distribution of endometriosis in 1350 women indicated that the predominant location was the pelvic cavity (96.4%) followed by the soft tissue (2.8%), gastrointestinal tract 0.3%) and urinary tract (0.2%), however, the various sites within the pelvic cavity were not specified. [20] Therefore, as a primary conclusion we may understand that despite the variety of previous relative studies, there have not been many reports of exact anatomic location in all kinds of endometriosis evaluating also laterality and correlating symptoms, which may actually be considered the “added value” of the present report.

The ovary has been reported as the most common site of endometriosis implants in humans (54.9%), followed by the posterior broad ligament (35.2%), the anterior cul-de-sac (34.6%), the posterior cul-de-sac (34.0%) and the uterosacral ligament (28.0%). Endometriosis of the anterior compartment was significantly more common in patients with anterior uteri (40.7%) versus

patients with posterior uteri 11.8%, p< .005).[11] Our findings have shown the uterosacral ligament as the second most frequent site of endometriosis lesions, which was consistent with the previous reports for the majority of main sites affected : ovarian implants or OMAs (66.94%), uterosacral ligaments (45.51%), fossa ovarica (32.15%), and the Pouch of Douglas (29.52%). However, our study also indicated a higher percentage of uterosacral ligament localization of endometriosis lesions compared to previous works, which is one amongst few relative reports. The reason may actually be related with the higher rate of DIE diagnosed after the 1995 (Table 2).

Urinary tract endometriosis is presented more frequently in modern times than in past years and its occurrence varies from 0.3 to 12%.[21] In this series, the bladder was the site of SI or endometriotic nodes in 234 patients (21.5%), while ureteral endometriosis was found in 7 patients (0.6%). The Fallopian tube was also the site of endometriosis in 50 patients (4.54%), which is consitent with the findings of previous reports.[22]

DIE was identified in 14.44% of our patients, all of which had shown other associated endometriotic lesions, while the main distribution was the posterior compartment. However, the key point in our results is the evolution of DIE diagnosis rates that increased progressively by the years with a marked shift in 1995 and 2001 (P<.001) (Table 2.) The obvious arising question is whether this time shift is due to technological evolution combined with the increased acquired experience of the operators to diagnose the endometriosis sites or is associated with different environmental and/or related to the life style factors. Indeed, we may not actually be sure whether the incidence of DIE has progressively increased over years or whether better education of reproductive physicians leads to higher clinical suspicion and therefore, given the availability and the progress og technology, diagnosis is much more facilitated than in the past. Furthermore, during the study period, the technique of laparoscopy has improved substantially due to the introduction of digital camera's etc. This could have biased the results on presence of the disease during the earlier years. In any case, it is a fact that overall diagnosed rate of DIE has increased

dramatically throughout study years, a conclusion which has not been made by not many other published studies.

Evaluation of laterality indicated a left predominance for the majority of sites : OMA (56.3%), Fossa ovaria (67.50%), USL (60.71%) and bladder (57.76%). Our results are in agreement with previous reports for OMA, utero-sacral ligaments, peritoneum.[23-24] Nevertheless, diaphragmatic endometriosis is the exception of the above rule as a recent review has indicated the right side of the diaphragm being the predominant location of endometriosis development.[23]

The distribution of endometriosis lesions has been related to the pathogenesis and pathophysiology of endometriosis. The anatomical distribution of endometriosis within the peritoneal cavity favors the retrograde menstruation theory by Sampson in 1920. The influence of gravity explains the predominance of superficial endometriosis lesion in the posterior and the left compartment of the peritoneal cavity. In extroverted uteri, the upright or supine position enhances the flow from the anterior to the posterior compartment or the peritoneal cavity. The left predominance is probably due to the sigmoid colon acting as an obstacle to the diffusion of the menstrual effluent from the left fallopian tube and therefore promoting an implantation. However, the DIE lesions distribution is probably due to metaplasia of colon or Mullerian remnants metaplasia.[25]

Adhesions were found in 54.5%of our cases and adnexa was the commonest site affected (Table 5). In a cross-sectional study of patients with endometriosis and associated pain, adhesions were observed in 89.0% of cases and it was suggested that there is no overall association between the presence of adhesions and the degree of pain[15]. Surprisingly, adhesions were recorded in 46.5% of our cases with no history of endometriosis, pelvic infection or abdominal surgery, while in patients with reported history of pelvic infection the adhesions rate was significantly lower. The highest rate of adhesions was found in the group of patients with previous surgery for endometriosis (Table 5)

The main limitation of this study is the bias related to factors influencing recruitment and thus it does not necessarily reflect findings in a non oriented population. Up to 2000, our center recruited many patients with infertility, therefore our main interest may have not been focused on the category of patients with DIE. After 2000, because of own medical policy, our interest in endometriosis and especially laparoscopic management of DIE may have influenced the recruitment (reflected by an increasing prevalence of DIE along the years). This may be due to several factors: increase awareness, better tools for clinical diagnosis (MRI) and progressive referral effect, thus it does not necessarily reflect true prevalence of DIE. Another bias is due to some arbitrary criteria selected for lesion site coding. For example, only OMA of 3 cm diameter were coded or the sole USL nodes affecting the ureter were coded as DIE. All patients with DIE had associated other endometriotic lesions. In a series of 93 DIE, assosiated endometriotic lésions were found in 61.3% of patients.[26]

In conclusion, this prospective observational study reports on anatomic location and distribution on a large series of patients, including all types of endometriosis and examining all potential locations. It confirms that ovary is the commonest site affected by endometriosis followed by the uterosacral ligament. However, there are additional conclusions highlighted, namely the increase of DIE rates as well as the correlation of endometriosis with adhesion formation. Further prospective observational studies should be established in order to further elucidate on whether increase in DIE is true as well as examining the final outcome of endometriosis after laparoscopic surgery mainly on fertility status.

Disclosure

Authors report no conflict of interest

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Table 1. Indication (groups) for laparoscopy and stages AFS (1985).

Group / n. by Stage	Age (y.)	Stage I	Stage II	Stage III	Stage IV	Total
I-Pain	34.10	118	45	166	76	405
II-Sterility + Pain	31.23	105	53	137	80	376
III-Sterility	31.87	150	42	32	23	247
IV No pain or sterility	40.44	36	4	28	5	73
All groups (%)	33.06	409 (37.15%)	144 (13.08%)	363 (33.06%)	184(16.71%)	1101

Table 2. Anatomic distribution of endometriotic lesions.

Site	Patients (N)	Patients (%)
Total ovary	737	66.9
OMA + SI	485	65.8
SI	227	30.8
OMA	25	5.2
US Ligament	468	45.5
Fossa Ovarica	354	32.2
Pouch of Douglas	325	29.5
Bladder	234	21.4
DIE (All sites)	159	14.4
Uterus	94	8.5
Sigmoid (IS)	92	8.4
Fallopian Tube	50	4.5
Round Ligament	28	2.5

Lateral Wall	16	1.5
Sus mesocolic compt.	14	1.3

Table 3. Rate of DIE according to the period of survey.

Period of survey	n. patients with endometriosis	n. patients with DIE	%
1989-1994	489	18	3.7
1995-2000	333	56	16.8
2001-2006	279	85	30.4

Table 4. Laterality of endometriosis for some locations.

Location	n. unilateral	n. left side(%)	n. right side (%)
OMA	398	224(56.3%)	174(43.7%)
Fossa Ovarica	320	216(67.5%)*	104 (32.5%)
USL	196	119(60.7%)	77(39.3%)
Bladder	74	42(57.8%)	32(42.2%)
FallopianTube	41	17(41.5%)	24(58.5%)
Ovarian SI	258	116(45.0%)	142(55.0%)

*: significantly higher vs. fallopian tube and ovarian SI, P<.001

Table 5. Prevalence of adhesions according to past history

Group	n. patients	Patients with adhesions, n(%)
I = No past history	645	300 (46.5%)
II = Recurrent endometriosis	263	201 (76.4%)*
III =Prior pelvic infection	64	26 (40.6%)
IV= Prior other pelvic surgery	129	73 (56.6%)
Total	1101	600 (54.5%)

*****: significantly higher vs. other categories, P<.001

Table 6. Anatomic distribution of adhesions in relative diagnosed cases (600 overall cases)

Adhesions Distribution	Patients, n(%)
Adnexa	522 (47.4%)
Sigmoid	204 (18.5%)
Pouch of Douglas	158 (14.4)
Uterus	156 (14.2%)