Accepted Manuscript

Title: The Isolated Ovarian Endometrioma: a History between Myth and Reality

Author: Caterina Exacoustos, De Felice Giovanna, Alessandra Pizzo, Giulia Morosetti, Lucia Lazzeri, Gabriele Centini, Emilio Piccione, Errico Zupi

PII: S1553-4650(18)30042-6
DOI: https://doi.org/10.1016/j.jmig.2017.12.026
Reference: JMIG 3395

To appear in: *The Journal of Minimally Invasive Gynecology*

Received date: 17-9-2017
Revised date: 19-12-2017
Accepted date: 21-12-2017

Please cite this article as: Caterina Exacoustos, De Felice Giovanna, Alessandra Pizzo, Giulia Morosetti, Lucia Lazzeri, Gabriele Centini, Emilio Piccione, Errico Zupi, The Isolated Ovarian Endometrioma: a History between Myth and Reality, *The Journal of Minimally Invasive Gynecology* (2018), https://doi.org/10.1016/j.jmig.2017.12.026.

The isolated ovarian endometrioma: a history between myth and reality

Caterina Exacoustos MD, PhD, De Felice Giovanna, MD, Alessandra Pizzo, MD, Giulia Morosetti, MD, Lucia Lazzeri, MD, PhD, Gabriele Centini, MD, Emilio Piccione, MD, and Errico Zupi, MD

From the Department of Biomedicine and Prevention, Obstetrics and Gynecological Clinic, University of Rome "Tor Vergata", Roma, Italy (Drs Exacoustos, Morosetti, Piccione, and Zupi), Department of Molecular and Developmental Medicine, Obstetrics and Gynecological Clinic University of Siena, Siena, Italy (Drs Giovanna, Pizzo, Lazzeri, and Centini).

Running Title: Endometriosis-associated endometrioma

Correspondence to
Lucia Lazzeri, MD, PhD, Department of Molecular and Developmental Medicine, Obstetrics and Gynecological Clinic, University of Siena, Siena 53100, Italy
E-mail: lucialazzeri@email.it

Conflict of interest: The authors declare no conflicts of interest.

Precis: Ovarian endometriomas may be an indicator of other endometriotic lesions, and proper ultrasonographic diagnosis is necessary to guide surgical, medical, and hormonal therapy to preserve fertility and avoid unnecessary procedures.

Comment [A1]: AUTHOR: Two different versions of Precis section were provided and the one in the manuscript has been used. Please check and confirm that it is correct

ABSTRACT

Study Objective: To assess the association between ovarian endometriomas detectable at transvaginal ultrasound (TVS) and other specific extra-ovarian lesions including adhesions, deep infiltrating endometriosis, and adenomyosis.

Design: Retrospective observational study (Canadian Task Force classification II-2).

Setting: Two university hospitals.

Patients: 255 symptomatic women with at least one ovarian endometrioma found on ultrasound after presentation with pain or irregular menstruation.

Interventions: Patients underwent TVS followed by either medical or surgical treatment.

Measurements and Main Results: Two hundred and fifty-five women, aged 20 to 40 years, underwent TVS and were found to have at least one endometrioma with a diameter > 20 mm. Associated sonographic signs of pelvic endometriosis (adhesions, deep infiltrating endometriosis, and adenomyosis) were recorded, and a subgroup of patients (n = 50) underwent laparoscopic surgery within 3 months of TVS. Mean endometrioma diameter was 40.0 ± 18.1 mm, and bilateral endometriomas were observed in 65 patients (25.5%). Transvaginal ultrasound showed posterior rectal deep infiltrating endometriosis in 55 patients (21.5%) and a thickening of at least one uterosacral ligament in 93 patients (36.4%). One hundred eighty-six patients (73%) had adhesions, and 134 patients (53%) showed signs of myometrial adenomyosis on TVS. Thirty-eight patients (15%) exhibited only a single isolated endometrioma with a mobile ovary and no other signs of pelvic endometriosis/adenomyosis at TVS.

Conclusion: Ovarian endometriomas are indicators for pelvic endometriosis and are rarely isolated. Particularly, left endometriomas were found to be associated with rectal deep infiltrating endometriosis and left uterosacral ligament localization, and bilateral endometriomas correlated with adhesions and pouch of Douglas obliteration while no correlation was found between endometrioma size and deep infiltrating endometriosis. Determining appropriate management, whether clinical or surgical, is critical for ovarian endometriomas and concomitant adhesions, endometriosis, and adenomyosis in patients desiring future fertility.

Keywords: Adenomyosis, Deep endometriosis, Pain, Transvaginal ultrasound

Introduction

Endometriosis is a chronic disease affecting about 10% of reproductive-age women, leading to significant morbidity and ultimately a major public health concern [1,2]. Ovarian lesions are the most frequent localizations, manifesting as typical ovarian cysts known as endometriomas. Through transvaginal ultrasound (TVS), endometriomas can be easily diagnosed [3]. The main diagnostic challenge is the detection of extra-ovarian endometriotic lesions such as peritoneal disease, adhesions, deep infiltrating endometriosis (DIE), and adenomyosis [4–7]. Identifying severe adenomyosis at ultrasound may help explain symptoms such as abnormal uterine bleeding, pelvic pain, or infertility [8–10]. However, non-ovarian endometriosis is much more difficult to diagnose and requires evaluation by experienced sonographers [11]. Recently, Guerriero et al showed that TVS is a fair imaging method to diagnose endometriosis involving the uterosacral ligaments (USLs), recto-vaginal septum, vagina, and bladder [5].

Ovarian endometriomas are highly associated with other endometriotic lesions [12], such as adhesions [13] and DIE, and simultaneous treatment of both types of lesions is effective in restoring pain, fertility, and reducing recurrence. Undiagnosed DIE associated with an endometrioma is the main cause for incomplete surgical excisions [12]. Accurate TVS results and detailed ultrasonographic mapping of lesions should be sent with patients to tertiary centers to determine appropriate surgical or medical therapy [14,15].

This underestimation or misdiagnosis of extensive adhesions and DIE could result in incomplete management, specifically in infertile women, where diagnosis may be delayed until the need for assisted reproductive technologies (ART) and may lead to repeated failed in vitro fertilization (IVF) cycles [16,17]. Several studies [18,19] have shown that symptomology and clinical history in the presence of an endometrioma may predict DIE lesions and that TVS is the first-line investigative tool for diagnosis [20].

The aim of the current study was to assess the association between the sonographic diagnosis of ovarian endometrioma and TVS detection of specific extra-ovarian lesions including adhesions, DIE, and adenomyosis.

Materials and Methods

Two hundred and fifty-five women were enrolled in a multicenter, retrospective observational study following ultrasonographic diagnosis of ovarian endometrioma owing to presentation of pain or irregular menstruation. All women underwent TVS and clinical or surgical management in two different endometriosis centers in Italy (Rome and Siena) between January 2014 and December 2016. The study was approved by the institutional review board, and full ethical review was not required owing to the retrospective and observational nature of the study.

Inclusion criteria were women from 20 to 40 years of age, the presence of an ovarian cyst with typical sonographic appearance of an endometrioma ≥ 20 mm diameter, accurate evaluation of the disease according to a previously published ultrasound mapping modality for pelvic endometriosis [21], the presence of symptoms such as pelvic pain (including dysmenorrhea, dyspareunia, dyschezia, and dysuria), chronic pelvic pain and/or infertility, no previous pelvic surgeries.

Fifty of the 255 patients underwent laparoscopic surgery within 3 months after TVS, and surgical mapping of lesions was compared with the preoperative TVS to evaluate the accuracy of the ultrasonographic diagnosis. The remaining 205 women were managed according to their symptoms and fertility desire either with medical therapy or ART.

Clinical examination

Medical, surgical, obstetric, and infertility history were documented for each patient as well as the following: dysmenorrhea, dyspareunia, bowel dysfunction, urinary tract symptoms (dysuria, urgency, and hematuria), chronic pelvic pain, and abnormal uterine bleeding. Pain severity was evaluated with the visual analog scale (VAS) system, using a 10-cm line with the extreme points 0 and 10 corresponding to ‘‘no pain’’ and ‘‘maximum pain,’’ respectively.

Ultrasound Examination

All sonographs were performed by two experienced examiners (CE and LL). All possible locations of endometriosis were evaluated and recorded using the mapping sheet named Endometriosis Surgical Ultrasonographic System, developed to assess the extent of endometriosis by accurately noting lesion locations and measuring the size and depth of the lesions at the various pelvic sites [21]. The TVS was performed with either a Voluson E6 or Voluson E8 (General Electric

Healthcare GE, Zipf, Austria), using a wideband 5- to 9-MHz endocavitary transducer at any time of the menstrual cycle. The TVS diagnosis of ovarian endometrioma was defined by the presence of a unilocular or multilocular cyst (< 5 locules) characterized by a homogeneous low-level echogenicity (ground glass echogenicity) of the cyst fluid and absent or moderate vascularization of the cystic walls [3] (Fig. 1). Following the detection of the ovarian endometrioma, TVS was repeated within 2 months to confirm a persistent ovarian lesion. Measurements in three orthogonal planes (longitudinal, anteroposterior, and transverse) for each endometrioma were recorded, and the maximum diameter was considered for statistical analysis. All potential locations of non-ovarian endometriosis were examined. Sonographic signs of coexisting adhesions and tubal pathology were evaluated. Adhesions were suspected and abdominal palpation was conducted during the TVS examination if the ovaries and/or uterus appeared fixed to the adjacent structures (Fig. 2). The presence of pelvic fluid, fine septa, or strands of tissue (adhesions) between the ovary, endometrioma, uterus, or the peritoneum of the pouch of Douglas [14,22,23] were recorded. The pouch of Douglas obliteration was assessed using the sliding sign by gently pressing on the cervix with the TVS probe or palpating the uterus abdominally with a hand to determine whether the rectosigmoid would glide freely over the posterior wall of the upper uterus/fundus [24–26].

The diagnosis of DIE was made if at least one structure in the anterior or posterior compartment showed the presence of an abnormal retroperitoneal hypoechoic linear or nodular thickening with irregular contours and no vascular Doppler signals, according to previously described and validated ultrasonographic criteria [20].

The pelvis was investigated in both the anterior and posterior compartments, and DIE lesions of the bladder, ureter, parametria, posterior vaginal fornix, torus uterinus, USLs, rectovaginal septum, caudal and cranial rectal walls were considered for this study according to the mapping system for pelvic endometriosis [21] (Fig. 3). During TVS, all possible sonographic findings of uterine adenomyosis [6,27,28] were evaluated. The diagnosis of adenomyosis was made if ≥ 2 of the following features were present: asymmetrical myometrial thickening, myometrial cysts, linear striations, hyperechoic islands, or an irregular and thickened endometrial-myometrial junction zone on either two-dimensional or three-dimensional imaging [28].

Surgery

Patients with indication for surgery underwent laparoscopy that was performed by two surgeons (EZ and GC) experienced in laparoscopic radical resection of DIE. Indications for surgery were dysmenorrhea and dyspareunia unresponsive to medical treatment (n = 12), pain and associated bowel obstructive symptoms (n = 21), and infertility (n = 17).

Surgical diagnosis of endometriosis was based on visualization, measurement with multiples of 5-mm probes and radical resection of all tissue with endometriotic involvement followed by histological confirmation.

Lesions of the rectosigmoid were removed by shaving or resection depending on the size of the lesion and the infiltration depth of the bowel wall. After surgery, the surgeon completed the mapping sheet with definitive endometriosis localizations. The mean operating time of each surgical procedure was recorded.

Statistical analysis

All continuous variables for population characteristics were expressed in terms of mean ± standard deviation while categorical variables were expressed in terms of frequency and percentage. Prevalence of endometriotic lesions at surgical and TVS evaluation were calculated.

The baseline characteristics in the two groups (no surgery versus surgery) were compared using chi-square tests for categorical variables and independent sample t tests or Mann-Whitney tests as appropriate for continuous data.

Surgical and histological findings were compared with the ultrasonographic preoperative diagnosis. Sensitivity, specificity, positive and negative predictive values, test accuracy, and positive and negative likelihood ratios were calculated with the CatMaker statistical software (Douglas Badenoch, Centre for Evidence-Based Medicine, Oxford, UK) for each site of possible endometriotic localization.

Results

Patient clinical characteristics and symptoms are shown in Table 1.

The most common symptom for all patients (N = 255) with endometriomas at TVS was

dysmenorrhea (88.2%), and 30% of patients suffered from infertility. Bilateral endometriomas were observed in 65 patients (25.5%), and unilateral endometriomas were on the left side in 115 patients (45%).

Patients who underwent laparoscopic surgery after TVS showed a statistically significant higher percentage of bowel and urinary symptoms.

Sixty percent of patients showed endometriomas with the largest diameter < 4 cm (managed with conservative medical treatment) and did not undergo surgical treatment to avoid the risk of an iatrogenic reduction of the ovarian reserve [29].

The patients who underwent surgery (n = 50) had larger endometriomas and more medically resistant symptoms compared with the group of patients who received conservative management (n = 205). No statistically significant differences in age and fertility were observed between groups.

The TVS findings of endometriosis are shown in Table 2. In the 255 patients included in this study, 186 patients (73%) showed pelvic adhesions and 134 patients (53%) had myometrial adenomyosis.

Only 57 patients (22%) showed a single ovarian lesion with a mobile ovary and without any other ultrasound signs of pelvic endometriosis or adhesions, and in 19 of them adenomyosis was found at TVS, resulting in a completely isolated endometrioma seen in only 38 women (15%).

Of the 255 women, 55 patients (21.5%) showed posterior rectal DIE and 93 patients (36.4 %) exhibited a thickening of at least one USL at TVS. The presence of DIE (anterior and posterior) was detected in 113 patients (44.3%) with endometriomas.

Comparing laparoscopic and histological findings to TVS mapping, despite the low number of patients who underwent surgery, the accuracy in diagnosing endometriosis in different pelvic locations ranged from 88% to 100%. Sensitivity ranged from 71% to 100%, specificity from 89% to 100%, and overall accuracy for the different single pelvic locations is similar to our previous study [21]. Endometriomas without any other DIE or adhesions were not found at laparoscopy. No statistically significant difference in the percentage of DIE localizations was observed in the two groups, except for bladder DIE.

Left endometriomas were more commonly associated with adhesions, rectosigmoid DIE (cranial and caudal rectum) and endometriotic infiltration of the left USL compared with right

endometriomas (Table 2). Bilateral endometriomas showed a higher percentage of pouch of Douglas obliteration and cranial rectum DIE. Unilateral endometriomas with the largest diameter ≥ 4 cm presented more adhesions compared with smaller ones.

Regarding endometrioma size no significant differences in mean endometrioma diameters were observed when comparing left and right endometriomas (38.7 ± 2.5 mm vs 34.8 ± 5.3 mm). However, endometriomas with a maximum diameter of ≥ 4 cm were more frequently found on the left side (56%) compared with the right side (32%). No correlation was found between the size of the endometrioma or an endometrioma with a maximum diameter of ≥ 4 cm and the presence of DIE.

Discussion

Ovarian endometriomas are present in approximately one-third of patients with endometriosis and can appear as cysts with ground glass echogenicity [30-32]. Transvaginal sonography is a first-line imaging technique used to accurately diagnose endometriosis even by an inexperienced sonographer, although endometriosis that is not ovarian is more difficult to diagnose. Treatment options depend on patient symptoms, age, and fertility wishes and include expectant management, medical and/or surgical treatment, and in vitro fertilization [33]. Typically, surgery is preferred treatment for endometriosis associated pain [29] although associated adenomyosis and DIE impact pain intensity and fertility. Because treatment options differ, the sonographer must search for all endometriotic lesions to map all disease within the pelvis and postulate an accurate plan for the patient whether it be surgical, medical, or fertility-focused. Despite high accuracy of TVS, lack of knowledge or skill regarding this condition can result in underestimation of the physical aspects of the disease and consequently inadequate treatment [4,21]. The current study showed isolated endometriomas in only 15% of patients and a clear association of endometriomas and localization in other areas of the pelvis. Particularly, left endometriomas were associated with rectal DIE and left USL localization. Further, bilateral endometriomas correlated with adhesions and Douglas obliteration, and no correlation was found between the size of the endometrioma and the presence of DIE. This is useful information to guide the sonographer in the specific evaluation of the pelvis and improve the diagnostic accuracy of the exam.

Studies have shown that DIE is more severe when ovarian endometriomas are present leading to the hypothesis that endometriomas indicate more extensive pelvic disease, especially DIE [12,18,19]. In addition, the relationship between DIE and chronic pelvic pain was clearly demonstrated by Chapron et al who evaluated the intensity of pelvic pain in a population of women with endometriomas [12]. Lafay Pillet et al [18] and Parello et al [19] used clinical scores and calculations to determine the probability of finding DIE in patients with endometriomas based on pelvic pain intensity, number of previous surgeries, and number of previous pregnancies. The probability of accurately detecting DIE in the presence of endometriomas without any detail regarding the site and size of the lesions seems incongruous. Other studies have tried to predict DIE using TVS to evaluate the immobility of the ovary or pouch of Douglas obliteration by means of the absence of the sliding uterus and ovaries [24,26,34]. Gerges et al [34] suggested that ovarian immobility is a sonographic 'soft marker' of DIE. The overall accuracy in diagnosing DIE in the 74 patients was only 63% [34].

The current study results clearly underline the importance of an accurate TVS pelvic evaluation and precise mapping of the pelvic sites, and not only soft markers. Furthermore, a thorough TVS investigation must be completed in all women with endometriomas, not just those planning to undergo surgical treatment but also patients planning medical or ART management. More than half of the women in the current study with small endometriomas had adhesions and adenomyosis that could decrease fertility. Indeed, in the 44% of current patients with endometriomas and associated DIE, TVS detected the exact locations of concomitant adhesions. Also in the current study, adenomyosis and adhesions were found in 52% and 72% of women with endometriomas implying that TVS could be useful in asymptomatic women with endometriomas who do not desire pregnancy.

The current study presented some limitations. There was a possible selection bias owing to specificity of the study design, as it only included symptomatic patients in two referral centers specialized in endometriosis management. Moreover, the surgical confirmation of endometriosis was available only for a small group of patients (n = 50).

In conclusion, ovarian endometriomas are indicators for pelvic endometriosis and are rarely isolated. Particularly, left endometriomas were found to be associated with rectal DIE and left USL localization, and bilateral endometriomas correlated with adhesions and pouch of Douglas obliteration

while no correlation was found between endometrioma size and DIE. When identified at TVS, it is important to explore for all possible pelvic endometriosis localizations or concomitant uterine adenomyosis. Many patients undergo surgery or medical treatment without any other information about the presence of deep endometriotic lesions, adhesions, or uterine pathologies possibly owing to missed detection in the diagnostic approach. Ovarian endometriomas are easy to recognize, even a small one; adhesions and DIE require a skilled imaging professional both for TVS and magnetic resonance imaging.

Determining appropriate management, whether clinical or surgical, is critical for ovarian endometriomas and concomitant adhesions, endometriosis, and adenomyosis in patients desiring future fertility. To overcome the challenges in TVS diagnosis of concomitant lesions of ovarian endometriomas, it is our hope that dedicated training for sonographers can take place to alert professionals regarding detailed lesion mapping in this patient population.

Acknowledgements We acknowledge Francesca Conway for English revision.

References

1. Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. *Fertil Steril*. 2012;98:511–519.
2. Centini G, Lazzeri L, Dores D, et al. Chronic pelvic pain and quality of life in women with and without endometriosis. *J Endometr Pelvic Pain Disord*. 2013;5:27–33.
3. Van Holsbeke C, Van Calster B, Guerriero S, et al. Endometriomas: their ultrasound characteristics. *Ultrasound Obstet Gynecol*. 2010;35:730–740.
4. Guerriero S, Ajossa S, Minguez JA, Jurado M, Mais V, Melis GB, Alcazar JL. Accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in uterosacral ligaments, rectovaginal septum, vagina and bladder: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2015;46:534–545.
5. Guerriero S, Ajossa S, Orozco R, Perniciano M, Jurado M, Melis GB, Alcazar JL. Accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in the rectosigmoid: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2016;47:281–289.
6. Naftalin J, Hoo W, Pateman K, Mavrelos D, Holland T, Jurkovic D. How common is adenomyosis? A prospective study of prevalence using transvaginal ultrasound in a gynaecology clinic. *Hum Reprod*. 2012;27:3432–3439.
7. Di Donato N, Montanari G, Benfenati A, et al. Prevalence of adenomyosis in women undergoing surgery for endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2014;181:289–293.
8. Lazzeri L, Di Giovanni A, Exacoustos C, et al. Preoperative and postoperative clinical and transvaginal ultrasound findings of adenomyosis in patients with deep infiltrating endometriosis. *Reprod Sci*. 2014;21:1027–1033.
9. Vercellini P, Consonni D, Dridi D, Bracco B, Frattaruolo MP, Somigliana E. Uterine adenomyosis and in vitro fertilization outcome: a systematic review and meta-analysis. *Hum Reprod*. 2014;29:964–967.
10. Naftalin J, Hoo W, Nunes N, Holland T, Mavrelos D, Jurkovic D. Association between ultrasound features of adenomyosis and severity of menstrual pain. *Ultrasound Obstet*

Gynecol. 2016;47:779–783.

11. Hudelist G, English J, Thomas AE, Tinelli A, Singer CF, Keckstein J. Diagnostic accuracy of transvaginal ultrasound for non-invasive diagnosis of bowel endometriosis: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2011;37:257–263.
12. Chapron C, Pietin-Vialle C, Borghese B, Davy C, Foulot H, Chopin N. Associated ovarian endometrioma is a marker for greater severity of deeply infiltrating endometriosis. *Fertil Steril*. 2009;92:453–457.
13. Guerriero S, Ajossa S, Garau N, Alcazar JL, Mais V, Melis GB. Diagnosis of pelvic adhesions in patients with endometrioma: the role of transvaginal ultrasonography. *Fertil Steril*. 2010;94:742–746.
14. Exacoustos C, Zupi E, Carusotti C, Rinaldo D, Marconi D, Lanzi G, Arduini D. Staging of pelvic endometriosis: role of sonographic appearance in determining extension of disease and modulating surgical approach. *J Am Assoc Gynecol Laparosc*. 2003;10: 378–378.
15. Hudelist G, Keckstein J. The use of transvaginal sonography (TVS) for preoperative diagnosis of pelvic endometriosis. *Praxis*. 2009;98:603–607.
16. Muzii L, Achilli C, Bergamini V, et al. Comparison between the stripping technique and the combined excisional/ablative technique for the treatment of bilateral ovarian endometriomas: a multicentre RCT. *Hum Reprod*. 2016;31:339–344.
17. Venturella R, Lico D, Sarica A, et al. OvAge: a new methodology to quantify ovarian reserve combining clinical, biochemical and 3D-ultrasonographic parameters. *J Ovarian Res*. 2015;8:21.
18. Lafay Pillet MC, Huchon C, Santulli P, Borghese B, Chapron C, Fauconnier A. A clinical score can predict associated deep infiltrating endometriosis before surgery for an endometrioma. *Hum Reprod*. 2014;29:1666–1676.
19. Perelló M, Martínez-Zamora MA, Torres X, et al. Markers of deep infiltrating endometriosis in patients with ovarian endometrioma: a predictive model. *Eur J Obstet Gynecol Reprod Biol*. 2017;209:55–60.

20. Guerriero S, Condous G, van den Bosch T, et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol*. 2016;48:318–332.

21. Exacoustos C, Malzoni M, Di Giovanni A, Lazzeri L, Tosti C, Petraglia F, Zupi E. Ultrasound mapping system for the surgical management of deep infiltrating endometriosis. *Fertil Steril*. 2014;102:143–150.

22. Okaro E, Condous G, Khalid A, Timmerman D, Ameye L, Huffel SV, Bourne T. The use of ultrasound-based 'soft markers' for the prediction of pelvic pathology in women with chronic pelvic pain--can we reduce the need for laparoscopy? *BJOG*. 2006;113:251–256.

23. Holland TK, Yazbek J, Cutner A, Saridogan E, Hoo WL, Jurkovic D. Value of transvaginal ultrasound in assessing severity of pelvic endometriosis. *Ultrasound Obstet Gynecol*. 2010;36:241–248.

24. Reid S, Lu C, Casikar I, Mein B, Magotti R, Ludlow J, Benzie R, Condous G. The prediction of pouch of Douglas obliteration using offline analysis of the transvaginal ultrasound 'sliding sign' technique: inter- and intra-observer reproducibility. *Hum Reprod*. 2013;28:1237–1246.

25. Hudelist G, Fritzer N, Staettner S, Tammaa A, Tinelli A, Sparic R, Keckstein J. Uterine sliding sign: a simple sonographic predictor for presence of deep infiltrating endometriosis of the rectum. *Ultrasound Obstet Gynecol*. 2013;41:692–695.

26. Menakaya U, Infante F, Lu C, et al. Interpreting the real-time dynamic ‘sliding sign’ and predicting POD obliteration: an inter-, intra-observer, diagnostic accuracy and learning curve study. *Ultrasound Obstet Gynecol*. 2016;48:113–120.

27. Exacoustos C, Brienza L, Di Giovanni A, Szabolcs B, Romanini ME, Zupi E, Arduini D. Adenomyosis: three-dimensional sonographic findings of the junctional zone and correlation with histology. *Ultrasound Obstet Gynecol*. 2011;37:471–479.

28. Van den Bosch T, Dueholm M, Leone FP, et al. Terms and definitions for describing myometrial pathology using ultrasonography. *Ultrasound Obstet Gynecol*. 2015;46:284–298.

29. Muzii L, Tucci CD, Feliciantonio MD, et al. Management of endometriomas. *Semin Reprod Med*. 2017;35:25–30.

30. Practice Committee of the American Society for Reproductive Medicine. Treatment of pelvic pain associated with endometriosis: a committee opinion. *Fertil Steril*. 2014;101:927–935.

31. Piketty M, Chopin N, Dousset B, et al. Preoperative work-up for patients with deeply infiltrating endometriosis: transvaginal ultrasonography must definitely be the first-line imaging examination. *Hum Reprod*. 2009;24:602–607.

32. Exacoustos C, Manganaro L, Zupi E. Imaging for the evaluation of endometriosis and adenomyosis. *Best Pract Res Clin Obstet Gynaecol*. 2014;28:655–681.

33. Endometriosis Treatment Italian Club. Ovarian endometrioma: what the patient needs. *J Minim Invasive Gynecol*. 2014;21:505–516.

34. Gerges B, Lu C, Reid S, Chou D, Chang T, Condous G. Sonographic evaluation of immobility of normal and endometriotic ovary in detection of deep endometriosis. *Ultrasound Obstet Gynecol*. 2017;49:793–798.

Fig. 1 Typical ultrasound appearance of an ovarian endometrioma: a unilocular cyst with ground glass echogenicity. Note the normal ovarian tissue around the cyst and the deep infiltrating endometriosis of the uterosacral ligament adherent to the ovary.

Fig. 2 Left endometrioma with adhesions to the lateral pelvic wall (white arrows).

Fig. 3 Longitudinal (a) and transverse (b) section of the pelvis with left endometriomas and rectal deep infiltrating endometriosis. Note how the endometrioma is adherent to the rectal deep infiltrating endometriosis and the retrocervical space is completely obliterated on the left side by the disease.

Table 1
Patient demographics and characteristics

	Total study population (N = 255)	Patients with only TVS mapping (n = 205)	Patients with TVS mapping followed by LPS surgery (n = 50)	p value*
Mean age, years (± SD)	34.2 ± 6.6	34.1 ± 6.5	34.5 ± 6.1	.6930
Body mass index, kg/m^2 (± SD)	21.5 ± 3.0	21.3 ± 2.9	22.1 ± 2.9	.0800
Parity, n (%)				
0	191 (74.9%)	161 (78.5%)	34 (68%)	.1360
1	32 (12.5%)	22 (10.7%)	8 (16%)	.3280
≥ 2	32 (12.5%)	22 (10.7%)	8 (16%)	.3280
Menarche, mean age (± SD)	12.2 ± 1.5	12.2 ± 1.5	12.3 ± 1.6	.6760
Endometrioma, mean maximum diameter (mm ± SD)	40.0 ± 18.1	36.6 ± 15.6	48.3 ± 21.4	.0001
Endometrioma maximum diameter, n (%)				
≥ 3 cm	177 (69.4%)	138 (67.3%)	40 (80.0%)	.0799
≥ 4 cm	102 (40.0%)	74 (36.0%)	30 (60.0%)	.0036
Previous medical treatment for endometriosis, n (%)	105 (41.1 %)	75 (36.5%)	30 (60.0%)	.0037
Endometrioma site, n (%)				
Left	115 (45.0 %)	104 (50.7%)	11 (22.0%)	.0002
Right	75 (29.4 %)	49 (23.9%)	26 (52.0%)	.0002
Bilateral	65 (25.5 %)	52 (25.3%)	13 (26.0%)	1.0000
Infertility, n (%)	77 (30.2%)	56 (27.3%)	21(42.0%)	.0579

Dysmenorrhea, n (%)	225 (88.2%)	180 (87.8%)	45 (90.0%)	.8091
Dyspareunia, n (%)	90 (35.3%)	65 (31.7%)	25 (50.0%)	.0204
Dyschezia and bowel functional symptoms, n (%)	51 (20.0%)	30 (14.6%)	21 (42.0%)	.0001
Dysuria, n (%)	16 (6.3%)	9 (4.4%)	7 (14.0%)	.0203

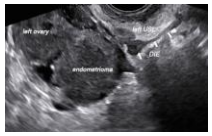
*Patients with TVS and no surgery (n = 205) vs TVS and surgery (n = 50).
SD = standard deviation; TVS = transvaginal sonography; LPS = laparoscopy.

Table 2
Endometrioma characteristics

Pelvic endometriosis sites	Total study population, n (%) (N = 255)	Unilateral endometrioma, n (%) (n = 190)	Left endometrioma, n (%) (n = 115)	Right endometrioma, n (%) (n = 75)	Unilateral endometrioma < 4 cm, n (%) (n = 120)	Unilateral endometrioma ≥ 4 cm, n (%) (n = 70)	Bilateral endometrioma total, n (%) (n = 65)	Bilateral endometrioma ≥ 4 cm, n (%) (n = 32)	Bilateral endometrioma < 4 cm, n (%) (n = 33)
Isolated endometrioma	38 (14.9%)	38 (20.0%)	21 (18.2%)	17 (22.7%)	28 (23%)	10 (14.3%)	–	–	–
Adenomyosis	134 (52.5%)	94 (49.5%)	58 (50.4%)	36 (48.0%)	63 (52.5%)	31 (44.3%)	40 (61.5%)	21 (65.6%)	19 (57.6%)
Tubal pathology (hydrosalpinx, sactosalpinx hematosalpinx)	1 (0.4%)	1 (0.5%)	1 (0.9%)	0	0	1 (1.4%)	0	0	0
Bladder infiltration	3 (1.2%)	2 (1.1%)	2 (1.7%)	0	2 (1.7%)	0	1 (1.5%)	1 (3.1%)	0
Right USL	38 (14.9%)	28 (14.7%)	12 (10.4%)	16 (21.3%)	17 (14.2%)	11 (15.7%)	10 (15.4%)	6 (18.8%)	4 (12.1%)
Left USL	67 (26.3%)	52 (27.4%)	46 (40.0%)	6 (8.0%)	33 (27.5%)	19 (27.1%)	15 (23.1%)	8 (25.0%)	7 (21.2%)
Torus uterinus	30 (11.8%)	21 (11.1%)	16 (13.9%)	5 (6.7%)	12 (10.0%)	9 (12.9%)	9 (13.8%)	4 (12.5%)	5 (15.2%)
Recto-vaginal septum	24 (9.4%)	19 (10.0%)	13 (11.3%)	6 (8.0%)	12 (10.0%)	7 (10.0%)	5 (7.7%)	3 (9.4%)	2 (6.1%)
Vagina	5 (2.0%)	2 (1.1%)	1 (0.9%)	1 (1.3%)	1 (0.8%)	1 (1.4%)	3 (4.6%)	1 (3.1%)	2 (6.1%)
Cranial rectum	56 (22.0%)	33 (17.4%)*	26 (22.6%)†	7 (9.3%)†	23 (19.2%)	10 (14.3%)	23 (35.4%)*	12 (37.5%)	11 (33.3%)
Caudal rectum	28 (11.0%)	21 (11.1%)	17 (14.8%)†	4 (5.3%)†	12 (10%)	9 (12.9%)	7 (10.8%)	2 (6.3%)	2 (6.1%)
Right parametrium	7 (2.7%)	6 (3.2%)	2 (1.7%)	4 (5.3%)	2 (1.7%)	4 (5.7%)	1 (1.5%)	1 (3.1%)	0
Left parametrium	12 (4.7%)	10 (5.3%)	9 (7.8%)	1 (1.3%)	7 (5.8%)	3 (4.3%)	2 (3.1%)	2 (6.3%)	0
Right ureter	4 (1.6%)	4 (2.1%)	1 (0.9%)	3 (4.0%)	3 (2.5%)	1 (1.4%)	0	0	0
Adhesions	186 (72.9%)	133 (70.0%)	83 (72.2%)	50 (66.7%)	77 (64.2%)‡	56 (80.0%)‡	53 (81.5%)	27 (84.4%)	26 (78.8%)
Obliteration of the pouch of Douglas	69 (27.1%)	40 (22.1%)*	29 (25.2%)	11 (14.7%)	20 (16.7%)	20 (28.6%)	29 (44.6%)*	19 (59.4%)§	10 (30.3%)§

USL = uterosacral ligament.
*Unilateral vs bilateral p < .05; †Unilateral left vs right, p < .05; ‡Unilateral < 4 cm vs ≥ 4 cm, p < .05; §Bilateral < 4 vs ≥ 4 cm, p < .05.

391

392 

393 Figure 1_bestsetConverted.png

394

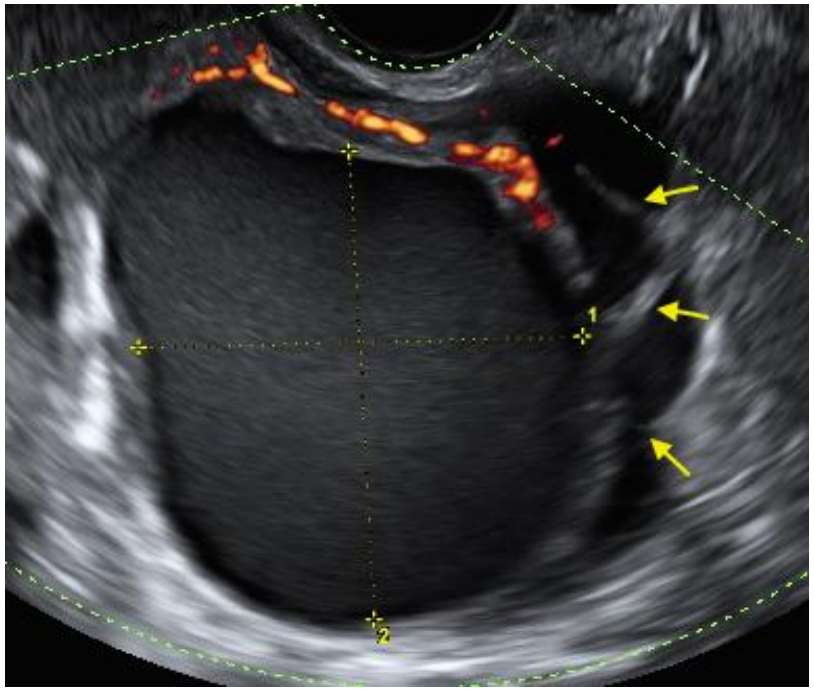


Figure 2_bestsetConverted.png

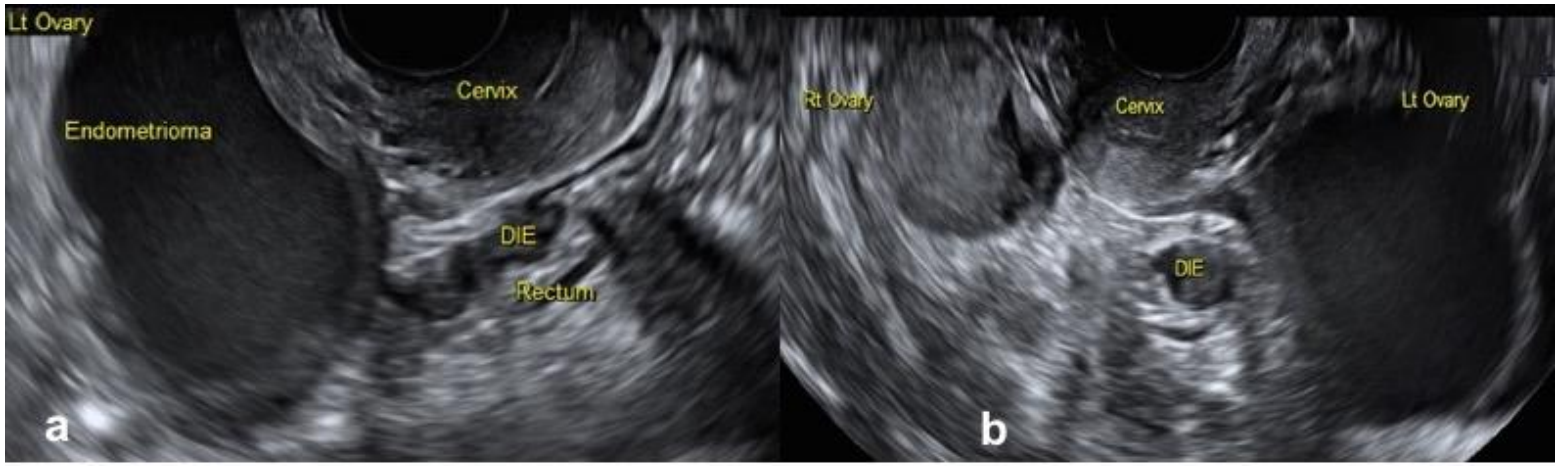


Figure 3_bestsetConverted.png