Best Practice & Research Clinical Obstetrics and Gynaecology 59 (2019) 48–55

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

5

Modern approaches to surgical management of endometrioma

S. Gordts*, R. Campo

Leuven Institute for Fertility & Embryology, Schipvaartstraat 4, 3000 Leuven, Belgium

Keywords:
Ovarian endometrioma
Surgery
Fertility preservation

A B S T R A C T

Formation of the ovarian endometrioma consists of implantation, invagination of the ovarian cortex, and adhesion formation. Progression is characterized by repeated injury and repair with degenerative changes. Already with a partially deprived ovarian reserve, resulting from the disease, surgical treatment carries a potential risk of further follicular deprivation. Surgery should therefore be performed with microsurgical precision by experienced hands.

Early treatment can possibly prevent further progression. The adverse impact on ovarian reserve of the ablative approach has to be balanced against a lower recurrence rate of a cystectomy. Adapted surgical approaches like a two-step approach or a combination of excisional and ablative surgery has to be considered in case of a large endometrioma. Further studies on the possibility and advantages of sclerotherapy are warranted. Fertility preservation by cryopreservation of ovarian cortex should be part of the informed consent with the patient.

Introduction

Endometriosis is a common gynecological disease with an estimated incidence in the infertile population ranging from 20% to 50% [1] (Moen et al.). In case of ovarian endometrioma, however, epidemiological data do not exist. Implantation theory of retrograde-shredded menstrual endometrial cells is the most widely accepted pathogenesis [2]. Regurgitated endometrial cells may implant on the ovarian surface, thereby causing local bleeding and adhesions. Hughesdon [3] demonstrated the

* Corresponding author.
E-mail address: stephan.gordts@lifeexpertcentre.be (S. Gordts).

https://doi.org/10.1016/j.bpobgyn.2018.12.013
1521-6934/

invaginated cortex with fibrosis and adhesion formation. As such, the ovarian endometrioma is an extraovarian pseudocystic structure without a real cystic wall but delineated by the fibrotic tissue. With the aging of the endometrioma, the invaginated cortex gradually thickens by smooth muscle metaplasia and fibrosis. Structural tissue alterations and fibrosis were described by Kitajima et al. [4] in endometriotic cysts as small as 4 cm. Intraovarian inspection of cysts as small as 1–2 cm clearly shows the aggression of the disease expressed by inflammation and neoangiogenesis [5,6]. In the absence of accurate markers, progressivity is difficult to predict, and surgical removal of the lesions is tempting. The complexity of the disease, however, clearly distinguishes it from other benign ovarian cysts and makes surgical treatment challenging. In the absence of clear data, discussion is going on whether early treatment causes less damage and whether a wait-and-see attitude will not carry the risk of exacerbation of the disease. We know from peritoneal implants that they can appear and disappear and can be considered to some extent as a normally occurring phenomenon [7]; however, this has never been described in the case of a small endometrioma.

Impact of endometriosis on the ovarian reserve

The presence of ovarian endometriomas, even in the absence of any kind of surgery, has a detrimental impact on the ovarian follicular reserve, and this impairing effect seems to be even more pronounced in younger women. In a recent publication [8], the difference in the concentration of AMH was more pronounced in younger women aged 18–27 years with bilateral ovarian endometrioma versus control or unilateral endometrioma than in older women. Although the impact of the size of the endometrioma on the ovarian reserve is less clear [9,10], the bilateralism of endometrioma has a detrimental impact on the ovarian reserve [8]. Kuroda et al. [11] correlated the density of the follicles in the ovarian tissue retrieved at the moment of cystectomy with the age of the patients. In women aged <35 years, the relative density of follicles in healthy ovarian tissues was consistently lower in the endometriotic cyst group than in the nonendometriotic cyst group. At the age of 20 years, there was already a reduction in follicular density of 35.4%, with a reduction in density of 62.7% at the age of 35 years. They concluded that ovarian endometriomas have a detrimental impact on the follicle reserve in young patients and that laparoscopic cystectomy for endometriomas may accelerate the rate of oocyte loss associated with aging. In accordance with the findings of Kitajima are the observations by Qiu et al. [12]; they reported microvascular injuries and progression through increased interstitial fibrosis. Using color Doppler flow, they described a higher vascular flow resistance in the interstitial ovarian vascularization in the presence of an ovarian endometriotic cyst.

Endometriosis is a progressive disease

Although progressivity of the disease is difficult to predict, aggressiveness of the lesions even in a small cyst should not be underestimated as shown by the presence of pronounced neoangiogenesis and inflammation in the cyst with a diameter <2 cm by intracystic exploration while performing transvaginal laparoscopy [5]. With the reported high frequency of severe forms of endometriosis in adolescents, it remains unclear why we are missing this progression and why the evolution from minor to severe forms never has been described.

Recent studies on endometriosis in adolescents show clearly that the disease is no longer characterized by subtle superficial lesions but by the presence of ovarian adhesions and endometriomas [6]. Depending on the studied cohort of patients, the presence of severe forms of endometriosis in adolescents was reported to be as high as 5–50%. In adolescents with dysmenorrhea and chronic pelvic pain or complaining of pathognomonic symptoms for endometriosis such as dyschezia or bladder complaints, factors possibly indicating a higher risk of severity or progression should be excluded.

One of the major reasons that adolescents come to search for medical help is dysmenorrhea. In the study conducted by Ragab et al. [13], 48.9% of the adolescent schoolgirls had dysmenorrhea, with severe forms in 68.8% (220/230). Ultrasound findings suggestive of endometriosis were present in 25.5%. In 34 patients, laparoscopy was performed for histologic-proven endometriosis in 79.4%; those patients declining laparoscopy were referred for an MRI ($n = 22$), and they showed suggestive signs for endometriosis in 77.3%.

The high incidence of dysmenorrhea reflects a significant health problem, which deserves great attention. These findings support the idea that severe forms of dysmenorrhea should be considered as the expression of the presence of endometriosis until proven otherwise. Harell, in his paper, states that *"If dysmenorrhea does not improve within 6 months of treatment with NSAIDs* (nonsteroidal anti-inflammatory drugs), *and OC (oral contraception), a laparoscopy is indicated to look for endometriosis*" [14]. If laparoscopy is declined, ultrasound and/or MRI can be used as a minimally invasive procedure.

In view of the recent findings, the occurrence of NUB should be excluded because of the possible role of the transport of stem/progenitor cells to the peritoneal cavity through retrograde menstruation [15]. As the incidence of NUB is elevated in the presence of utero-placental ischemia, special attention should be paid to the history of low birth weight, pre-eclampsia, postmaturity, and ABO incompatibility.

Ovarian endometriotic cyst progression is characterized by continuous infiltration and invasion of the ovarian interstitium surrounding the cyst, resulting in injury to the ovarian tissue structure and vascular distribution.

Surgical management

Small endometrioma

The delay between the first symptoms and the final diagnosis of endometriosis has been reported to be between 3 and 11 years. Reasons can be the lack of awareness by the adolescents and clinicians and the necessity to perform a laparoscopy to obtain an exact diagnosis [16]. Indirect imaging and more particular transvaginal ultrasound can now be used for the early detection of endometriosis and may reduce this delay in diagnosis. Frequently, these small endometriomas do not cause pain, but they are regularly detected in patients suffering from infertility. In our center, transvaginal laparoscopy is routinely performed in patients as part of the routine exploration for infertility. By performing systematically a transvaginal ultrasound before the transvaginal laparoscopic exploration, it is our experience that cysts <15 mm are missed in 45% of the patients (unpublished data). In the treatment of these small endometriotic cysts, the transvaginal laparoscopy allows an easy access to the anterolateral side of the ovaries and the fossa ovarica without supplementary manipulation. As a watery solution is used as the distension medium, hydroflotation allows an accurate and detailed visualization of small lesions and adhesions. It is remarkable that adhesions with the lateral pelvic wall are always present even in case of these small endometriotic cysts, and frequently, an adenomyotic plaque is identified in the lateral pelvic wall. Treatment consists first of performing an adhesiolysis to restore normal anatomy. Second, the cyst is opened using 5Fr scissors, thereby allowing the outflow of the chocolate fluid. Intracystic inspection shows the presence of endometrial-like tissue, neo-angiogenesis, and a strong inflammatory reaction (Fig. 1). Consecutively, an ablative treatment is performed using a 5Fr bipolar probe (Karl Storz, Germany). As the whole procedure is performed under water, no carbonization occurs, clearly showing the white color of the base of the invaginated cortex comparable with a normal ovarian surface (Fig. 2) [5]. This early treatment can be discussed, but as there are no markers available, indicating the progressivity of the disease, it is barely defendable not to treat. The treatment is minimally atraumatic because of the cyst size; operative technique; and use of Ringer lactate as the distension medium, which protects against adhesion formation.

Larger endometrioma

Reproductive surgery aims for the restoration of the tubo-ovarian anatomy and the elimination of the diseased areas of endometriosis. Spontaneous pregnancy rates of 50%–60% are obtained after the surgical correction of ovarian endometriosis [17–19]. The discussion remains between the believers of the cystectomy and the ablative surgical approach. The systematic use of cystectomy is mainly based on a Cochrane review by Hart et al. [20] in 2008, wherein they concluded that cystectomy for endometriomas results in lower recurrence rates and higher spontaneous pregnancy rates than drainage and ablation. This analysis, however, was based only on three randomized studies using bipolar coagulation without prospective evaluation of the ovarian reserve. It was questioned whether this conclusion was

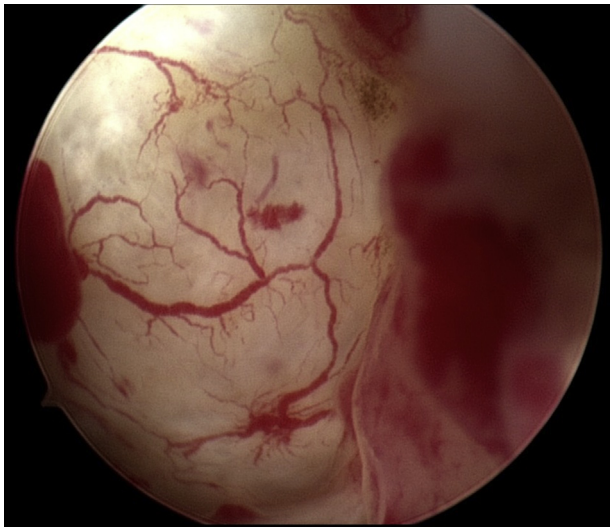

Fig. 1. Intracystic inspection of a small endometriotic cyst by transvaginal laparoscopy showing the presence of endometrial-like tissue and neoangiogenesis.

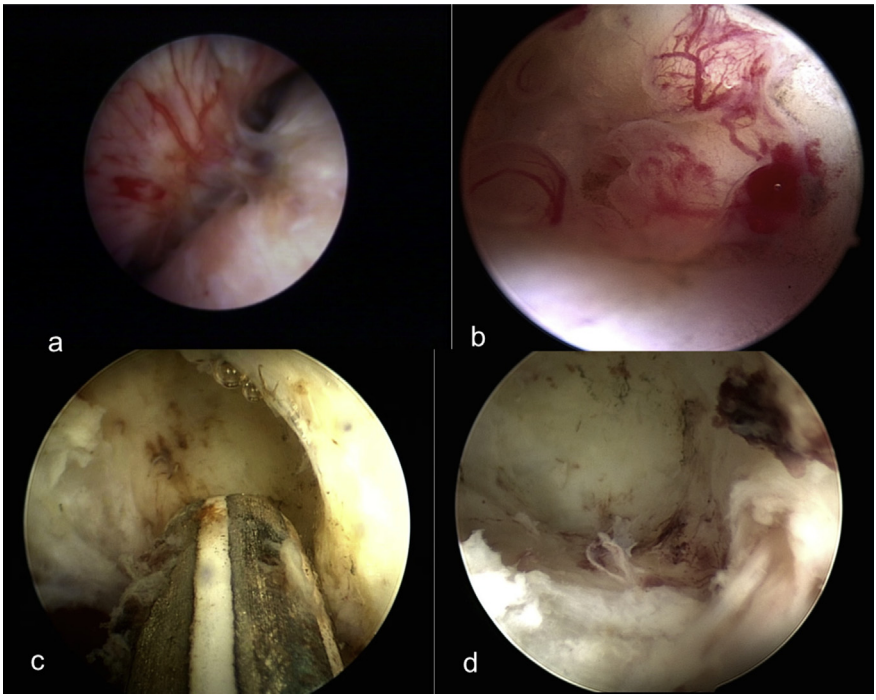

Fig. 2. Ablative surgery of a small endometriotic cyst by transvaginal laparoscopy. a: small cyst adherent to the pelvic wall. b: inside view of the cyst shows the presence of endometrial like tissue; c: use of a 5Fr bipolar probe for ablative surgery; final result: remark the white color of the basis of the cyst and absence of carbonization after the ablative surgery. d: final result; presence of white color of basis and absence of carbonization.

not taken as too hasty [21]. In contrast with cystectomy for a benign ovarian cyst, there is histological evidence of the systematic removal of ovarian follicles after cystectomy for ovarian endometrioma [22,23] with a direct proportional relationship with the size of the endometrioma [24].

Ablative surgery can be performed using bipolar coagulation, CO_2 laser, or PlasmaJet. In our experience, the bipolar coagulation probe (K. Storz, Germany), which combines coagulation, irrigation, and aspiration, is easy to use; it has a depth of penetration comparable with the CO_2 laser (unpublished data) (Fig. 3). The ablative surgery seems to cause less damage to the ovarian reserve than the cystectomy [25]. Certainly, in a large endometrioma (>5 cm), the decrease in AMH levels is more consistent after cystectomy than after ablative surgery [9]. These findings are also confirmed with the use of PlasmaJet [26]. These data are important to gynecologists in counseling the patients with further desire of pregnancy. Because of this deleterious effect of surgery on the ovarian reserve in case of a large endometrioma, a two-step operative procedure was suggested [27,28], which limits the first step to drainage followed by treatment with a gonadotropin-releasing hormone agonist for 3 months. The second procedure consisted of laparoscopic cystectomy. This two-step procedure resulted in better preservation of the ovarian reserve. In the same philosophy, a combined technique was described [29,30], starting with cyst excision of the lateral walls and ablation close to the hilus. Ovarian volume and antral follicular count (AFC) did not show any difference compared the control group. Histologic examination of the removed specimen did show the presence of follicles only in 2%, and the recurrence rate after 8.3 months was 2%. The reported spontaneous pregnancy rate was 41%. Recently, reported data on the use of ablation using PlasmaJet did not show any difference in pregnancy rates compared to cystectomy and showed beneficial in preserving the ovarian reserve [26].

Sclerotherapy

To preserve ovarian function, ultrasound-guided transvaginal sclerotherapy was described. Although several substances such as tetracyclines and methotrexate can be applied, ethanol was the most frequently used. In a recent meta-analysis [31], results showed higher levels of AFC and anti-Mullerian hormone (AMH) than cystectomy. Although more oocytes were harvested after sclerotherapy, pregnancy rates after in vitro fertilization did not show any significant difference. Depending on the technique used, the recurrence rates were 3.47 times higher when only irrigation and no retention technique were used. In the latter, the reported recurrence rate was 9.1% when the retention time was >10 min. Abdominal pain occurred in 1.8%–15.3% of patients; the risk of intracystic abscess reported in one study was 2%. Recently, an adapted technique of laparoscopic ethanol sclerotherapy avoiding any spillage was presented [32]. A recent publication [33] recommended concentrating more on the development of the intracystic application of hormonal and nonhormonal medications in an attempt to control the disease and to avoid the risks of ovarian surgery.

In case of frozen pelvis with severe forms of endometriosis and in cases of recurrence of endometrioma, an oophorectomy can become unavoidable. In these cases, we have to consider either to perform an orthotopic transplantation of the ovarian tissue [34] or to offer the patient the possibility of cryopreservation of the ovarian cortex [35,36]. Ovarian cortex can be obtained by dissection of the remaining healthy ovarian cortex from the endometriotic tissue.

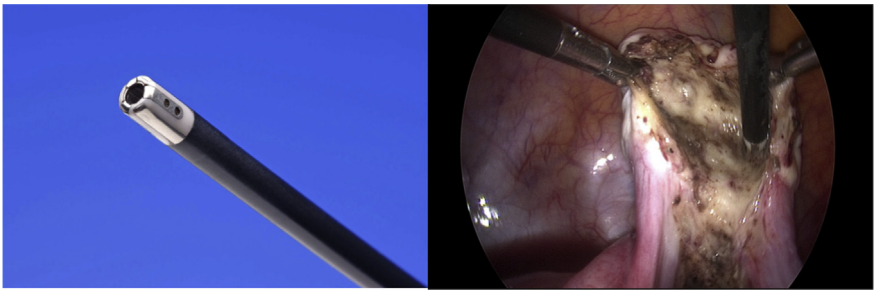

Fig. 3. At laparoscopy: use of a bipolar probe (Karl Storz, Germany) for ablative surgery.

Conclusion

Independent of the pathogenesis of the ovarian endometrioma, in the majority of cases, it constitutes an extraovarian pseudocystic structure with no cystic wall but surrounded by fibrosis with underlying ovarian cortical follicles. As such, it is part of a pleiotropic pathology and differs from other benign ovarian cysts. The disease by itself results in an impaired ovarian reserve with a very severe impact in case of bilateral ovarian endometrioma. As each surgical technique is critical and carries the risk of follicle loss, surgery therefore should be performed meticulously by experienced hands. Ablative surgical techniques seem to have less impact on the ovarian reserve than the excision techniques but possibly carrying a slightly higher risk of recurrence. This has to be balanced against the potential of better preservation of the ovarian reserve and patient has to be well informed. In case of a small endometrioma (<2 cm), the transvaginal approach allows treatment at an early stage with minimum ovarian damage and hopefully avoids progression to more severe forms. Dealing with larger endometrioma (>5 cm), a two-step technique or the combined technique of ablation and cystectomy is recommended. The pros and cons of ovarian endometriosis surgery should be clearly discussed with the patient, and an individualized treatment is necessary. In severe forms of endometriosis, the informed consent of the patient should mention the possibility of cryopreservation of the ovarian tissue.

Practice points

- The ovarian endometrioma is most frequently an extraovarian cyst and differs as such from other benign ovarian cysts with the absence of a real cystic wall.
- As part of a pleiotropic disease, the endometrioma by itself causes a reduced ovarian reserve, especially in the case of a bilateral ovarian endometrioma.
- Ovarian endometriosis surgery carries an intrinsic risk of ovarian damage and should be performed by experienced surgeons.

Research agenda

- Creating awareness of the disease and its impact on later fertility in adolescents.
- Need for the development of markers to predict risks of progressivity of the disease.
- Assess whether early treatment can reduce risks of further progression of the disease and reduce deleterious impact on fertility.
- Further studies are warranted to evaluate the place of intracystic application of hormonal and nonhormonal medications in the treatment of ovarian endometrioma.

Conflict of interest statement

Both the authors are consultants at Karl Storz, Germany.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bpobgyn.2018.12.013.

References

[1] Moen MH. Endometriosis in women at interval sterilization. Acta Obstet Gynecol Scand 1987;66:451–5.
[2] Sampson JA. Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. Am J Obstet Gynecol 1927;14:422–69.

[3] Hughesdon PE. The structure of endometrial cysts of the ovary. J Obstet Gynaecol Br Emp 1957;44:481–7.
*[4] Kitajima M, Dolmans M-M, Donnez O, Masuzaki H, Soares M, Donnez J. Enhanced follicular recruitment and atresia in cortex derived from ovaries with endometriomas. Fertil Steril 2014;101:1031–7.
*[5] Gordts S, Campo R, Brosens I. Experience with transvaginal hydrolaparoscopy for reconstructive tubo-ovarian surgery. Reprod Biomed Online 2002;4(Suppl 3):72–5.
[6] Brosens I, Gargett CE, Guo SW, Puttemans P, Gordts S, Brosens JJ, et al. Origins and progression of adolescent endometriosis. Reprod Sci 2016 Oct;23(10):1282–8.
[7] Evers JL. Endometriosis does not exist; all women have endometriosis. Hum Reprod 1994 Dec;9(12):2206–9.
*[8] Nieweglowska D, Hajdyla-Banas I, Pitynski K, Banas T, Grabowska O, Juszczyk G, et al. Age-related trends in anti-Mullerian hormone serum level in women with unilateral and bilateral ovarian endometriomas prior to surgery. Reprod Biol Endocrinol 2015 Nov 24;13:128.
[9] Giampaolino P, Bifulco G, Di Spiezio Sardo A, Mercorio A, Bruzzese D, Di Carlo C. Endometrioma size is a relevant factor in selection of the most appropriate surgical technique: a prospective randomized preliminary study. Eur J Obstet Gynecol Reprod Biol 2015;195:88–93.
[10] Tang Y, Chen SL, Chen X, He YX, Ye DS, Guo W, et al. Ovarian damage after laparoscopic endometrioma excision might be related to the size of cyst. Fertil Steril 2013;100(2):464–9.
*[11] Kuroda M, Kuroda K, Arakawa A, Fukumura Y, Kitade M, Kikuchi I, et al. Histological assessment of impact of ovarian endometrioma and laparoscopic cystectomy on ovarian reserve. J Obstet Gynaecol Res 2012;38:1187–93.
*[12] Qiu Jun-Jun, Liu Man-Hua, Zhang Zhong-Xin, Chen Li-Ping, Yang Qi-Chang, Liu Hong-Bing. Transvaginal color Doppler sonography predicts ovarian interstitial fibrosis and microvascular injury in women with ovarian endometriotic cysts. Acta Obstet Gynecol Scand 2012;91:605–12.
[13] Ragab A, Shams M, Badawy A, Alsammani MA. Prevalence of endometriosis among adolescent school girls with severe dysmenorrhea: a cross sectional prospective study. Int J Health Sci 2015;9(3):273–81.
[14] Harel Z. Dysmenorrhea in adolescents and young adults: etiology and management. J Pediatr Adolesc Gynecol 2006;19:363–71.
[15] Gargett CE, Schwab KE, Brosens JJ, Puttemans P, Benagiano G, Brosens I. Potential role of endometrial stem/progenitor cells in the pathogenesis of early-onset endometriosis. Mol Hum Reprod 2014 Jul;20(7):591–8.
*[16] Hadfield R1, Mardon H, Barlow D, Kennedy S. Delay in the diagnosis of endometriosis: a survey of women from the USA and the UK. Hum Reprod 1996;11(4):878–80.
[17] Rizk B, Turki R, Lotfy H, Ranganathan S, Zahed H, Freeman AR, et al. Surgery for endometriosis-associated infertility: do we exaggerate the magnitude of effect? Facts Views Vis Obgyn 2015;7(2):109–18.
[18] Vercellini P, Fedele L, Aimi G, De Giorgi O, Consonni D, Crosignani PG. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. Hum Reprod 2006 Oct;21(10):2679–85.
[19] Gordts S, Boeckx W, Brosens I. Microsurgery of endometriosis in infertile patients. Fertil Steril 1984 Oct;42(4):520–5.
[20] Hart R, Hickey M, Maouris P, Buckett W. Excisional surgery versus ablative surgery for ovarian endometriomata. Cochrane Database Syst Rev 2008;16:CD004992.
[21] Donnez J, Squifflet J, Donnez O. Minimally invasive gynecologic procedures. Curr Opin Obstet Gynecol 2011;23(4):289–95.
[22] Dogan E, Ulukus EC, Okyay E, Ertugrul C, Saygili U, Koyuncuoglu M. Retrospective analysis of follicle loss after laparoscopic excision of endometrioma compared with benign non-endometriotic ovarian cysts. Int J Gynaecol Obstet 2011;114:124–7.
*[23] Muzii L, Bianchi A, Bellati F, Cristi E, Pernice M, Zullo MA, et al. Histologic analysis of endometriomas: what the surgeon needs to know. Fertil Steril 2007;87:362–6.
*[24] Roman H, Tarta O, Pura I, Opris I, Bourdel N, Marpeau L, et al. Direct proportional relationship between endometrioma size and ovarian parenchyma inadvertently removed during cystectomy, and its implication on the management of enlarged endometriomas. Hum Reprod 2010;25:1428–32.
[25] Var T, Batioglu S, Tonguc E, Kahyaoglu I. The effect of laparoscopic ovarian cystectomy versus coagulation in bilateral endometriomas on ovarian reserve as determined by antral follicle count and ovarian volume: a prospective randomized study. Fertil Steril 2011;95(7):2247–50.
[26] Roman H, Auber M, Mokdad C, Martin C, Diguet A, Marpeau L, et al. Ovarian endometrioma ablation using plasma energy versus cystectomy: a step toward better preservation of the ovarian parenchyma in women wishing to conceive. Fertil Steril 2011;96(6):1396–400.
[27] Pados G1, Tsolakidis D, Assimakopoulos E, Athanatos D, Tarlatzis B. Sonographic changes after laparoscopic cystectomy compared with three-stage management in patients with ovarian endometriomas: a prospective randomized study. Hum Reprod 2010 Mar;25(3):672–7.
[28] Donnez J1, Nisolle M, Gillet N, Smets M, Bassil S, Casanas-Roux F. Large ovarian endometriomas. Hum Reprod 1996;11(3):641–6.
[29] Donnez Jacques, Lousse Jean-Christophe, Jadoul Pascale, Donnez Olivier, Squifflet Jean. Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery. Fertil Steril June 2010;94(1):28–32.
*[30] Muzii L, Achilli C, Bergamini V, Candiani M, Garavaglia E, Lazzeri L, 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(2):339–44.
[31] Cohen A1, Almog B2, Tulandi T. Sclerotherapy in the management of ovarian endometrioma: systematic review and meta-analysis. Fertil Steril 2017;108(1):117–24.
[32] De Cicco Nardone A, De Cicco Nardone C, Carfagna P, Ussia A, Marana R, De Cicco Nardone F. Laparoscopic ethanol sclerotherapy of ovarian endometrioma: a new minimal invasive procedure. In: Description of the technique and preliminary results. ESGE; 2018. Annual meeting ES27-0302 – Best Selected Abstracts.

*[33] Benagiano G, Petraglia F, Gordts S, Brosens I. A new approach to the management of ovarian endometrioma to prevent tissue damage and recurrence. RBM Online 2016;32:556–62.
[34] Donnez J, Squifflet J, Dolmans MM, Martinez-Madrid B, Jadoul P, Van Langendonckt A. Orthotopic transplantation of fresh ovarian cortex: a report of two cases. Fertil Steril 2005;84(4):1018.
[35] Donnez J, Dolmans MM, Demylle D, Jadoul P, Pirard C, Squifflet J, et al. Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. Lancet 2004 Oct 16-22;364(9443):1405–10.
[36] Rosendahl M, Schmidt KT, Ernst E, Rasmussen PE, Loft A, Byskov AG, et al. Cryopreservation of ovarian tissue for a decade in Denmark: a view of the technique. Reprod Biomed Online 2011;22(2):162–71.