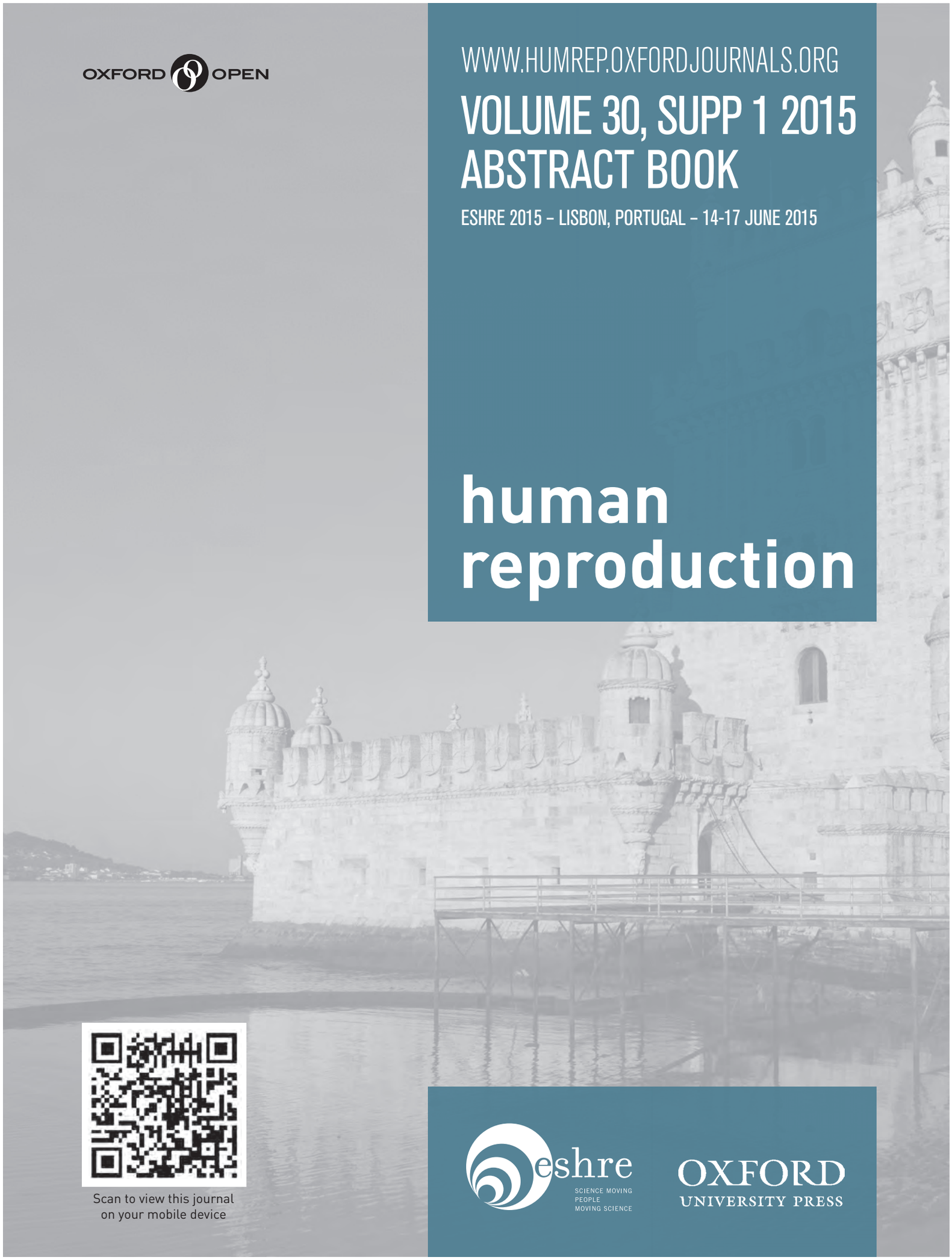

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ABSTRACT BOOK

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Study question: to evaluate whether iron contained in ovarian endometriomas may diffuse through the cyst wall to follicular fluids and affect ovarian function.
Summary answer: Iron content did not differ in follicular fluids belonging to ovaries with and without endometriomas, while ferritin concentration resulted significantly higher in affected gonads compared to controls.
What is known already: Endometriotic cysts contain huge amount of free iron that can mediate the production of Reactive Oxygen Species (ROS) potentially harmful to the surrounding cells. The amount of oxidative stress in the ovarian cortex surrounding an endometrioma and in granulosa cells from patients with endometriosis was shown to be higher compared to controls. It has been hypothesized that factors present in the endometriomas, and iron in particular, may diffuse in the surrounding tissue causing ROS generation.
Study design, size, duration: A prospective case series, between January 2012 and January 2013. Sample size was decided considering as biologically relevant an Odds Ratio of having levels of iron/ferritin in the affected gonad above the 90th percentile of the distribution in the intact gonad ≥ 3. On these bases, thirty-nine women were recruited.
Participants/materials, setting, methods: Women undergoing IVF/ICSI with unilateral ovarian endometriomas (≥ 10 mm) at transvaginal ultrasound the month preceding the stimulation; age 18-42 years; absence of non-endometriotic ovarian cysts. Iron and ferritin were measured on an automatic platform in pools of follicular fluids obtained from affected and contralateral intact gonads.
Main results and the role of chance: The median (IQR) concentration of iron in the affected and unaffected ovaries was 59 (44-74) and 59 (47-73) µg/dL, respectively ($p = 0.77$). The median (IQR) concentration of ferritin was 57 (31-146) and 33 (23-67) µg/mL, respectively ($p = 0.026$). Ferritin concentration was above the 90th percentile of the distribution in unaffected ovaries (132 µg/mL) in 3 (8%) intact and 11 (28%) affected gonads ($p = 0.021$). No differences emerged when considering iron. Follicular concentration of iron correlated between the two ovaries (Rho = 0.76, $p < 0.001$). A similar figure emerged for follicular ferritin (Rho = 0.55, $p < 0.001$). A significant correlation was documented when correlating ferritin and iron in the 78 available gonads (Rho = 0.42, $p < 0.001$). No statistically significant correlations emerged between follicular iron and ferritin and variables reflecting ovarian responsiveness and oocyte developmental competence.
Limitations, reason for caution: We lack an histological diagnosis of endometriosis but his limitation is of scanty relevance given the high accuracy of transvaginal ultrasound. We exclusively recruited women with indication to IVF. Inferences of our findings to the whole population of women with ovarian endometriomas should therefore be made with caution.
Wider implications of the findings: Iron may diffuse from ovarian endometriomas into the adjacent ovarian tissue. However, this phenomenon does not markedly affect ovarian function because of some effective biological mechanisms such as ferritin storage that properly counterbalance the potentially highly detrimental effects of free iron.
Study funding/competing interest(s): Funding by hospital/clinic(s) – Fondazione IRCCS Ca' Granda.
Trial registration number: NA.
Keywords: endometrioma, endometriosis, follicular fluid, iron, ferritin

P-349 sperm oviduct interaction in the human – new insights using live cell imaging

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Study question: How do spermatozoa interact with the oviductal epithelium under near in vivo conditions?
Summary answer: Only spermatozoa with high membrane integrity bind to the cilia of the oviductal epithelium. As soon as sperm quality is impaired by a disruption in general health, sperm binding is also impaired. Inflammation of the fallopian tube also results in decreased sperm binding.
What is known already: In animals spermatozoa form a sperm reservoir in the isthmus by binding with their head to the cilia of the uterine tube. Thus they maintain their capacity to fertilize for days (most mammals), months (birds) or even years (reptiles). Due to the lack of imaging technologies for investigating the human fallopian tube under *in vivo* conditions, the sperm oviduct interaction has not been investigated in the human fallopian tube up to now.
Study design, size, duration: Using a digital video microscopic system, this pre-clinical randomized study was designed to characterize the human sperm-oviduct interaction under near *in vivo* conditions. Experiments were performed, over 9 months, on the ampulla and isthmus of 5 premenopausal women undergoing hysterectomy and in one pregnant woman undergoing caesarean section.
Participants/materials, setting, methods: The fallopian tubes of the premenopausal women and the pregnant woman were investigated immediately after surgery. Ampulla and isthmus with and without co-incubation with a) fresh and b) frozen thawed spermatozoa were examined qualitatively and quantitatively using a digital video microscopic analysis system and scanning electron microscopy (SEM).
Main results and the role of chance: Human spermatozoa bind to the epithelial cells of the fallopian tube as soon as they enter the oviduct. This binding capacity is not confined to the isthmus – it also takes place in the ampulla. Where there is a disruption in general health, e.g., inflammatory joint disease, sperm binding is impaired. Similarly inflammations of the fallopian tube, which in most cases are only seen microscopically, reduce sperm binding and sperm survival time. Accumulations of mucus in the fallopian tube, which may be drug related, result in the 'sticking' of sperm and thus decreased sperm vitality.
Limitations, reason for caution: Medications and in particular hormones influence the sperm oviduct interaction and have to be taken into account.
Wider implications of the findings: Our studies show movies of the human sperm oviduct interaction for the first time, under near *in vivo* conditions. The fact that only spermatozoa of high quality are able to bind to the oviduct point to it playing a pivotal role in sperm selection. Impairments in general health, both in male and in female result in reduced sperm binding and survival time- a major cause of decreased fertility.
Study funding/competing interest(s): Funding by University(ies) – School of Medicine, University College Dublin, Ireland.
Trial registration number: NA.
Keywords: human, sperm, fallopian tube

P-350 Review of performance of patients with endometriosis in in-vitro-fertilisation (IVF) as compared to tubal factor infertility-Retrospective Cohort study

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Study question: To compare the performance of patients with endometriosis related infertility in IVF to patients with tubal factor infertility.
Summary answer: In comparison to tubal factor infertility, patients with endometriosis perform well in IVF with a reasonable clinical pregnancy rate, comparable implantation rate and number of good quality embryos generated.
What is known already: There is debate in the studies about IVF performance in endometriosis patients. Some studies are quoting reduced pregnancy rate and poor quality embryo in patients with endometriosis. However, data emerging from larger database such as human fertilisation and embryology authority (HFEA) suggests better performance.
Study design, size, duration: Retrospective review of the women undergoing IVF treatment between January 2012 to December 2013 in the assisted reproductive unit (ARU) at Hartlepool university Hospital. 41 patients with endometriosis were identified and compared to 321 patient with tubal factor infertility matched for age and duration of infertility.
Participants/materials, setting, methods: Endometriosis was confirmed by laparoscopy and staging following the American Society for Reproductive Medicine (ASRM), 73% minimal to mild endometriosis and 27% moderate to severe. The outcome measures were clinical pregnancy, implantation, embryo quality, on going pregnancy and multiple pregnancy rates. Statistical analysis was completed using GraphPad Prism ® 2015.
Main results and the role of chance: There was no statistically significant difference between the two groups regarding the clinical pregnancy rate per cycle started (*P*: 0.53, Relative Risk (RR): 0.83, 95% Confidence Interval (CI): 0.52–1.3), per cycle completed (*P*: 0.63, RR 0.87, 95% CI: 0.55–1.4), Implantation rate (*P*: 0.10, RR: 1.4, 95% CI: 0.96–2.1), miscarriage rate (*P*: 1.00, RR: 0.74, 95% CI: 0.10–5.2), ongoing pregnancy rate (*P*: 1.00, RR: 0.97, 95% CI: 0.61–1.5), and Twin pregnancy rate (*P*: 0.64, RR: 1.4, 95% CI: 0.37–5.5).

Endometriosis patients had a comparable percentage of good quality embryos (Grade 1 and 2) generated (83% versus 80%).

Limitations, reason for caution: The study is retrospective in nature. The sample size of endometriosis group is small as compared to the tubal factor group; however, all the patients were diagnosed with Laparoscopy. We also identified an unequal distribution of the severity of endometriosis in the study group.

Wider implications of the findings: The findings from our study suggest that women with endometriosis perform fairly well in IVF in term of embryo quality, implantation, and multiple pregnancy rates as compared to women with tubal factor infertility. Clinical pregnancy and ongoing pregnancy rates in endometriosis patients are lower but not statistically different from patients with tubal factor infertility.

Study funding/competing interest(s): Funding by hospital/clinic(s) – North Tees and Hartlepool NHS Foundation Trust.

Trial registration number: This study was registered with clinical audit department (CG 156).

Keywords: IVF, endometriosis, fallopian tubes, implantation, embryo quality

P-351 miRNA expression of the endocervix as a biomarker for endometrium receptivity in patients undergoing assisted reproductive technologies

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Study question: To compare the miRNA expression in the endocervix and the endometrium during implantation window in patients undergoing *in vitro* fertilization (IVF) treatment? Could endocervix miRNA expression be a new less-invasive method to assess the implantation window of infertile patients undergoing *in vitro* fertilization (IVF) treatments?

Summary answer: The miRNA expression in endocervix was not totally concordant with the endometrium in infertile patients during the implantation window. However, we identified five microRNAs differentially expressed in both the endometrium and in the endocervix in patients who became pregnant and may be considered potential candidates for biomarkers of endometrium receptivity.

What is known already: Despite of high technology used to IVF treatments, the function of endometrium remains little explored in the assisted reproductive field. The endometrial gene expression has been recently used to identify the implantation window. miRNA are small molecules and may act as a post-transcriptional gene expression regulator. Endometrial biopsy constitutes an invasive method and cannot be applied to an ongoing cycle. Biomarkers for endometrial receptivity in the endocervix could represent a less-invasive approach and may be performed during the IVF treatment.

Study design, size, duration: This prospective cohort study included 32 good prognosis infertile women undergoing fresh IVF treatment cycles using standard conventional protocol, at an University Center from July 2012 to December 2013.

Participants/materials, setting, methods: Women candidates to IVF treatment underwent an endometrial biopsy and endocervical brush during the luteal phase (implantation window) in the menstrual cycle prior to IVF treatment. The endometrial and endocervix samples were submitted to RNA purification and were analyzed by miRNA PCR-array (miScript miRNA PCR Array, Qiagen).

Main results and the role of chance: It is interesting to note that among 86 miRNA evaluated, 14 miRNA were significantly downregulated in the endocervix in relation to endometrium, 11 miRNA were significantly upregulated in the endocervix in relation to endometrium, and 61 miRNA were similar between two kind of samples. We can suppose that about one-third of miRNA evaluated were differentially expressed between endometrium and endocervix, and hence, endocervix miRNA expression does not accurately represent the endometrium. On the other hand, when comparing pregnant and non-pregnant patients, pregnant patients revealed five miRNA downregulated in endometrium and upregulated in endocervix. So, those miRNA in the endocervix, could represent, in an inverse way, a possible new biomarker profile of implantation window, since the endocervical cells are not suitable for invasion. If the efficiency of those markers would be proved, it is also possible to perform the exam during the cycle.

Limitations, reason for caution: This study is a screening of miRNA expression in endometrium and endocervix of infertile patients undergoing IVF cycles in a limited sample size. The concordant miRNA expressed can represent a biomarker profile in the endocervix, and must be validated in a higher number of samples in an ongoing cycle.

Wider implications of the findings: Considering that human endometrial study constitutes an invasive method for embryo implantation assessment and cannot be applied to an ongoing cycle, this study offers endocervix miRNA expression as a less-invasive possible marker for implantation window. It may have wide implication in clinical practice and could be a decisive factor for either transferring embryos in same cycle and cryopreserving them and postponing transfer to subsequent cycle if endometrium is not well prepared.

Study funding/competing interest(s): Funding by national/international organization(s) – This study was funded by "Fundação de Amparo à Pesquisa do Estado de São Paulo", Brazil (FAPESP) Proc. number 2012/16911-0. There is no interest conflict related to this study.

Trial registration number: NA.

Keywords: endometrium, endocervix, microRNA, implantation window, IVF

P-352 Ethanol sclerotherapy of ovarian endometriomas before IVF: long term data on safety and efficacy

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Study question: To evaluate long-term safety and efficacy of ethanol sclerotherapy (EST) in the treatment of ovarian endometriosis before IVF.

Summary answer: EST of endometriomas appears to be a safe procedure associated with a low recurrence rate and a good fertility outcome.

What is known already: Conventional surgical treatment of endometriomas may decrease ovarian reserve and response to subsequent fertility treatments. This is particularly true in patients with advanced stage endometriosis, who have had multiple previous ovarian surgeries. In recent years, minimal invasive techniques like ethanol sclerotherapy were developed to minimize the effect of surgery on ovarian tissue. However, reports on safety and efficacy are still lacking.

Study design, size, duration: A prospective cohort study was conducted from October 2004 to December 2014, including a total number of 107 patients undergoing 129 ethanol sclerotherapy procedures. The mean follow-up period was about two years (range from 0.5 to 7.5 years). Six patients were lost to follow-up.

Participants/materials, setting, methods: Candidates for IVF presenting with severe endometriosis and one to four endometriomas with a large diameter of 25 to 65 mm, were included in the study. After 12 days of pituitary desensitization by GnRH agonists, EST was performed in an outpatient basis and ovarian stimulation was started 15 days later.

Main results and the role of chance: The mean patients' age was 33.2 years. The mean diameter of endometrioma was 44.6 mm. The procedure was successful in 95.4% of cases, and was globally well tolerated (visual analog scale of 2.9) under local anesthesia. We did not observe any major complication (infection, hemorrhage, ...), and all cysts' fluid cytologies were benign.

Recurrence rate, defined on ultrasound as a cystic image of more than 20 mm on the previously treated ovary, was estimated at 7.0% (8/115) on the 3-months' visit and at 13.8% (16/116) at the end of follow-up. Risk factors for recurrence were analysed by a Cox proportional hazards model. Pregnancy rate was 45.6% (36/79) after the first cycle of IVF and cumulative pregnancy rate at 1 year was 64.4% (47/73), including nine spontaneous pregnancies.

Limitations, reason for caution: Follow-up period which varied between patients and cases lost to follow up might underestimate recurrence rate. Analysis of survival data accounting for censored observations was consequently done.

Wider implications of the findings: This is one of the biggest series of EST in women undergoing fertility treatments. Results on safety and efficacy encourage us to consider this treatment as an alternative option to conventional surgery prior to IVF in future randomized trials.