Prevalence of Endometriosis and Peritoneal Pockets in Women with Infertility and/or Pelvic Pain

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ABSTRACT

Objective: To evaluate the prevalence of endometriosis and peritoneal pockets and to analyze whether these pockets are associated with pain.

Methods: Analysis of prospectively registered data of all women undergoing laparoscopy for infertility or pelvic pain between 1988 and 2011 at KU Leuven University Hospital.

Results: Of 4497 women, 191 had 238 pockets, with a prevalence of 4.7% in women with infertility only, 4.9% in women with infertility and pelvic pain, and 3.5% in women with pelvic pain only ($P = 0.045$ for all infertility vs. pelvic pain only). Prevalence did not vary by age. Pockets were associated with endometriosis ($P < 0.0001$), which was found in 77% of women with pockets. Among women with infertility only, the prevalence of endometriosis was higher in women with pockets ($P = 0.0001$) than in women without. The prevalence of endometriosis was similar in women with infertility and pelvic pain or pelvic pain only. Pelvic pain as an indication for surgery was associated simultaneously (through logistic regression) with endometriosis ($P < 0.0001$) and pockets ($P = 0.040$). Pelvic pain severity was associated simultaneously with pockets ($P = 0.0026$) and the severity of subtle ($P = 0.001$), typical ($P = 0.030$), cystic ovarian ($P = 0.051$), and deep endometriosis ($P < 0.0001$). Pelvic pain severity was not associated with endometriosis in the pockets or the diameter or location of pockets.

Conclusions: The prevalence of pockets was low, at between 3.5% and 5%. Women with infertility only and pockets had more endometriosis than women without. Severe pelvic pain and pelvic pain as an indication for surgery were associated with the presence of pockets as well as the presence and severity of endometriosis.

Keywords: endometriosis; Allen-Masters; peritoneal pocket; peritoneal lacerations; pelvic pain

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RÉSUMÉ

Objectif : Évaluer la prévalence de l'endométriose et des poches péritonéales et analyser si ces poches sont associées à la douleur.

Méthodologie : Analyse des données enregistrées prospectivement de toutes les femmes ayant subi une laparoscopie en raison d'une infertilité ou de douleurs pelviennes entre 1988 et 2011 au KU Leuven University Hospital.

Résultats : Sur un total de 4 497 femmes, 191 avaient 238 poches; la prévalence était de 4,7 % chez les femmes atteintes d'infertilité seulement, de 4,9 % chez les femmes atteintes d'infertilité et de douleurs pelviennes et de 3,5 % chez les femmes souffrant de douleurs pelviennes seulement ($p = 0,045$ pour toutes les infertilités vs douleurs pelviennes seulement). La prévalence ne variait pas en fonction de l'âge. Les poches étaient associées à l'endométriose ($p < 0,0001$), ce qui a été observé chez 77 % des femmes avec

poches. Chez les femmes atteintes d'infertilité seulement, la prévalence de l'endométriose était plus élevée chez celles avec poches (p = 0,0001) que chez celles n'en ayant pas. La prévalence de l'endométriose était semblable chez les femmes atteintes d'infertilité et de douleurs pelviennes ou de douleurs pelviennes seulement. Les douleurs pelviennes comme indication de l'intervention chirurgicale étaient associées simultanément (par régression logistique) à l'endométriose (p < 0,0001) et aux poches (p = 0,040). L'intensité des douleurs pelviennes était associée simultanément aux poches (p = 0,0026) et à la gravité des lésions endométriosiques subtiles (p = 0,001), typiques (p = 0,030), ovariennes kystiques (p = 0,051) et profondes (p < 0,0001). L'intensité des douleurs pelviennes n'était pas associée à l'endométriose dans les poches ni au diamètre ou à l'emplacement des poches.

Conclusions : La prévalence des poches était faible, soit entre 3,5 et 5 %. Les femmes atteintes d'infertilité seulement et ayant des poches avaient plus d'endométriose que les femmes sans poche. Les douleurs pelviennes intenses et les douleurs pelviennes comme indication de l'intervention chirurgicale ont été associées à la présence de poches ainsi qu'à la présence et à la gravité de l'endométriose.

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INTRODUCTION

The term *peritoneal pockets* (pockets) is used to designate depressions in the pelvic peritoneum (Figure 1) as described initially by Sampson[1] and Chatman[2] and recently by Yeung et al.,[3] Ferrari et al.,[4] Ilnitsky et al.,[5] and Carranco et al.[6] Pockets include small defects, defects extending to the perineal body, fluid-filled pockets with a small opening, cryptic pockets, and lateral pockets bordered by a medial ureter (Figure 2).[6–8] Pockets have been used synonymously, albeit erroneously, with Allen-Masters lacerations[9,10] and have been confused with broad ligament hernias[11–13] and sciatic hernias.[14,15] It is unclear whether these various descriptions represent one or several pathologies. In this manuscript, we will use the term *pockets* unless discussing literature that equates it with other terms.

Peritoneal pockets associated with endometriosis were described in women with pelvic pain (PP)[1,2,16–19] or cyclic sciatalgia.[20] Chatman[2] reported that of women with PP, 3% had pockets, 10% had endometriosis, and 2.5% had both. Later, he reported prevalences of 15%, 42%, and 12%, respectively.[16] Redwine[17] found pockets in 18% and endometriosis in 66%. In these pockets, endometriosis was diagnosed macroscopically in 60% to 70%[2,3,5] and by histology in an additional 30%.[3] Batt et al.[18,19] emphasized the association with specific histologic phenotypes of endometriosis such as "spiders" and organoid lesions. In Allen-Masters lacerations,[9,10,21–26] the presence of endometriosis was variable[10] or rare.[24] There is little descriptive data on endometriosis in pockets with a small opening or no opening in the peritoneum.[3,7] The literature reports pockets as a cause of bowel obstructions or strangulations.[12,13,27–33]

Figure 1. (A) Small peritoneal pocket in the pouch of Douglas with endometriosis lesion in the base (courtesy of L. Flavio Fernandes and A. Liceaga). (B) Pocket in the ovarian fossa lined medially by the ureter and demonstrating a thin and more transparent peritoneum. (C and D) Peritoneal pocket in the vesico-uterine fold with a tiny communication with the peritoneal cavity (arrow) before and after excision.

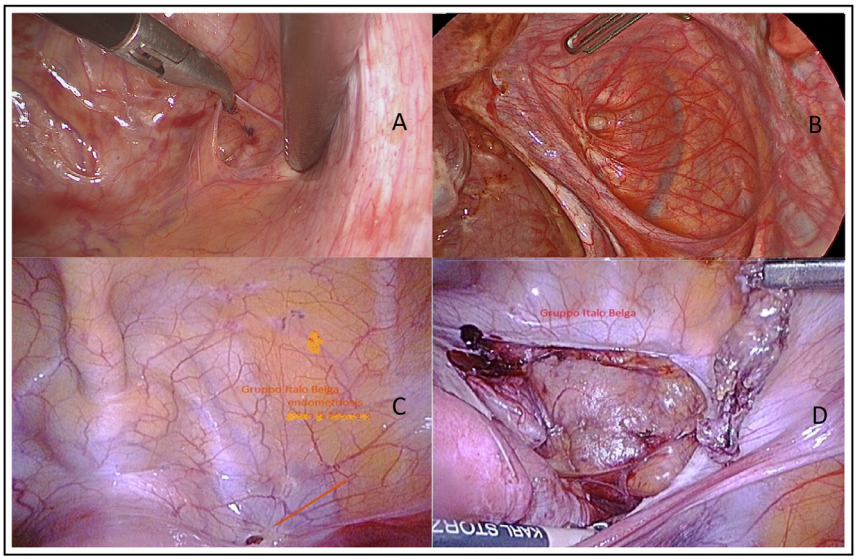
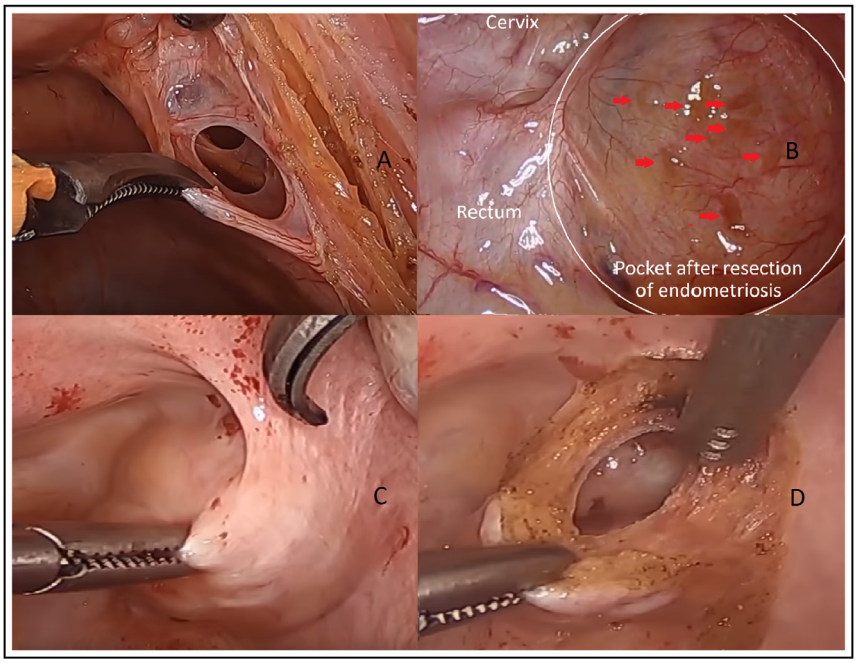


Figure 2. (A) Multilocular pockets with a smaller opening to the peritoneum[8] (used with permission). (B) Right perirectal post-excision pocket 5 years after excisional surgery. Arrows indicate flat endometriosis and stromal endometriotic polyps. The flat and polypoid nature can be seen in the video[36] beginning at 5:55 minutes (used with permission). (C and D) Hidden pocket before and during surgery[8] (used with permission).



The pathophysiology of peritoneal pockets is unclear. Redwine[17] and Batt et al.[18,19] suggested that pockets were congenital defects. Pockets can develop after surgery or excision.[7] The traumatic lacerations that Allen and Masters described in women with PP[9,10] may be misidentified pockets or pockets like those seen after the biopsy or excision of endometriosis[34–36] (Figure 2). However, Allen-Masters syndrome did not require visible lacerations, which were only seen in six of their 28 patients.[9,10]

It is believed that peritoneal pockets are a cause of PP because PP improved after surgical excision of endometriosis and pockets.[3] However, it remains unclear whether pockets without endometriosis are associated with PP and whether they should be treated. We therefore reviewed our database to evaluate the prevalence of endometriosis and pockets in women undergoing laparoscopy for infertility or pelvic pain and to analyze whether pockets are associated with PP in addition to endometriosis.

METHODS

Review of PP and Pockets

PubMed and SCOPUS were searched for "Allen-Masters" OR "peritoneal pockets" OR "broad ligament hernia" OR "peritoneal defect" in the title or abstract. After hand-searching (P.R.K.) 161 articles for an association of pockets with endometriosis or PP or the repair of a pocket after excision, 54 relevant articles were identified.

Registration of Endometriosis and Pockets

All women who underwent surgery by or directly supervised by P.R.K. between 1988 and 2011 at KU Leuven University Hospital were registered in a database. The indication for surgery and descriptive data were entered immediately after surgery when writing the operation report, as described by Koninckx et al.[37] Up to seven entries different endometriosis lesion could be entered. For each lesion the type of lesion, the location, the macroscopic appearance, the diameter, the depth, and the number of similar lesions were registered. The location was described as the ovarian fossa, the sidewall, the uterosacral ligaments, the vesico-uterine fold, the pouch of Douglas, the diaphragm, the sigmoid, the rectum, the ischial spine, and so forth. The macroscopic appearance of each endometriosis lesion was described as white or red vesicles, polypoid or flame-like lesions, black puckered lesions in a white sclerotic area, or pockets. Location and appearance were described using one letter (i.e., P [pocket], T [typical], or S [subtle]). The depth and diameter of lesions were estimated by comparison with the distance of openings at the end of the suction irrigation probe.[37] The diameter and depth of deep lesions were estimated after excision. To facilitate the calculation of the peritoneal surface and the volume of deep and cystic

lesions, the diameter and the depth of deep lesions were approximated as if their peritoneal surfaces and volumes were circular and spherical, respectively. A superficial lesion of 5 × 15 mm thus was approximated and as a lesion of 10 mm in diameter, which is an approximation with a less than 5% error. For deep endometriosis lesions, depth and diameter estimations were made after "en bloc" excision, after which most lesions had become more spherical by contraction. The severity of dysmenorrhea, chronic PP, deep dyspareunia, dyschezia, and mictalgia (painful urination) was scored as 0, 1, 2, or 3.[38]

This Study on the Prevalence of Peritoneal Pockets and PP

All women for whom the indication for laparoscopy was registered as infertility and/or PP (n = 4497) were included in this study. Women with other indications (e.g., myomectomy, hysterectomy) were excluded. Of the women included, 10.1% had undergone a previous surgery elsewhere.

The registration of peritoneal pockets had been routine in the registration of endometriosis lesions since, in 1989, pockets were (erroneously) considered a type of endometriosis at KU Leuven. The registration of the type of lesion with one letter permitted entry of pockets together with subtle or typical endometriosis lesions in the pockets. As a consequence, the depth of the pockets was not registered because depth was defined as the depth of endometriosis lesions under the peritoneum. For the same reason, the number and diameter of subtle and typical lesions in the pocket were not registered because the number and diameter referred to the pockets. To avoid inconsistencies, the database was kept unchanged over the years. Because the location on the uterosacral ligaments was identified by the letter U, it was specified in the database that pockets with the entry U identified a pocket that was medial but close to the uterosacral ligaments. This was different from lesions in the middle or on the right or left side of the pouch of Douglas, identified with the letters D, DR, and DL, respectively.

PP was registered as dysmenorrhea, chronic PP, deep dyspareunia, dyschezia, and mictalgia on a 0 to 3 scale.[38]

The database review was registered with the institutional review board of University Hospital Gasthuisberg (S63491), and the database was kept as a General Data Protection Regulation compliant SAS file.[39]

Analysis and Statistics

The database files (Visual FoxPro) were imported into SAS[39]: 1896 women underwent laparoscopy for infertility only (I), 648 for infertility and pelvic pain (I&PP), and 1953 for PP only (PP). All women with infertility thus are in groups I and I&PP. All women with PP are in groups I&PP and PP. Using the raw data, we first calculated derived variables. For each woman, we calculated the number and location of pockets and, for each pocket, the presence and type of endometriosis lesions in the pocket. White and red vesicles and polypoid and flame-like lesions were grouped as subtle lesions. Gun-shot lesions with or without a white sclerotic area and with or without subtle lesions were grouped as typical lesions. Lesions deeper than 5 mm were considered deep lesions.[40,41] With the number, appearance, diameter, and depth of endometriosis lesions, we calculated for each woman the total number, the total pelvic area, and the total volume of subtle, typical, cystic ovarian, and deep endometriosis lesions. The total pain score was the sum of the scores for dysmenorrhea, chronic PP, deep dyspareunia, dyschezia, and mictalgia.

Statistical analysis began with descriptive statistics and associations (chi-square and Spearman correlations) and a two-way analysis of variance (Proc GLM). Multivariate analysis (proc logistic) then was used to evaluate whether the presence of pockets (yes/no) was an independent variable in predicting pelvic pain, in addition to the presence of endometriosis or the presence or severity of the different types of endometriosis lesions (i.e., is PP predicted by pockets AND endometriosis; is PP predicted by pockets AND by subtle AND typical AND cystic AND deep endometriosis). PP was used either as the indication for surgery (i.e., women with I&PP plus those with PP versus those with I) or as the total pain score, defined as the sum of dysmenorrhea, chronic PP, deep dyspareunia, dyschezia, and mictalgia. The severity of endometriosis lesions was defined by the number of subtle lesions, the pelvic area of typical lesions, the volume or diameter of cystic ovarian endometriosis, and the total volume of deep endometriosis. Thus, the results are a summary of many sequential and consistent analyses. As an example, when PP was found to be associated both with pockets and endometriosis, endometriosis was replaced with the presence and then with the severity of the different types of endometriosis lesions. Each analysis was done as a model including all variables and a stepwise backwards or a stepwise forwards analysis of the most predictive variables. A stepwise forwards analysis identified the most predictive variable, followed by the second most predictive and so on, until no other variables added significantly to the prediction. This resulted in a final model including all predictive variables reaching a significance level of $P < 0.05$. It is important to realize that strongly associated variables carry at least partially similar information and thus are not completely independent

variables. In a logistic model, often either variable can enter the model but not both variables, and variables entering a model simultaneously are independent variables carrying different information. Infertility was not analyzed separately because parameters such as the duration of infertility and male infertility were not reliably available in the database.

Statistical analysis was done using SAS and included chi-square, two-way analysis of variance (Proc GLM), and multivariate logistic regression (proc logistic). Means and standard deviations are given unless indicated otherwise. *P* values were rounded to three decimals because otherwise *P* values such as 0.054 could have been rounded to *P* = 0.05, which is considered significant.

RESULTS

Among 4497 women, 191 women had 238 pockets; one, two, three, and four pockets were found in 152, 32, six, and one woman, respectively. The age of women with pockets was similar among women with one, two, three, or four pockets: 30.6 ± 5.3, 29.6 ± 5.5, 28.2 ± 4.0, and 29.3 years, respectively. Age also did not vary with the indication of laparoscopy, being 29.9 ± 3.9, 32.0 ± 7.0, and 28.4 ± 2.6 years for women undergoing surgery for I, I&PP, and PP, respectively. The prevalence of pockets did not vary with age, at 3.5%, 4.5%, 5.3%, 4.2%, and 3.1% in women 15 to 20, 21 to 25, 26 to 30, 31 to 35, and 36 to 40 years old, respectively. The prevalence of pockets was 4.7%, 4.9%, and 3.5% in women undergoing laparoscopy for I, I&PP, and PP, respectively. All women with infertility (I and I&PP) had more pockets (*P* = 0.045) than women with PP only (Table). The presence of pockets did not correlate (Spearman) with any other numeric demographic variables in the database, such as weight, height, body mass index, previous pregnancies, or previous surgery.

Women with one, two, and three pockets had a similar prevalence of endometriosis: 79%, 69%, and 83%, respectively. In the 191 women with pockets, only 42 did not have endometriosis, and two had subtle lesions in the pocket only.

In women with I only, those with a pocket more frequently had endometriosis (chi-square *P* < 0.0001), as well as more subtle (*P* = 0.04) and more typical endometriosis (*P* < 0.0001), than women without pockets. However, in women with PP (I&PP + PP), the prevalence of endometriosis was not different (Not significant: NS) in those with and without pockets.

To evaluate whether pockets were independently associated with PP in addition to endometriosis, we analyzed PP as an indication for surgery (yes/no; i.e., I&PP + PP vs I) and as the total pain score. By two-way analysis of variance (Proc GLM), pelvic pain as an indication for surgery was simultaneously associated with pockets (*P* = 0.054) and endometriosis (*P* < 0.0001). In addition, by logistic regression (proc logistic), pelvic pain as an indication for surgery was associated simultaneously with the presence of pockets (*P* = 0.040) and endometriosis (*P* < 0.0001). If endometriosis was substituted in this model with the presence of subtle, typical, cystic ovarian, and deep endometriosis, aside from pockets, only deep (*P* < 0.0001) and typical endometriosis (*P* < 0.0001) were significant.

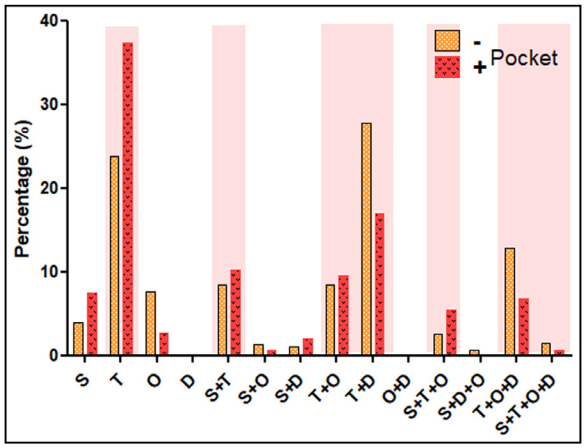
Results were similar when the total pain score was analyzed. The total pain score was associated with the presence of a pocket (*P* = 0.043) and the presence of endometriosis (*P* < 0.0001), more specifically the presence of deep (*P* < 0.0001) and typical endometriosis (*P* < 0.0001). When, instead of the presence of endometriosis lesions, the number, pelvic area, or volume of each type of endometriosis lesion was entered into the model, the total pain score was associated simultaneously with the presence

Table. Prevalence of subtle, typical, cystic ovarian, and deep endometriosis lesions in women with (P+) and without (P−) peritoneal pockets

	Total; n = 4497	Infertility only; n = 1896	All pain[a]; n = 2601	Pelvic pain; n = 1953	Infertility and pelvic pain; n = 648
Pockets, no. (%)	191 (4.2)	90 (4.7)	101 (3.9)	69 (3.5)	32 (4.9)
Endometriosis, %, P+; P−	77; 63 (*P* = 0.0001)	76; 50 (*P* < 0.0001)	76; 76 (NS)	75; 68	84; 86
Subtle	24; 16 (*P* = 0.006)	23; 16 (*P* = 0.04)	23; 24 (NS)	20; 16	31; 19
Typical	67; 54 (*P* = 0.0002)	66; 42 (*P* < 0.0001)	68; 66 (NS)	64; 58	72; 74
Cystic ovarian	20; 22 (NS)	14; 13 (NS)	14; 25 (NS)	19; 22	38; 44
Deep	20; 27 (*P* = 0.04)	8; 9 (NS)	30; 37 (NS)	30; 37	31; 54

[a] Women with pelvic pain and those with pelvic pain and infertility as the indication for surgery. NS: not significant.

Figure 3. The prevalence of subtle (S), typical (T), cystic ovarian (O), and deep (D) endometriosis and of their combinations in women with (P+) and without (P-) peritoneal pockets. The variable associations, as highlighted by the percentages of T, T + S, T + O, T + D, S + T + O, T + O, and S + T + O + D, illustrate the necessity of multivariate statistical analysis to investigate which factors are independent variables predicting pelvic pain. In a model "pelvic pain = pocket subtle typical cystic deep," the severity of pelvic pain is associated with the presence of pockets ($P = 0.0026$), the number of subtle lesions ($P = 0.001$), the pelvic area of typical lesions ($P = 0.030$), the diameter of cystic ovarian endometriosis ($P = 0.051$) and the volume of deep endometriosis ($P < 0.0001$).



of pockets ($P = 0.0026$), the number of subtle lesions ($P = 0.001$), the pelvic area of typical lesions ($P = 0.030$), the diameter of cystic ovarian endometriosis ($P = 0.051$), and the volume of deep endometriosis ($P < 0.0001$). To interpret these analyses, it is important to realize that endometriosis lesions are found in all combinations of type (Figure 3) and severity of lesions in women with and without pockets.

PP was not significantly associated with the presence of subtle or typical endometriosis lesions in the pockets, nor with the diameter or location of pockets. Pockets contained macroscopically typical endometriosis lesions, subtle lesions, and both in 7.8%, 1.6%, and 1.0%, respectively. Pocket diameter in the 190 women with a single pocket and the largest diameter in the 20 women with more than one pocket were 17.1 + 11.4 mm (10th and 90th percentile: 5 and 30 mm) and 15.1 + 9.8 mm (5 and 27 mm), respectively. The largest pockets were localized in the pouch of Douglas in 20.4%, in the right and the left side of the pouch of Douglas in 5.7% and 3.7%, in the right and left ovarian fossa in 25.1% and 22.0%, medial to the right and left uterosacral ligament in 10.5% and 7.8%, and in the vesicouterine fold in 4.2%.

Because pockets were vaporized with an 80 W CO2 laser in defocus, pathology results were not available. The peritoneum of the rare pockets with a tiny opening to the peritoneal cavity was excised, but endometriosis was not detected either macroscopically or on pathology. The follow-up for PP after surgery was not systematically studied. Thus, no conclusion can be reached regarding symptomatic outcome after surgery.

DISCUSSION

These data confirm that not only women with PP but also women with I only have pockets in 3% to 5%.[2] Reported prevalences of 15% and 18%[16,17] might be due to different definitions or specific interests. The finding that women with I only have a slightly higher prevalence of pockets than all women with PP might be an observation bias in women with severe endometriosis and adhesions. The similar incidence in women with I only and our observation that the prevalence of pockets does not change with age supports the hypothesis that most pockets are congenital rather than acquired defects.[17–19] Our data also confirm the association of peritoneal pockets with pelvic endometriosis. Furthermore, the type of pelvic endometriosis does not differ between women with and without a pocket. It is unclear why pockets and endometriosis are associated. Accumulation of retrograde menstruation in pockets, with locally increased oxidative stress leading to endometriosis,[42] and scarring and retraction have been suggested.[2,6,8,16,43,44] The clinical observation that the peritoneal lining of pockets is thinner, more transparent, and more loosely attached to the underlying tissue than the normal peritoneum (Figure 1) points to a congenital mechanism.

This analysis illustrates the difficulty of understanding rare events such as pockets that occur in only 3% to 5% of women. A series of 4477 laparoscopies and 191 women with pockets was barely sufficient for the multivariate analysis that demonstrated that pockets were an independent variable in predicting PP in addition to subtle, typical, cystic ovarian, and deep endometriosis.

The mechanism of the pocket-associated PP is unclear. The peritoneum in the pockets could be stretched, causing PP.[45] Because pelvic endometriosis is associated with low-grade inflammation and tenderness up to a 2.7-cm distance, the bottom of the pockets might be sufficiently close to the inferior hypogastric plexus to cause PP.[46] That PP is not found to be higher in women with endometriosis in their pockets could be explained by a lack of power in this small series of 191 pockets. In addition, macroscopic inspection without histology could have missed lesions in the pockets.[7]

Clinically, whether pockets should be treated is an important question. Excising or destroying deep, cystic ovarian, and typical endometriosis lesions seems well established.[47] The inflammatory reaction[36] around subtle lesions, which are painful during conscious pain mapping,[46] suggests treatment of subtle lesions. Peritoneal pockets being an independent variable associated with PP suggests excising, vaporizing, or coagulating the peritoneum of the pocket. That endometriosis is found by histology in 30% of normal-looking peritoneum in pockets[3] is an additional argument for treatment. In the absence of data describing the repair of pockets after surgery and the associated pain relief, the preferred technique and the necessity of suturing large defects[20] will remain a surgical decision, considering the ease of stripping the peritoneum and the risk of bleeding.

Our data do not permit discussion of peritoneal pockets with a tiny opening to the peritoneal cavity because these were not entered into the database as a separate entity. However, our clinical observation suggests that they are rare and occasionally large, extending up to the sacrum, and that they rarely contain endometriosis lesions.[6]

CONCLUSION

Women with PP or I can be expected to have endometriosis at a prevalence of 70% and peritoneal pockets at a prevalence of 3% to 5%. In women with I only, those with pockets have a similar prevalence of endometriosis compared with women with PP. That pockets are an independent variable predicting PP suggests treatment of the peritoneum of pockets.

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