

# The role of ovarian fossa evaluation in patients with ovarian endometriosis

Carlo De Cicco Nardone<sup>1</sup> · Corrado Terranova<sup>1</sup> · Francesco Plotti<sup>1</sup> · Roberto Ricciardi<sup>1</sup> · Stella Capriglione<sup>1</sup> · Daniela Luvero<sup>1</sup> · Donatella Caserta<sup>2</sup> · Massimo Moscarini<sup>2</sup> · Pierluigi Benedetti Panici<sup>2</sup> · Roberto Angioli<sup>1</sup>

Received: 13 September 2014 / Accepted: 7 April 2015 / Published online: 16 April 2015  
© Springer-Verlag Berlin Heidelberg 2015

## Abstract

**Purpose** The aim of this study is to evaluate prospectively the presence of endometriosis in the peritoneum of the ovarian fossa of patients affected by endometriomas and its correlation with the adhesion between this peritoneum and endometrioma.

**Methods** Patients presenting ovarian endometriomas and candidate to laparoscopy were considered for inclusion in the study. Patients underwent laparoscopic excision of endometriomas. The presence of adherence of the ovarian fossa to endometrioma was investigated. In all patients, the removal of a peritoneum fragment from the ovarian fossa of the affected ovary was carried out.

**Results** 68 patients were enrolled in the study. 48 patients presented adhesions to the ovarian fossa. Histopathologic examination of the peritoneum of the ovarian fossa revealed the presence of endometriosis in 87 % of patients presenting adhesions of the endometriomas with ovarian fossa; surprisingly it was present only in 15 % of patients not presenting this condition ( $p < 0.0001$ ). Pain symptoms were more frequent in patients with endometriomas adhesion to the ovarian fossa. CA125 levels were not statistically significantly different between groups. At 12-month follow-up, four patients presented endometrioma recurrence. All of them presented adhesion of the ovarian fossa to the endometrioma in the first operation.

**Conclusions** There is a strong association between adhesion of the endometriomas to the ovarian fossa and the presence of endometriosis on the peritoneal surface of the fossa. This condition significantly correlates with pain symptoms and may predict endometrioma recurrence. The removal of this peritoneum in case of adherent endometrioma may potentially reduce the incidence of recurrence.

**Keywords** Endometriosis · Ovarian fossa · Laparoscopy · Peritoneum

## Introduction

Endometriosis is defined as the presence of endometrial-like tissue outside the uterus, which induces a chronic, inflammatory reaction. The condition is predominantly found in women of reproductive age, from all ethnic and social groups. The associated symptoms can impact on general physical, mental, and social well-being [1, 2]. Some women, however, have no symptoms at all [3].

Some evidence shows that genetic, endocrine, immunological, and environmental factors play a crucial role in the genesis and development of endometriosis [4, 5].

The most commonly affected sites are the pelvic organs and peritoneum, although other parts of the body such as the lungs are occasionally affected. The extent of the disease varies from a few, small lesions on otherwise normal pelvic organs to large, ovarian endometriotic cysts (endometriomas) and/or extensive fibrosis and adhesion formation causing marked distortion of pelvic anatomy [3]. Endometriomas usually contain thick fluid-like tar; such cysts are often densely adherent to the peritoneum of the

✉ Roberto Ricciardi  
ricciardi.roberto@hotmail.it

<sup>1</sup> Department of Obstetrics and Gynecology, “Campus Bio-Medico” University of Rome, Via Álvaro del Portillo, 200, 00128 Rome, Italy

<sup>2</sup> Department of Obstetrics and Gynecology, Sapienza University of Rome, Rome, Italy

ovarian fossa and the surrounding fibrosis may involve the tubes and bowel [3].

Excisional surgery for endometriomas should be considered the preferential surgical approach [6]. To decrease the risk of recurrence (or possible persistence) of endometriosis, the complete eradication of the disease is mandatory [7].

Endometriosis is rarely confined exclusively to the ovaries and the presence of an endometrioma seems to be a marker for more extensive disease [8].

The aim of our study is to prospectively evaluate the presence of endometriosis in the peritoneum of the ovarian fossa of patients affected by endometriomas and its correlation with the adhesion between this peritoneum and the endometrioma.

## Materials and methods

From January to December 2012, consecutive >18 years old patients with ultrasonographic evidence of ovarian endometriomas and candidate to laparoscopy were considered for inclusion in the study. Inclusion criteria were no contraindications to laparoscopic surgery, signed informed consent, presence of one or more endometriomas with maximal diameter >3 cm estimated by ultrasound. Exclusion criteria were presence of deep endometriosis, previous pelvic surgery, previous or present gynecologic neoplasms, BMI >40, ongoing or recent history of PID and menopausal status.

All women gave informed consent for participation in the study, and approval from the institutional ethics committee was obtained.

Pre-operative pain symptoms (dysmenorrhea, mid-cycle pain, dyspareunia, dysuria and dyschezia) were evaluated by a visual analog scale (VAS) with a 10-point rating from 1 (lack of pain) to 10 (unbearable pain). Significant pain was rated as VAS score  $\geq 4$  [9].

Before surgery, all patients underwent at least two transvaginal ultrasonographic scans at least 8 weeks apart to confirm the presence of ovarian cysts with ultrasonographic features of endometriomas. No patient had previously undergone any surgical treatment for endometriosis. None of the patients had been taking oral contraceptives for the previous 6 months.

The day before surgery, blood samples were obtained to dose preoperative CA125 levels. Normal levels of CA125 were considered to be less than 35 U/mL. Furthermore, patients will undergo to CA125 dosage within 48 h after discharge and starting from primary surgery every 3 months for the first year.

Before surgery, patients were submitted to mechanical bowel preparation, deep venous thrombosis prophylaxis

with low molecular weight heparin (from the evening before the operation and postoperatively until complete deambulation). Short-term antibiotic prophylaxis was performed at the beginning of the operation (cefazolin, 2 g).

The patients underwent laparoscopic excision of ovarian endometriomas by the stripping technique, as previously reported [10, 11]. The presence of adherence between the peritoneum of the ovarian fossa and the endometrioma was investigated and recorded. At the end of the procedure, the removal of a peritoneum fragment (at least  $3 \times 3$  mm) from the ovarian fossa of the affected ovary was carried out.

All surgical specimens were sent for histological examination. The histological diagnosis of endometriotic cysts and of peritoneal endometriosis was made when the internal surface of cyst removed at laparoscopy was lined, totally or partially, by endometrial epithelium with or without stroma [12]. Operative data, intra-operative and postoperative complications and length of hospital stay were recorded. Intra-operative blood loss was estimated subtracting the volume of used normal saline for irrigation (mL) from the waste irrigation fluid volume (mL).

After surgery, all patients not desiring pregnancy underwent treatment with cyclic monophasic combined oral contraceptives (ethinyl estradiol 0.030 mg, and gestodene 0.075 mg, daily for 21 days followed by a 7-day interval) for at least 6 months [13].

All patients were clinically evaluated 1, 6, and 12 months after surgery. Follow-up consisted of pelvic examination, transvaginal ultrasound, and pain symptoms evaluation.

The diagnostic criteria adopted for ovarian endometrioma were those reported by Kupfer et al. [14]: (1) homogeneous contents of low echogenicity, (2) the echoes present in 1 cyst or in various cysts in different positions, and (3) confirmation of the suspected mass by repeat ultrasonography in the early follicular phase.

Student's or Mann–Whitney's *t* tests were used for quantitative variables, according to their pattern of distribution. Qualitative variables were compared by means of the Chi square test or Fisher's test, according to the assumptions to be verified. Statistical significance was set at a *p* value less than 0.05.

## Results

68 patients affected by ovarian endometriomas and candidate to laparoscopy were enrolled in this study. Patients characteristics are summarized in Table 1. Concerning pain symptoms, dysmenorrhea was reported by 42 patients (62 %) with a mean VAS score of  $6.1 \pm 1.7$ , mid-cycle pain was reported by 27 patients (40 %) with a mean VAS

**Table 1** Patients characteristics and laparoscopic findings

Characteristic	Data <sup>a</sup>
Total number of patients	68 (100 %)
Age	31.9 ± 7.4 (18–46)
Body Mass Index	24.7 ± 3.3 (18–32)
<i>Parity, number</i>	
0	45 (66 %)
1	18 (26 %)
2	5 (8 %)
<i>Pain symptoms<sup>b</sup></i>	
Dysmenorrhea	42 (62 %); pre-operative VAS score 6.1 ± 1.7
Mid-cycle pain	27 (40 %); pre-operative VAS score 5.7 ± 1.6
Dyspareunia	8 (12 %); pre-operative VAS score 5.2 ± 1.4
Dyschezia	3 (4 %); pre-operative VAS score 5.7 ± 1.5
Dysuria	1 (1 %); pre-operative VAS score 6
<i>Laparoscopic findings</i>	
<i>Feature, n</i>	
Total number of endometriomas	87
Patients with monolateral endometrioma	40 (59 %)
Patients with bilateral endometrioma	19 (28 %)
Patients with more than one endometrioma per ovary	9 (13 %)
Patients with endometriomas adherent to ovarian fossa	48 (71 %)

<sup>a</sup> Values are given as mean ± SD (range) or number (percentage)

<sup>b</sup> Some patients had more than 1 symptom

score of 5.7 ± 1.6, dyspareunia was reported by 8 patients (12 %) with a mean VAS score of 5.2 ± 1.4, dyschezia was reported by 3 patients (4 %) with a mean VAS score of 5.7 ± 1.5 and dysuria was reported by 1 patient (1 %) with a VAS score of 6.

Laparoscopic findings are shown in Table 1. A total of 87 endometriomas were laparoscopically removed: 19 patients had bilateral endometriomas, and 40 had monolateral endometriomas; 9 of the patients presenting monolateral endometrioma had 2 cysts per ovary. Among the 68 patients submitted to laparoscopy, 48 (71 %) of them presented adhesions to the ovarian fossa; in all the other cases (20 patients) no adhesion was found between ovarian fossa and endometriomas.

Histopathologic examination of the ovarian cysts revealed endometriosis in all cases. Concerning histopathologic examination of the peritoneum of the ovarian fossa, it revealed the presence of endometriosis in 42 (87 %) of the 48 patients presenting adhesions of the endometriomas with ovarian fossa; surprisingly it was present only in 3 (15 %) of the 20 patients not presenting adhesions of the endometriomas with ovarian fossa ( $p < 0.0001$ ).

Pain symptoms were more frequent in patients with endometriomas adhesion to the ovarian fossa; within the 48

patients with adhesion, 42 (87 %) presented at least 1 significant pain symptom, whereas on 20 patients not presenting adhesion, 13 (65 %) presented significant pain symptoms ( $p = 0.03$ ). Concerning CA125 levels are shown in Table 2; we found that mean values were not statistically significantly different between patients with endometriomas adherent to ovarian fossa and patients not presenting this condition ( $p = 0.31$ ).

Concerning intra- and postoperative features, mean operative time was 84.4 ± 19.5 min; mean blood loss was 86.2 ± 38.2 mL; no intra-operative or post-operative complications were detected and the mean hospital stay was 1.2 ± 0.4 days.

All patients returned to follow-up examination. At 12-month follow-up, in four patients (6 %) recurrence of endometrioma was detected. Only two of these patients were submitted to operative laparoscopy because of the dimension of endometriomas (>3 cm). In all the two patients the endometriotic nature of the cyst was confirmed. All of the patients presenting recurrence, presented adhesion of the ovarian fossa to the endometrioma in the first operation and higher CA125 mean values, but not statistically significant ( $p = 0.08$ ).

**Table 2** Patients characteristics and CA125 levels

Characteristic	CA125 (UI/mL) <sup>a</sup>
Total number of patients ( <i>n</i> = 68)	80.6 ± 27.8
Patients with endometriomas adherent to ovarian fossa ( <i>n</i> = 48)	83.6 ± 28.1
Patients with endometriomas not adherent to ovarian fossa ( <i>n</i> = 20)	76.5 ± 27.3

<sup>a</sup> Values are given as mean ± SD

## Discussion

Laparoscopy represents today the leading surgical approach in case of symptomatic and/or large ovarian endometriomas. Comparative studies have shown that the results in terms of pregnancy rates or recurrence are comparable to or better than those obtained with laparotomy [15–17].

The development of more accurate diagnostic tools and refined laparoscopic techniques has almost eliminated diagnostic laparoscopy from the contemporary management of endometriosis [18]. Modern operative laparoscopy allows, at the same time, to confirm the diagnosis and treat the disease modulating, based on anatomic results of surgery, the decision of postoperative medical treatment [19, 20]. Disease recurrence is, in fact, seen in 8–40 % of patients treated with conservative surgery and is a main concern for the gynecological surgeon [21, 22].

Concerning our data, 87 endometriomas were laparoscopically removed: 19 patients had bilateral endometriomas, and 49 had monolateral endometriomas. Among the 68 patients submitted to laparoscopy, 48 (71 %) of them presented adhesions to the ovarian fossa; in all the other cases no adhesion was found between ovarian fossa and endometriomas.

According to literature data, ovarian endometriosis accounts for 35 % of benign cysts and, even though the ovary is not the most common location of pelvic endometriosis [23, 24], it occurs in 17–44 % of patients with this disease [25, 26]. In the study conducted by Redwine [23], among a population of 1785 patients with surgically treated endometriosis, only 19 (1 %) of patients had exclusively ovarian involvement, finding that support the concept that adequate surgical treatment of ovarian endometrioma requires surgical treatment of all of the pelvic areas involved, especially of deep endometriotic lesions. It has been well demonstrated that, to decrease the risk of recurrence (or possible persistence) of endometriosis, the best surgical approach should be one that completely removes all of the visible disease [27]. Therefore, if improvement in patient symptoms, reduction of recurrence, enhancement of fertility, and patient satisfaction are intended, the complete eradication of endometriosis is mandatory [7, 28–30]. At laparoscopy, deeply infiltrating endometriosis may have the appearance of minimal disease [31]; thus, the isolated

identification of ovarian endometriosis and its single excision can lead to under-diagnosis and under-treatment.

According to our data, histopathologic examination of the peritoneum of the ovarian fossa revealed a statistically significant difference in the presence of endometriosis between patients presenting adhesions of the endometriomas with ovarian fossa and patients not presenting it (87 and 15 %, respectively;  $p < 0.0001$ ).

Furthermore, the rate of patients presenting pain symptoms (dysmenorrhea, mid-cycle pain, dyspareunia, dyschezia, and dysuria) was significantly higher in the group of patients presenting adhesions between peritoneum of ovarian fossa and endometrioma (87 and 65 %, respectively;  $p = 0.03$ ). As reported by Mereu et al., the presence of adnexal endometriosis and adhesions could be a cause of painful ovulation and might explain the high incidence of this symptom among patients affected by endometriosis and/or adhesions at the level of adnexa and posterior broad ligament. The high rate of mid-cycle pain might be explained by the formation of adnexal adhesions between two damaged surfaces: the ovary and the posterior broad ligament [8].

Moreover, according to our series, at 12-month follow-up in three patients endometriomas recurred; surprisingly all these patients presented adhesion of the endometrioma to the peritoneum of the ovarian fossa during first operation.

In conclusion, there is a strong association between adhesion of the endometriomas to the ovarian fossa and the presence of endometriosis on the underlying peritoneal surface. Furthermore, this condition significantly correlates with the symptomatology of the patients.

Furthermore, the presence of endometriosis in the peritoneum of the ovarian fossa may predict endometrioma recurrence. Concerning CA125 levels, we found that CA125 values do not correlate with endometriosis on the peritoneal surface of the fossa and endometrioma recurrence. These data confirm that CA125 concentration is grossly increased in non-malignant conditions such as various abdominal conditions [32].

Considering that adequate surgical treatment of endometriosis should require removal of all concomitant pelvic endometriotic lesions, the removal of ovarian fossa peritoneum in case of endometrioma adherent to the underlying fossa may potentially help the complete removal

of the disease; furthermore, it could potentially reduce the incidence of endometrioma recurrence.

**Conflict of interest** The authors have no conflict of interest or financial ties to disclose.

## References

- Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, Jenkinson C, Kennedy SH, Zondervan KT, World Endometriosis Research Foundation Global Study of Women's Health consortium (2011) Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 96(2):366–373
- Melis I, Agus M, Pluchino N, Di Spiezo Sardo A, Litta P, Melis GB, Angioni S (2014) Alexithymia in women with deep endometriosis? A pilot study. *J Endometriosis Pelvic Pain Dis* 6(1):26–33
- Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, Hummelshoj L, Prentice A, Saridogan E, ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group (2005) ESHRE guideline for the diagnosis and treatment of endometriosis. *Hum Reprod* 20(10):2698–2704
- Kobayashi H, Yamada Y, Morioka S, Niuro E, Shigemitsu A, Ito F (2014) Mechanism of pain generation for endometriosis-associated pelvic pain. *Arch Gynecol Obstet* 289(1):13–21
- Locci R, Nisolle M, Angioni S, Foidart JM, Munaut C (2013) Expression of the gamma 2 chain of laminin-332 in eutopic and ectopic endometrium of patients with endometriosis. *Reprod Biol Endocrinol* 26(11):94
- Hart R, Hickey M, Maouris P, Buckett W, Garry R (2005) Excisional surgery versus ablative surgery for ovarian endometriomata: a cochrane review. *Hum Reprod* 20(11):3000–3007
- Vignali M, Bianchi S, Candiani M, Spadaccini G, Oggioni G, Busacca M (2005) Surgical treatment of deep endometriosis and risk of recurrence. *J Minim Invasive Gynecol* 12(6):508–513
- Mereu L, Florio P, Carri G, Pontis A, Petraglia F, Mencaglia L (2012) Clinical outcomes associated with surgical treatment of endometrioma coupled with resection of the posterior broad ligament. *Int J Gynaecol Obstet* 116(1):57–60
- Keele KD (1948) The pain chart. *Lancet* 2(6514):6–8
- Marana R, Caruana P, Muzii L, Catalano GF, Mancuso S (1996) Operative laparoscopy for ovarian cysts: excision versus aspiration. *J Reprod Med* 41:435–438
- Muzii L, Marana R, Caruana P, Mancuso S (1996) The impact of preoperative gonadotropin-releasing hormone agonist treatment on laparoscopic excision of ovarian endometriotic cysts. *Fertil Steril* 65:1235–1237
- Busacca M, Marana R, Caruana P, Candiani M, Muzii L, Calia C, Bianchi S (1999) Recurrence of ovarian endometrioma after laparoscopic excision. *Am J Obstet Gynecol* 180(3 Pt 1):519–523
- Muzii L, Marana R, Caruana P, Catalano GF, Margutti F, Panici PB (2000) Postoperative administration of monophasic combined oral contraceptives after laparoscopic treatment of ovarian endometriomas: a prospective, randomized trial. *Am J Obstet Gynecol* 183(3):588–592
- Kupfer MC, Schwiimer RS, Lebovic J (1992) Transvaginal sonographic appearance of endometriomata: spectrum of findings. *J Ultrasound Med* 11:129–132
- Bateman BG, Kolp LA, Mills S (1994) Endoscopic versus laparotomy management of endometriomas. *Fertil Steril* 62:690–695
- Catalano GF, Marana R, Caruana P, Muzii L, Mancuso S (1996) Laparoscopy versus microsurgery by laparotomy for excision of ovarian cysts in patients with moderate or severe endometriosis. *J Am Assoc Gynecol Laparosc* 3:267–270
- Adamson GD, Subak LL, Pasta DJ, Hurd SJ, Von Franque O, Rodriguez BD (1992) Comparison of CO<sub>2</sub> laser laparoscopy with laparotomy for treatment of endometriomata. *Fertil Steril* 57:965–973
- Hornstein MD, Hemmings R, Yuzpe AA, Heinrichs WL (1997) Use of nafarelin versus placebo after reductive laparoscopic surgery for endometriosis. *Fertil Steril* 68:860–864
- Angioni S, Pontis A, Dessole M, Surico D, De Cicco Nardone C, Melis I (2015) Pain control and quality of life after laparoscopic en-block resection of deep infiltrating endometriosis (DIE) vs. incomplete surgical treatment with or without GnRHa administration after surgery. *Arch Gynecol Obstet* 291:363–370
- Angioni S, Cofelice V, Pontis A, Tinelli R, Socolov R (2014) New trends of progestins treatment of endometriosis. *Gynecol Endocrinol* 30(11):769–773
- American College of Obstetricians and Gynecologists (1993) Endometriosis. *Int J Gynecol Obstet* 43:221–227
- Canis M, Mage G, Wattiez A, Chapron C, Pouly JL, Bassil S (1992) Second-look laparoscopy after laparoscopic cystectomy of large ovarian endometriomas. *Fertil Steril* 58:617–619
- Redwine DB (1999) Ovarian endometriosis: a marker for more extensive pelvic and intestinal disease. *Fertil Steril* 72(2):310–315
- Sampson JA (1927) Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obstet Gynecol* 14:422–469
- Gruppo italiano per lo studio dell'endometriosi (1994) Prevalence and anatomical distribution of endometriosis in women with selected gynaecological conditions: results from a multicentric Italian study. *Hum Reprod* 9(6):158–162
- Jenkins S, Olive DL, Haney AF (1986) Endometriosis: pathogenetic implications of the anatomic distribution. *Obstet Gynecol* 67(3):335–338
- Busacca M, Vignali M (2009) Endometrioma excision and ovarian reserve: a dangerous relation. *J Minim Invasive Gynecol* 16(2):142–148
- Strowitzki T (2005) Infertility treatment and endometriosis—risk and benefit of assisted reproductive techniques. *Zentralbl Gynakol* 127(5):314–319
- Chapron C, Pietin-Vialle C, Borghese B, Davy C, Foulot H, Chopin N (2009) Associated ovarian endometrioma is a marker for greater severity of deeply infiltrating endometriosis. *Fertil Steril* 92(2):453–457
- Chapron C, Chopin N, Borghese B, Malartic C, Decuypere F, Foulot H (2004) Surgical management of deeply infiltrating endometriosis: an update. *Ann N Y Acad Sci* 1034:326–337
- Koninckx PR, Oosterlynck D, D'Hooghe T, Meuleman C (1994) Deeply infiltrating endometriosis is a disease whereas mild endometriosis could be considered a non-disease. *Ann N Y Acad Sci* 734:333–341
- Grover S, Quinn MA, Weideman P, Koh H (1992) Factors influencing serum CA 125 levels in normal women. *Obstet Gynecol* 79(4):511–514