Which is worse? Comparison of ART outcome between women with primary or recurrent endometriomas

Baris Ata[1], Sezcan Mumusoglu[2], Kiper Aslan[3], Ayse Seyhan[4], Isıl Kasapoglu[2], Berrin Avcı[4], Bulent Urman[4], Gurkan Bozdag[2], and Gurkan Uncu[4,*]

[1]Department of Obstetrics and Gynecology, Koc University School of Medicine, Davutpasa Caddesi No 4, Topkapi, Istanbul 34010, Turkey [2]Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Sıhhiye, Ankara 06100, Turkey [3]Department of Obstetrics and Gynecology, Uludag University School of Medicine, Gorukle, Bursa 16059, Turkey [4]Women's Health and Assisted Reproduction Center of the American Hospital of Istanbul, Guzelbahce Sokak, Nisantasi, Istanbul 34365, Turkey

*Correspondence address. Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Uludag University School of Medicine, Gorukle, Bursa, Turkey. Tel: +90-224-295-0000; E-mail: guncu@gurkanuncu.com

STUDY QUESTİON: Are live birth rates (LBR) different after ART cycles between women with primary or recurrent endometrioma?

SUMMARY ANSWER: Women with recurrent endometrioma have similar LBR as compared to patients with primary endometrioma.

WHAT IS ALREADY KNOWN: Recurrence rate can be as high as 29% after endometrioma excision. Prior studies on management of endometrioma before ART involve primary endometriomas. There is limited information regarding the prognosis of women with recurrent endometriomas.

STUDY DESIGN, SIZE, DURATION: A multicenter retrospective cohort study, including 76 women with primary and 82 women with recurrent endometriomas treated at the participating centers over a 6-year period.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Women with endometrioma who underwent ART at three academic ART centers. Couples with another indication for ART were excluded.

MAIN RESULTS AND THE ROLE OF CHANCE: Female age, median number of prior failed ART cycles, proportion of patients with bilateral endometrioma (28 versus 28.9%), ovarian stimulation protocols, and total gonadotropin consumption were similar between the study groups. Numbers of metaphase two oocytes (5 versus 6), number of embryos transferred, and the proportion of patients undergoing blastocyst transfer were similar across the study groups. Clinical pregnancy rates (36.6 versus 34.2%, absolute difference 2.4%, 95% CI: −12.5 to 17.3%, P = 0.83) and LBR (35.4 versus 30.3%, absolute difference 5.1%, 95% CI: −9.5 to 19.7%, P = 0.51) per started cycle in recurrent and primary endometrioma were similar. Comparable success rates were also confirmed with logistic regression analysis (OR: 1.14, 95% CI: 0.78–0.57, P = 2.3)

LIMITATIONS, REASONS FOR CAUTION: The retrospective design has inherent limitations. Some women with severely decreased ovarian reserve after primary endometrioma excision may not have pursued further treatment.

WIDER IMPLICATIONS OF THE FINDINGS: The management of endometrioma prior to ART is controversial but a different management strategy is not required for recurrent endometriomas. Since recurrent endometriomas do not have a worse impact on ART outcome than primary endometriomas, and repeat surgery has a higher risk for complications, conservative management without surgery can be justified.

STUDY FUNDING/COMPETING INTEREST(S): No funding or competing interests to declare.

TRIAL REGISTRATION NUMBER: None.

Key words: recurrent endometrioma / infertility / assisted reproduction / ovarian reserve / endometriosis / live birth

Introduction

Endometriosis is characterized by the presence of endometrial gland and stroma outside the uterine cavity. While some patients are asymptomatic, endometriosis can present with chronic pelvic pain, and/or infertility. The true prevalence of the disease is unknown but studies suggest that endometriosis affects 25–50% of infertile women (D'Hooghe *et al.*, 2003).

Ovarian endometriosis presents as a cystic formation, which contains a homogenous dark brown viscous liquid, and is named endometrioma. A total of 17–44% of infertile patients with endometriosis are diagnosed with ovarian endometrioma (Vercellini *et al.*, 2003). Surgical excision, cyst aspiration, hormonal treatment, ethanol injection as well as leaving the cysts *in situ* are management options of endometrioma in infertile women (Beretta *et al.*, 1998; Brown and Farquhar, 2014; McDonnell *et al.*, 2014; Garcia-Tejedor *et al.*, 2015). Yet, optimal management is still controversial.

ART is an effective treatment for endometriosis-associated infertility (Dunselman *et al.*, 2014). Although the presence of an endometrioma increases the risk of ART cycle cancellation, pregnancy rates appear to be similar compared to women without an endometrioma (Hamdan *et al.*, 2015a,b). Moreover, surgical excision of endometrioma prior to ART does not increase pregnancy rates and may decrease the number of collected oocytes (Hamdan *et al.*, 2015a,b).

A high recurrence rate in the absence of post-operative hormonal suppression of the disease process is a limitation of surgical excision in subfertile patients. Depending on patient characteristics and duration of follow-up recurrence rate can be as high as 16–29% even within 2 years after surgery (Guo, 2009; Sesti *et al.*, 2009; Seracchioli *et al.*, 2010). Prior studies on management of endometriomata before ART involve primary endometriomas (Yanushpolsky *et al.*, 1998; Suzuki *et al.*, 2005; Bongioanni *et al.*, 2011; Benaglia *et al.*, 2013). Thus, there is limited information about the optimal management of recurrent endometriomas prior to ART cycles. In this study, we aimed to compare ART outcome between women with primary and recurrent endometriomas.

Material and Methods

This multicenter retrospective cohort study was conducted at the Assisted Reproductive Technology Centers of the Uludag University School of Medicine, Hacettepe University School of Medicine and the American Hospital of Istanbul. Uludag University research ethics committee approved the study protocol. Electronic databases of the three clinics were screened to identify patients with endometriosis who underwent ART between the years 2011 and 2016. Patients who never had an endometrioma and couples with other etiology than endometriosis for infertility were excluded.

An endometrioma was defined by the visualization of an ovarian cyst with regular margins and ground-glass echogenicity on transvaginal ultrasound examination (Savelli, 2009; Exacoustos *et al.*, 2014). In all clinics, the presence of the cysts was confirmed at least on two separate examinations done at least 1 month apart. Surgical histories of women with endometrioma who underwent ART were retrieved from original patient charts. Women with a history of a prior endometrioma excision were included in the recurrent endometrioma group. They were matched with women without a history of endometrioma

excision. Women with multiple ART cycles were included only with the chronologically first cycle.

Protocols for controlled ovarian stimulation (COS) included GnRH antagonist protocol, microdose flare-up, long GnRH agonist, and ultra-long GnRH agonist protocol at the discretion of treating physicians. The stimulation protocols and trigger criteria were described elsewhere (Aslan *et al.*, 2015; Esinler *et al.*, 2015). Oocytes were retrieved transvaginally 34–36 h after the ovulation trigger. Fertilization was affected by ICSI in all cases. One or two embryos were transferred under transabdominal ultrasound guidance. Day of embryo transfer was decided based on the number of available embryos and embryo quality. We usually aim for a Day 5 transfer but patients who had an equal or smaller number of good quality cleavage stage embryos than the number allowed to transfer per local regulations underwent cleavage stage transfer. Cleavage stage transfer was also done when the patients' or the laboratory schedule did not allow for a day five transfer. Luteal phase was supported with vaginal micronized progesterone.

Clinical pregnancy was defined as the presence of at least one embryo with cardiac activity. Implantation rate (IR) was calculated as number of embryos with heartbeat divided by the number of embryos transferred. IR was calculated separately for each woman and treated as a continuous variable to address multiple implantations in a woman. Live birth was defined as the delivery of a live infant after 24th gestational week.

Distribution of variables was evaluated visually with histograms. Depending on distribution characteristics, continuous variables were defined with mean (standard deviation) or median (25th–75th percentile). Categorical variables were defined with numbers and percentages. Mann Whitney *U* and independent samples *t*-test were used to compare continuous and derivatives of chi-square test was used to compare categorical variables across the groups. A two-tailed P value < 0.05 was regarded as statistically significant. Logistic regression analysis including live birth as the dependent variable, treatment center, endometrioma recurrence and female age as the independent variables was done.

A sample size calculation was not done for this retrospective analysis, but all women meeting inclusion criteria were included in the analysis. The absolute differences between the two groups were presented with accompanying 95% CI to reflect the inherent imprecision of point estimates.

Results

A total of 158 patients with endometriosis were eligible for inclusion. They comprised 76 women with a primary endometrioma and 82 with recurrent endometrioma after excision.

Of the 82 women with a recurrent endometrioma, 67 had a laparoscopy and 15 had a laparotomy. While 59 (71%) of these patients had a unilateral endometrioma excision, 23 (28%) patients had a bilateral cystectomy. Six (26%) women with bilateral endometrioma excision had bilateral recurrence and the rest, 17 (74%), had unilateral recurrence. Overall, 14 (24%) women with unilateral excision had bilateral recurrence whilst, 78% (35/45) of unilateral recurrences were on the ipsilateral side and 17% (10/45) were on the contralateral side.

Female age (31.5 ± 4.1 versus 31.9 ± 4.8 years), number of prior failed ART cycles (0 versus 0), early follicular phase serum FSH levels (6.5 versus 6.8 IU/L), proportion of patients with bilateral

endometrioma (28 versus 29%), ovarian stimulation protocols and total gonadotropin consumption (3150 versus 3225 IU) were similar between the study groups. Baseline characteristics are presented in Table I.

Numbers of oocytes collected (7 versus 8), metaphase two oocytes (5 versus 6), two pronuclear fertilized oocytes (5 versus 4), proportion of patients reaching embryo transfer (87.8 versus 93.4%), number of embryos transferred (1 versus 1), and the proportion of patients undergoing blastocyst transfer (49 versus 35%) were similar across the study groups. Laboratory parameters are presented in Table II.

Overall embryo implantation rates (including both cleavage stage and blastocyst transfers) were 35 versus 34% in the recurrent and primary endometrioma groups, respectively ($P = 0.83$). Clinical pregnancy (37 versus 34%) and live birth (35 versus 30%) rates were similar in the study groups (Table III)

Logistic regression analysis revealed an odds ratio of 1.14 (95% CI: 0.57–2.3) for achieving a livebirth in women with recurrent endometriomas as compared to women with primary endometriomas.

Discussion

Our results show that women with primary and recurrent endometriomas have similar response to COS and ART outcome. To the best of our knowledge, this is the first study comparing live birth rates following ART between women with primary and recurrent endometriomas.

Retrospective design has its inherent limitations; however, it is impossible to conduct a randomized controlled trial since women cannot be randomized to have recurrent endometriomas or not. Yet, a prospective cohort study could provide a more reliable comparison.

Table I Participant characteristics and ovarian stimulation protocols. Data are mean ($\pm$SD), n (%) or median (quartiles).

	Recurrent endometrioma ($n = 82$)	Primary endometrioma ($n = 76$)	P
Age (y; mean)	31.5 ($\pm$4.1)	31.9 ($\pm$4.8)	0.55
Number of prior ART cycles	0 (0–1)	0 (0–0)	0.14
Early follicular phase serum FSH levels in IU/L	6.5 (5.4–8.2)	6.8 (5.1–9.8)	0.57
Patients with bilateral endometrioma	23 (28%)	22 (29%)	>0.99
Total gonadotropin dosage	3150 (2250–4500)	3225 (2400–4425)	0.89
Stimulation protocols (%)			
GnRH antagonist	23 (28%)	29 (38.2%)	0.39
Microdose flare[a]	5 (6.1%)	4 (5.3%)	
Long GnRH agonist	31 (37.8%)	26 (36.1%)	
Ultralong GnRH agonist	23 (28.1%)	17 (22.4%)	

[a]Microdose flare protocols are excluded from analyses to meet chi-square test assumptions.

Table II Assisted reproductive technology outcomes. Data are median (quartiles) or n (%).

	Recurrent endometrioma ($n = 82$)	Primary endometrioma ($n = 76$)	Absolute difference (95% CI)	P
No. of cycles canceled before oocyte collection	2 (3%)	0 (0%)	2.5% (−0.9% to 5.8%)	0.99
No. of oocytes	7 (4–11)	8 (5–11)	−0.9 (−2.6 to 0.8)	0.29
No. of metaphase two oocytes	5 (3–8)	6 (4–9)	−0.4 (−1.6 to 0.8)	0.36
No. of two-pronuclear fertilized oocytes	5 (2–7)	4 (3–7)	0.02 (−1.0 to 1.1)	0.84
Patients who had embryo transfer	72 (87.8%)	71 (93.4%)	−5.6% (−14.6% to 5.4%)	0.23
Number of embryos transferred	1 (1–2)	1 (1–2)	−0.05 (−0.3 to 0.2)	0.67
Blastocyst transfer (%)	35/72 (48.6%)	25/71 (35.2%)	13.4% (−2.6% to 29.4%)	0.11

Table III Pregnancy and live birth rates. Data are mean ($\pm$SD) or n (%).

	Recurrent endometrioma ($n = 82$)	Primary endometrioma ($n = 76$)	Absolute difference (95% CI)	P
Clinical pregnancy (%)	30 (37%)	26 (34%)	2.4% (−12.5 to +17.3)	0.87
Implantation rate (SD)	35% (45%)	34% (45%)	1.6% (−13.1 to +16.4)	0.83
Live births (%)	29 (35%)	23 (30%)	5.1% (−9.5 to +19.7)	0.51

We used strict inclusion criteria to collect study groups as homogenous as possible and include a relatively large sample and a multivariable analysis to adjust for the effects of other variables to the possible extent. The present data are also valuable for guiding future prospective studies on the subject.

Both the presence of endometrioma per se (Uncu et al., 2013) and endometrioma excision (Somigliana et al., 2008, 2012; Raffi et al., 2012; Urman et al., 2013) cause a decrease in ovarian reserve. Since surgical intervention can further decrease an already diminished ovarian reserve; one would expect lower ovarian response to COS, hence lower pregnancy rates in women with recurrent endometriomas. Nevertheless, we found a similar ovarian response to COS and ART outcome in the recurrent endometrioma group.

A similar number of oocytes being collected from women with recurrent versus primary endometriomas can be explained by several mechanisms. For example, if endometriomas arise from ovulatory events, one may speculate that if an ovary was severely injured during prior surgery this will have depleted its primordial follicle pool and it will be unlikely to develop a recurrent endometrioma, simply due to the absence of follicular growth and ovulation. Thus, only patients who have relatively better preserved ovarian reserve can be prone to recurrence (Somigliana et al., 2011).

Ovarian response to COS in women with recurrent and primary endometriomas was compared in two other studies. While, Xing et al. (2016) reported collecting significantly more MII oocytes from women with recurrent endometrioma (8.61 ± 5.61 versus 6.71 ± 4.27, $P < 0.05$) (Xing et al., 2016), Somigliana et al. (2011) reported similar number of oocytes being collected. Nevertheless, when only affected ovaries were compared, they also reported that ovaries with recurrent endometriomas yielded significantly more co-dominant follicles than those without recurrence (Somigliana et al., 2011). Secondly, ovaries with small, i.e. <3 cm, endometriomas were reported to yield similar numbers of oocytes when compared to healthy contralateral gonads (Esinler et al., 2012; Yang et al., 2015). Since the majority of women in our study had endometriomas <3 cm, it is possible that their ovarian reserve was more or less maintained. Many women in our study had a suboptimal to poor ovarian response, despite mean female age being ~30 years. Thus, failure to demonstrate a small difference from an already low comparator as statistically significant could be a false negative finding. Importantly, women with severely decreased ovarian reserve following primary endometrioma excision could have given up further treatment, and be underrepresented in the study populations. This could have led to overestimation of ovarian responsiveness in the recurrent endometrioma group. Indeed, the median number of oocytes collected and metaphase—two oocytes were one less in the recurrent endometrioma group than in the primary endometrioma group, and it should be noted that, our sample had only 18 and 9% power to demonstrate the observed differences in the number of oocytes and number of metaphase two oocytes between the study groups as statistically significant, respectively. Final possible explanation is based on the hypothesis that damage to ovarian cortex could promote follicle growth by suppressing the hippo-signaling pathway. The hippo-signaling pathway is an important intracellular signaling system that controls cell proliferation and determines organ size (Hsueh et al., 2015). This pathway consists of several negative growth regulators, and damaging and/or cutting ovaries could suppress the hypo-signaling pathway leading to increased recruitment from the primordial follicle pool to the growing antral follicle stage.

Regarding pregnancy and live birth rates, previous studies focused on the effect of second-line surgery. Spontaneous pregnancy rates after second-line surgery for endometriosis have been reported to be almost half that after primary surgery, but comparable with IVF cycles (Vercellini et al., 2009a,b). Whereas, Park et al. (2015) reported that second-line surgery have deleterious effect on ovarian response, implantation rate, and clinical pregnancy rates when compared with in situ recurrent endometriomas before ART cycle (Park et al., 2015). Moreover, additional deleterious effect of second-line surgery on ovarian reserve recently has been histologically confirmed (Muzii et al., 2015).

Our findings indicate that patients with recurrent endometriomas have similar ovarian response to COS, embryo implantation, clinical pregnancy and live birth rates as women with primary endometriomas. Surgical intervention for the sole purpose of improving ART outcome does not seen justified in women with recurrent endometriomas, since the risk of complications is substantially higher in women with prior abdominal surgery.

Authors' roles

Funding

Conflict of interest

References

Aslan K, Avci B, Uncu G, Saribal S, Ata B. Scheduling GnRH antagonist cycles by a short course of oral estradiol administration during early follicular phase: a comparative study with non-scheduled cycles. *Gynecol Endocrinol* 2015;**31**:465–468.

Benaglia L, Bermejo A, Somigliana E, Faulisi S, Ragni G, Fedele L, Garcia-Velasco JA. In vitro fertilization outcome in women with unoperated bilateral endometriomas. *Fertil Steril* 2013;**99**:1714–1719.

Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. *Fertil Steril* 1998;**70**:1176–1180.

Bongioanni F, Revelli A, Gennarelli G, Guidetti D, Delle Piane LD, Holte J. Ovarian endometriomas and IVF: a retrospective case-control study. *Reprod Biol Endocrinol* 2011;**9**:81.

Brown J, Farquhar C. Endometriosis: an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2014;**3**:Cd009590.

D'Hooghe TM, Debrock S, Hill JA, Meuleman C. Endometriosis and subfertility: is the relationship resolved? *Semin Reprod Med* 2003;**21**:243–254.

Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A *et al*. ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014;**29**:400–412.

Esinler I, Bozdag G, Arikan I, Demir B, Yarali H. Endometrioma </=3 cm in diameter per se does not affect ovarian reserve in intracytoplasmic sperm injection cycles. *Gynecol Obstet Invest* 2012;**74**:261–264.

Esinler I, Bozdag G, Esinler D, Lale KS, Yarali H. Luteal-long GnRH agonist versus flexible-multidose GnRH antagonist protocols for overweight and obese patients who underwent ICSI. *J Obstet Gynaecol* 2015;**35**:297–301.

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

Garcia-Tejedor A, Castellarnau M, Ponce J, Fernandez ME, Burdio F. Ethanol sclerotherapy of ovarian endometrioma: a safe and effective minimal invasive procedure. Preliminary results. *Eur J Obstet Gynecol Reprod Biol* 2015;**187**:25–29.

Guo SW. Recurrence of endometriosis and its control. *Hum Reprod Update* 2009;**15**:441–461.

Hamdan M, Dunselman G, Li TC, Cheong Y. The impact of endometrioma on IVF/ICSI outcomes: a systematic review and meta-analysis. *Hum Reprod Update* 2015a;**21**:809–825.

Hamdan M, Omar SZ, Dunselman G, Cheong Y. Influence of endometriosis on assisted reproductive technology outcomes: a systematic review and meta-analysis. *Obstet Gynecol* 2015b;**125**:79–88.

Hsueh AJ, Kawamura K, Cheng Y, Fauser BC. Intraovarian control of early folliculogenesis. *Endocr Rev* 2015;**36**:1–24.

McDonnell R, Marjoribanks J, Hart RJ. Ovarian cyst aspiration prior to in vitro fertilization treatment for subfertility. *Cochrane Database Syst Rev* 2014;**12**:Cd005999.

Muzii L, Achilli C, Lecce F, Bianchi A, Franceschetti S, Marchetti C, Perniola G, Panici PB. Second surgery for recurrent endometriomas is more harmful to healthy ovarian tissue and ovarian reserve than first surgery. *Fertil Steril* 2015;**103**:738–743.

Park H, Kim CH, Kim EY, Moon JW, Kim SH, Chae HD, Kang BM. Effect of second-line surgery on in vitro fertilization outcome in infertile women with ovarian endometrioma recurrence after primary conservative surgery for moderate to severe endometriosis. *Obstet Gynecol Sci* 2015;**58**:481–486.

Raffi F, Metwally M, Amer S. The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2012;**97**:3146–3154.

Savelli L. Transvaginal sonography for the assessment of ovarian and pelvic endometriosis: how deep is our understanding? *Ultrasound Obstet Gynecol* 2009;**33**:497–501.

Seracchioli R, Mabrouk M, Frasca C, Manuzzi L, Montanari G, Keramyda A, Venturoli S. Long-term cyclic and continuous oral contraceptive therapy and endometrioma recurrence: a randomized controlled trial. *Fertil Steril* 2010;**93**:52–56.

Sesti F, Capozzolo T, Pietropolli A, Marziali M, Bollea MR, Piccione E. Recurrence rate of endometrioma after laparoscopic cystectomy: a comparative randomized trial between post-operative hormonal suppression treatment or dietary therapy versus placebo. *Eur J Obstet Gynecol Reprod Biol* 2009;**147**:72–77.

Somigliana E, Arnoldi M, Benaglia L, Iemmello R, Nicolosi AE, Ragni G. IVF-ICSI outcome in women operated on for bilateral endometriomas. *Hum Reprod* 2008;**23**:1526–1530.

Somigliana E, Benaglia L, Vercellini P, Paffoni A, Ragni G, Fedele L. Recurrent endometrioma and ovarian reserve: biological connection or surgical paradox? *Am J Obstet Gynecol* 2011;**204**:529.e521–525.

Somigliana E, Berlanda N, Benaglia L, Vigano P, Vercellini P, Fedele L. Surgical excision of endometriomas and ovarian reserve: a systematic review on serum antimullerian hormone level modifications. *Fertil Steril* 2012;**98**:1531–1538.

Suzuki T, Izumi S, Matsubayashi H, Awaji H, Yoshikata K, Makino T. Impact of ovarian endometrioma on oocytes and pregnancy outcome in in vitro fertilization. *Fertil Steril* 2005;**83**:908–913.

Uncu G, Kasapoglu I, Ozerkan K, Seyhan A, Oral Yilmaztepe A, Ata B. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. *Hum Reprod* 2013;**28**:2140–2145.

Urman B, Alper E, Yakin K, Oktem O, Aksoy S, Alatas C, Mercan R, Ata B. Removal of unilateral endometriomas is associated with immediate and sustained reduction in ovarian reserve. *Reprod Biomed Online* 2013;**27**: 212–216.

Vercellini P, Chapron C, De Giorgi O, Consonni D, Frontino G, Crosignani PG. Coagulation or excision of ovarian endometriomas? *Am J Obstet Gynecol* 2003;**188**:606–610.

Vercellini P, Somigliana E, Daguati R, Barbara G, Abbiati A, Fedele L. The second time around: reproductive performance after repetitive versus primary surgery for endometriosis. *Fertil Steril* 2009a;**92**:1253–1255.

Vercellini P, Somigliana E, Vigano P, De Matteis S, Barbara G, Fedele L. The effect of second-line surgery on reproductive performance of women with recurrent endometriosis: a systematic review. *Acta Obstet Gynecol Scand* 2009b;**88**:1074–1082.

Xing W, Lin H, Wu Z, Li Y, Zhang Q. Effect of pelvic endometriosis, endometriomas and recurrent endometriomas on IVF-ET/ICSI outcomes. *Mater Sociomed* 2016;**28**:91–94.

Yang C, Geng Y, Li Y, Chen C, Gao Y. Impact of ovarian endometrioma on ovarian responsiveness and IVF: a systematic review and meta-analysis. *Reprod Biomed Online* 2015;**31**:9–19.

Yanushpolsky EH, Best CL, Jackson KV, Clarke RN, Barbieri RL, Hornstein MD. Effects of endometriomas on oocyte quality, embryo quality, and pregnancy rates in in vitro fertilization cycles: a prospective, case-controlled study. *J Assist Reprod Genet* 1998;**15**:193–197.