Direct proportional relationship between endometrioma size and ovarian parenchyma inadvertently removed during cystectomy, and its implication on the management of enlarged endometriomas

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BACKGROUND: The aim of this study was to estimate whether or not the size of an endometrioma is related to the thickness of the ovarian parenchyma inadvertently excised along with the cyst wall.

METHODS: We performed a retrospective study including 35 women who had undergone endometrioma cystectomy, using an ovarian tissue sparing procedure. In total 38 specimens were studied by three pathologists as three women presented bilateral localizations, and all cyst diameters measured at least 30 mm. For each endometrioma, serial sections were performed, and on each section four different sites were randomly chosen to measure the thickness of glandular epithelium and stroma, of subjacent fibrosis, depending on the cyst, and of the ovarian parenchyma removed with the cyst. The diameter of the ovary was measured preoperatively either by MRI or ultrasound, and the area of the internal wall was then calculated. The relationships between the mean thickness of ovarian parenchyma removed and the variables were estimated and a multiple regression model identified independent predictors for ovarian parenchyma thickness.

RESULTS: Adjacent ovarian tissue was found in 37 cases (97%). The mean thickness of ovarian tissue removed was 1173 ± 711 μm and that of the cyst wall was 851 ± 499 μm. The thickness of the ovarian parenchyma removed presented a direct proportional relationship with cyst diameter (P = 0.015), and consequently with cyst wall area (P = 0.032). This relationship with cyst diameter was independent after adjustment on other variables (P = 0.032).

CONCLUSION: Endometrioma cystectomy even though performed with an accurate surgical technique leads to significant ovarian tissue removal, the thickness of which increases proportionally with cyst diameter.

Key words: endometrioma / ovarian parenchyma / excision / cystectomy / fertility

Introduction

The prevalence of endometriosis in the general population averages 5%, and involves ovaries in up to 44% of cases (Jenkins et al., 1986). Although surgical management of ovarian endometriosis is routinely performed all over the world, a better knowledge of the studies that evaluate the procedure efficiency by the rate of recurrences and consequences on ovarian function could, for many surgeons, lead to improvements in surgical procedures (Jones et al., 2002; Canis et al., 2003). Several authors have suggested that endometrioma cystectomy may be harmful for ovarian tissue and surgeons require knowledge of both surgical procedures and the specific physiopathology of endometriomas (Canis et al., 2003; Muzzi et al., 2007; Roman et al., 2009). Histopathologic studies have clearly shown that
Endometrioma size predicts ovarian tissue loss

Endometrioma cystectomy regularly leads to the removal of large fragments of adjacent ovarian tissue, particularly in areas close to the ovarian hilus (Muzii et al., 2002). Ovarian post-operative transvaginal sonographic evaluation shows that endometrioma cystectomy is associated with a significant decrease in residual ovarian volume that may result in diminished ovarian reserve and function (Exacoustos et al., 2004).

The aim of our retrospective study was to evaluate whether or not more ovarian parenchyma is inadvertently removed with increasing cyst size. We therefore studied the relationship between the size of the cyst and the thickness of the ovarian tissue removed along with the cyst wall, in women managed by an experienced surgeon using an ovarian tissue sparing technique.

Materials and Methods

We performed a retrospective study including women having undergone endometrioma excision, of diameter ≥30 mm, carried out over a 30 month period by one laparoscopist surgeon experienced in deep and ovarian endometriosis management, in the Department of Gynecology and Obstetrics of Rouen University Hospital (France). All women had benefited from preoperative medical treatment using GnRH analogs for 1–3 months. Histological specimens of excised endometriomas were reviewed by two pathologists (I.O. and O.T.), who carried out serial sections and randomly chose, for each section, four different sites to measure the thickness of glandular epithelium and stroma, of subjacent fibrosis, depending on the cyst, and of the ovarian parenchyma removed with the cyst (Figs 1 and 2). In accordance with the French regulations, this retrospective study was exempted from IRB approval.

The surgical procedure of endometrioma excision has been previously described by other authors as being an ovarian tissue sparing procedure (Muzii et al., 2005; Roman et al., 2009). This surgical technique takes into account the physiopathologic theories of the development of endometriomas (Hughesdon, 1957; Brosens et al., 1994; Donnez et al., 1996; Nisolle and Donnez, 1997). According to the theory of Hughesdon, an ovarian endometrioma is the result of cortex invagination linked to the accumulation of menstrual debris from bleeding of endometrial implants, which are located on the ovarian surface and adherent to the peritoneum (Hughesdon, 1957). This theory may be verified in more than 90% of ovarian endometriomas (Brosens et al., 1994). A second theory proposed by Nisolle and Donnez states that endometriomas originate from the metaplasia of celomic epithelium invaginated into the ovarian cortex, a theory which fits 100% of cases of ovarian endometriomas (Nisolle and Donnez, 1997). Both theories are of major importance for surgeons in that they suggest that the excision of an endometrioma does not require antimesial incision of the ovarian parenchyma, as it can be performed through a small area of the cyst, free of ovarian tissue (Roman et al., 2009).

During the removal of ovarian endometrioma, three distinct cyst areas are identifiable, each one requiring a different excision procedure (Muzii et al., 2005; Roman et al., 2009). The first area (A) from where the cyst invagination originates, measures 1 cm² on average and is located around the site of parietal adhesions. This area is revealed by lyses of adhesions between the ovary and the adjacent broad ligament, leading to characteristic ‘chocolate fluid’ evacuating from the cyst. The excision by scissors of area A allows the surgeon to identify a cleavage plane close to the cyst wall, which may be followed without significant bleeding (area B; Canis et al., 2001). Where adhesions are revealed in the cleavage plane, they should be coagulated and cut, so as not to strip the ovarian cortex. Close to the ovarian hilus, such adhesions may be frequent, requiring coagulation using bipolar current and section by scissors (area C), for complete cyst removal.

This technique is considered to be an ovarian tissue sparing procedure (Muzii et al., 2002). It is clear however, despite particular care taken by the surgeon, that ovarian tissue is frequently inadvertently excised. In order to estimate the removal of ovarian tissue during endometrioma cystectomy, for each endometrioma 14, four measures of thickness of the adjacent ovarian tissue were randomly performed (respectively t1, t2, t3, and t4), with the calculation of a mean thickness of removed ovarian parenchyma tm (Fig. 1). The first measurement was located close to the ovarian hilus, the second was antimesenterial, and the remainder was positioned midway between these two sites. To estimate in cm² the area a of the removed cyst (a = d² x π), we then used a preoperative measurement of the diameter d of the endometrioma t taken from an MRI or ultrasonography. Similarly, four thicknesses of the fibrous cyst wall were measured (f1, f2, f3, and f4), in order to estimate the mean thickness (f) of the fibrosis surrounding the endometrial layer. The thicknesses of endometrial epithelium and stroma were also measured (e1, e2, e3, and e4) and these results were used in the estimation of the mean thickness of the endometrial lining (em). Glandular structures arising along the endometrial lining were measured, along with the number of oocytes removed from each specimen.

Figure 1 For each endometrioma and on serial sections, four different sites were randomly chosen to measure both the thickness of glandular epithelium, stroma and subjacent fibrosis depending on the cyst (green line), and that of the ovarian parenchyma removed along with the cyst (red line).
Statistical analysis was performed using Stata 9.0 Software (Stata Corporation, 4905 Lakeway Drive, TX, USA). Median values, percentiles, mean values and SD were calculated for continuous variables, and numbers and percentages for categorical variables. The relationship between categorical variables and thickness was calculated using the Mann–Whitney test. The relationship between continuous variables and the thickness of ovarian parenchyma removed was calculated using a regression model and Spearman’s correlation test. A multivariate model was used to identify the independent predictors of the thickness of ovarian parenchyma removed. A P-value inferior to 0.05 was considered to be statistically significant.

Results

In total, 38 ovarian endometriomas in 35 women were managed by cystectomy following the procedure described above. All women expressed a desire to retain their fertility, thus particular care was taken to spare ovarian tissue during the procedure. In all cases, preoperative amenorrhoea had been induced for 4 to 12 weeks using GnRHa associated with add back therapy. The subjects mean age was 29.3 years and the SD 5.3 years. In 29 cases (76%), endometrioma cystectomy was performed in nulliparas. To date, only 10 women have post-operatively attempted to conceive: 7 women have already conceived naturally and in 3 cases IVF will be required due to Fallopian tube abnormalities.

In 24 cases (63%), the cyst was located on the left ovary and in 14 cases (37%) on the right ovary. Eight women presented with bilateral ovarian cysts; however, only in three cases both cysts were >30 mm respecting our inclusion criteria. In 18 women (47%), ovarian endometriomas were associated with deep rectovaginal or rectal endometriosis, which was excised at the same time. Mean and median values, SD and percentiles for the following parameters are shown in Table I: thickness of endometrial epithelium, fibrous cyst wall and removed ovarian parenchyma preoperative cyst diameter and area and the number of oocytes inadvertently removed. In one case (3%), no ovarian tissue was found on the endometrioma capsules. The presence of glandular structures arising along the endometrial layer was recorded in 25 specimens (66%).

There were no statistical significant relationships between the thickness of ovarian parenchyma removed and respectively bilateral endometrioma (P = 0.66), simultaneous management of deep

![Figure 2](https://academic.oup.com/humrep/article-abstract/25/6/1428/2915767/1430)
endometriosis \( (P = 0.10) \), and nullipara status \( (P = 0.59) \). We observed a tendency toward statistical significance between young age and an increase in the thickness of ovarian parenchyma removed \( (P = 0.06) \), while no significant relationship was found between age and number of oocytes or fibrosis thickness (respectively, \( P = 0.21 \) and \( P = 0.75 \)). The relationship between the number of oocytes excised and the thickness of ovarian parenchyma was statistically significant \( (P = 0.02) \), while that between the number of oocytes and the thickness of fibrosis was not \( (P = 0.17) \). Conversely, there was a significant statistical relationship between the thickness of ovarian parenchyma and both preoperative cyst diameter (correlation coefficient of 0.39, \( P = 0.015 \)) and cyst area (correlation coefficient of 0.35, \( P = 0.03 \)), and a tendency towards a negative correlation between fibrosis layer and ovarian parenchyma thickness (correlation coefficient of 0.29, \( P = 0.08 \)) (Table II, Fig. 3). Due to the dependent relationship between cyst diameter and area, we did not include both continuous variables in the multiple regression model at the same time, the results of which are presented in Table III. Our results suggest that an increase in cyst diameter of 1 cm leads to the removal of a supplementary thickness of the ovarian parenchyma averaging 200 \( \mu m \).

**Discussion**

We observed that endometrioma cystectomy despite an accurate surgical technique leads to ovarian tissue removal in a majority of cases. Furthermore, at the time of surgery the amount of ovarian parenchyma loss increases proportionally with increases in cyst diameter. This tissue loss averages 200 \( \mu m \) per centimetre increase in cyst diameter.

Unfortunately we were unable to estimate the volume of ovarian parenchyma removed from the data concerning ovarian parenchyma thickness measured on the specimen and preoperative cyst diameter. It should be noted that both the thickness of endometrioma capsules and that of the ovarian parenchyma are likely to be modified by the retraction of the tissues during the fixation process, while accurate measurement of post-operative cyst diameter presents obvious difficulties on a broken and fragmented cyst. Nevertheless, we can reasonably state that there is an increase in the volume of ovarian tissue removed with an increase in cyst diameter. As this volume is provided by the formula: thickness \( \times \) (post-operative diameter/2)^2 \( \times \pi \), it is clear that a simultaneous increase in thickness and diameter in an enlarged endometrioma leads to a consecutive increase in the absolute value of ovarian parenchyma removed, when compared with endometrioma of inferior diameter.

The inadvertent removal of endometrioma parenchyma during cystectomy has already been reported by numerous authors, and it appears to be a frequent occurrence (Donnez et al., 1996; Exacoustos et al., 2004). In a series of 122 women managed by experienced surgeons from Clermont Ferrand (France) using the ovarian tissue sparing technique, ovarian tissue was found on cyst wall specimens in a majority of women, and 10 times more frequently when compared with cystectomy in dermoid cysts (Matsouzaki et al., 2009). The volume of ovarian tissue lost may be as high as the post-operative volume of the ovary could decrease by 50\% when compared with the contralateral ovary (Exacoustos et al., 2004). Several authors have reported that inadvertent removal of ovarian tissue is even more frequent when surgeons considered that the stripping procedure was easy to perform (Hachisuga and Kawarabayashi, 2002). This means that the hypothetical cleavage plan, which surgeons might intraoperatively identify around the cyst, is in fact not located

![Figure 3](https://academic.oup.com/humrep/article-abstract/25/6/1428/2915767/1428)
between the endometrioma fibrous wall and ovarian parenchyma, but rather within the ovarian tissue itself, and is due to the strong fusion between the ovarian parenchyma and fibrosis (Donnez et al., 1996).

Our data suggest the possible benefits of treatment to decrease the size of ovarian endometrioma prior to cystectomy. Based on this hypothesis, Donnez et al. proposed a three-step surgical management of large endometriomas, rather than performing a cystectomy without delay. This three-step procedure begins with cyst drainage, followed by a 3-month treatment by GnRH analogs, and culminates in a curative surgery, by either ablation or excision, on a cyst whose diameter has been reduced by 50% (Donnez et al., 1996). To date, no comparative studies on enlarged endometriomas are available to support this strategy. It would be important to demonstrate that the expected advantages related to the performing of two surgical procedures instead of one are outweighed by a significant improvement in pregnancy and recurrence rates.

It is also evident that repetitive cystectomies in enlarged recurrent cysts must be avoided wherever possible, so as to reduce the risk of definitive infertility due to the repetitive excision of ovarian parenchyma. Surgeons carrying out the first cystectomy in a young patient with large endometrioma should be aware of the necessity for complete excision of the cyst wall in order to prevent endometrioma recurrences. Furthermore, in women not intending to conceive immediately after surgery, the systematic administration of continuous post-operative contraceptive pill treatment can prevent cyst recurrences, as has been demonstrated by a recent randomized trial (Seracchioli et al., 2010).

We consider that our results are of note for those surgeons who believe that endometrioma cystectomy could be harmful to the ovarian reserve, especially when the endometrioma is large. Our data indicates the importance of conducting a comparative trial between one-step and three-step cystectomy in women presenting with enlarged ovarian endometriomas only. Outcomes of this trial should not only include the preservation of ovarian tissue but also the multiple consequences on hormonal status and on both spontaneous and induced fertility.

### Authors’ roles

H.R. developed the original design and performed surgical procedures. I.O., O.T., I.P. and J.C.S. reviewed histological specimens. H.R. and O.T. participated in acquisition, analysis and interpretation of data. H.R. and N.B. wrote the first draft of the report. All authors contributed to the writing of the final manuscript.

### References


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**Table III** Relationship between the thickness of ovarian parenchyma lost, cyst diameter and thickness of the cyst wall (multivariate analysis, multiple regression model).

<table>
<thead>
<tr>
<th>Factor</th>
<th>β-Coefficient</th>
<th>95% CI of β-coefficient</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst diameter</td>
<td>20.8</td>
<td>1.9; 39.7</td>
<td>0.032*</td>
</tr>
<tr>
<td>Thickness of the fibrous cyst wall</td>
<td>-0.30</td>
<td>-0.75; 0.15</td>
<td>0.18</td>
</tr>
<tr>
<td>Constant</td>
<td>483</td>
<td>-554; 1519</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*Statistically significant.