

Transmyometrial oocyte recruitment: a safe surgical procedure alternative to the transvaginal retrieval when ovaries are inaccessible

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Research

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Abstract

Background: This study aims to investigate the intra-cytoplasmic semen injection (ICSI) outcomes and the potential complications of transmyometrial oocyte retrieval performed in patients with one or both inaccessible ovaries.

Methods: From January 2004 to December 2018 were evaluated 11,273 oocytes retrievals, of which 594 not conventional procedures for inaccessible ovaries through transvaginal retrieval. Despite alternative approaches tested by clinicians during the oocyte pick up (OPU), in 113 of these patients (Group A) were indispensable the needle's passage through the myometrium, compared to as many controls (Group B) from the 481 remaining women without this necessity. The two resulting groups were matched for their reproductive outcomes and the relative developed complications.

Results: No statistically significant differences were found between the two Groups in terms of number of eggs/embryos obtained, ongoing pregnancy rate and spontaneous miscarriage. A complete absence of complications as peritoneal and endometrial bleeding after 4 and 24 hours from the transmyometrial access was reported for the whole cohort.

Conclusions: This study shows that the transvaginal transmyometrial oocyte retrieval does not affect the OPU outcome even if the passage of the needle occurs through the endometrium, not inducing significant complications. Thus, here we support both efficacy and safety of transmyometrial follicular aspiration as a valid surgical approach in conditions of inaccessible ovaries.

Introduction

The original oocyte pick up (OPU) procedure has been long performed by laparoscopic access [1] comprising the insertion of three instruments into the women's abdomen by multiple surgical small incisions, respectively at the navel lower edge for the laparoscope, few centimeters above the pubic symphysis for grasping forceps, and in the lower right quadrant to insert the needle, necessary for aspiration and collection of both oocytes and follicular fluid [2].

This laparoscopic approach has been progressively discarded for intrinsic risks to expose patients to infections, internal organ damages and/or severe bleeding. On the other hand, the frequent scarcity of mature oocytes recruited, as well as the minor fertilization rate usually reported by OPU, led to a gradual substitution of the laparoscopy with a transabdominal (TAUS) or transvaginal (TVUS) ultrasound-guided oocyte retrieval [3–5]. In the last years, however, the TAUS has been progressively replaced by TVUS which is today considered a direct and safer approach for the oocyte retrieval since the needle passage does not occur through the abdomen.

During the TVUS oocyte recruitment, the transvaginal probe is properly utilized to assess the position of ovaries and the needle is attached to the ultrasound probe guide and carefully inserted into the follicle through the vaginal wall for both oocyte retrieval and follicular fluid aspiration. This approach employs

approximately 10–15 minutes and requires a slight sedation of the patients with a short assistance time after the procedure. However, although this procedure is largely adopted for the minor risks of surgical complications, several conditions as ovarian inaccessibility, transposed ovaries [6, 7], Müllerian agenesis [8], or hysterectomized patients, prevent its utilization for intrinsic drawbacks related to physical manual skills of the procedure in searching ovaries, and in these circumstances the TAUS should be thus preferred [9, 10].

Several studies have compared laparoscopy [11], TAUS and TVUS for the oocyte retrieval and provided evidence that TVUS is usually preferred for its shorter surgical time required and minor invasive intervention, although the laparoscopy still remains the conventional practice to recover ovarian cortical strips from oncological patients [12]. Nevertheless, besides the mentioned precluding conditions for TVUS, in less than 2% of patients with changed position of ovaries due to pelvic adhesions by pelvic inflammation or surgery as well as fibroids, endometriosis or congenital vaginal abnormalities [13], this procedure becomes impracticable for its failure [14]. In these cases, once the urinary bladder is empty, a vaginal scan probe manipulation with abdominal pressure in association with cervical traction by a tenaculum would improve the chance of oocyte recruitment even by transperitoneal needle passage [15].

In rare cases, during the OPU, it has been necessary to introduce the aspiration needle through the myometrium to access to the ovarian follicles. However, this procedure also applied to transmyometrial embryo transfer (ET), is not risk-free since uterine contractions due to endometrial injury may occur and results at lower pregnancy rate in women undergoing in vitro fertilization (IVF) protocols [16–19]. However, data concerning the reproductive outcomes are still controversial in line with the scarcity of defined information regarding the relative complications.

Therefore, our study was aimed at both comparing the efficacy of the transmyometrial pick up (TPU) with respect to standard transvaginal oocyte retrieval in terms of reproductive outcomes particularly in women with inaccessible ovaries, in a cohort of infertile patients. Also, we explored advantages and drawbacks of TPU.

Methods

Patients - Female patients aged within 38yrs, candidate to IVF/intracytoplasmic sperm injection (ICSI) at “*Momò Fertilife - Center for Reproductive Medicine*” in Bisceglie (Italy) and at “*Santa Maria Hospital*” in Bari were enrolled after written informed consent in line with standard criteria of the study which was approved by the local Ethical Committee (code n. 0612). A specific accepted note of the informed consent reported that in case of inaccessible ovaries an alternative surgical approach requiring the oocyte transmyometrial retrieval should have be performed. From January 2004 to December 2018 at both infertility centers 594 women with one or both inaccessible ovaries were planned for standard transvaginal OPU from a cohort of 11,273 ICSI-cycles performed. To avoid other concurrent infertility settings, only couples with male partners showing normal semen parameters according to WHO (World Health Organization) were considered suitable for the study, and females coupled with males claiming

azoospermia, severe oligo-astheno-teratozoospermia or known reproductive genes' alterations were excluded. All females were conventionally treated with gonadotropin-releasing hormone (GnRH) antagonists (Cetrotide, Merck Serono), then stimulated with a recombinant follicle stimulating hormone (FSH) preparation (GONAL-f, Merck Serono) and induced to ovulation by a choriogonadotropin alfa (Ovitrelle 250, Merck Serono).

Oocyte-recruitment procedures - To retrieve oocytes, patients underwent procedural sedation by intravenously injection of a general anesthetic (Propofol 1%, TEVA). Eggs were transvaginally retrieved through follicular puncture using a 17-gauge aspiration needle (COOK Medical) connected to a guide on the ultrasound transvaginal probe (Aloka, Toshiba, GE), whereas for the male partners the semen was collected in sterile containers after 3/4 days of sexual abstinence and maintained at 37 °C for 30 min until use. The female population with inaccessible ovaries included 594 women who were primarily referred to standard OPU, and in case of failure to supportive procedures as induction of a vaginal pressure on the fornix, use of reverse Trendelenburg position, traction of cervix or ultimately a transabdominal access. In case of unreachable ovaries even by such OPU facilities, we approached the oocytes recruitment through transmyometrial insertion of the needle under ultrasound guide. This alternative surgical procedure included the trasabdominal access of the aspiration needle through the fundal myometrium using an ultrasound color-Doppler device to avoid the blood vessels injury particularly on the uterus' sites potentially leading to severe pelvic hemorrhages when damaged [21].

Therefore, in relation to the method employed for allow the oocyte retrieval, all patients were divided into two groups: group A including patients who underwent transmyometrial follicular aspiration and group B of patients, homogeneous in number and etiology of infertility, treated with standard transvaginal OPU even implemented with supportive variants.

Therefore, both groups were compared with respect of several aspects as stimulation days, levels of Estradiol and follicles' number on the day of hCG injection, number of retrieved as well inseminated eggs, fertilization rate and, ultimately, the reproductive outcomes.

Furthermore, a subset from group A including 24 patients in whom the needle was transendometrially was also investigated to assess whether or not this procedural variant can affect IVF outcomes in relation to the possible injury of the endometrial mucosa capable to prevent the subsequent embryo's nesting.

In all instances, eggs were retrieved by a single ovarian puncture 36 hrs after the choriogonadotropin alfa administration. Therefore, cumulus-oocyte complexes were exposed to Hyaluronidase solution (25 IU/ml) to remove the corona radiata, and putative oocytes were inspected and evaluated under a stereomicroscope (Nikon SMZ 1500) to select those in metaphase II (MII). These eggs were then incubated in LGGF medium (Fertilization Global) and injected 38–40 hrs following the Ovitrelle treatment of patients. In both A and B groups, the ICSI procedure was performed at 37 °C under an inverted microscope (Nikon eclipse, TE 200) using a microinjection system at 400X magnification. After the insemination, the fertilized oocytes were cultured in LGGG medium (Global) for 3 days.

Statistical analysis - Data between groups were calculated as mean values (M) ± SD whereas ANOVA was performed by using Statistica version 8.0 (StatSoft Italia Srl, Padova) and compared by Student's t-test using a P-value < 0.05 as significance limit.

Results

Patients and TVUS oocyte-recruitment procedures - The first analysis of our study was devoted to investigate the major reasons of ovaries inaccessibility in our cohort of infertile women for which they underwent additional measures up to the trans-myometrial access to ovaries. As mentioned, in these patients the traditional TVUS technique failed to the egg retrieval since the ubication of both ovaries was unreachable by ultrasound recognition.

We retrospectively revisited by anamnestic data the potential causes of ovaries ultrasound inaccessibility and Table 1 details the major pathogenic conditions in 113 patients. As shown, several diseases as endometriosis and previous pelvic surgery predominantly recurred in this group of patients although unknown causes were largely present in inducing the ovarian unreachability.

Table 1
Causes of inaccessible ovaries in a cohort of infertile women undergoing OPU.

	Numer of patients
Previous salpingitis	17
Pelvic inflammatory disease	3
Endometriosis	25
Previous surgery	18
Laparoscopic diagnosis of adhesions	16
Unknown	35

We thus adopted other actions to improve the efficacy of standard TVUS retrieval including the increased pressure on the vaginal fornix by the probe, reverse Trendelenburg accommodation of patients, traction of the cervix and others up to the trans-myometrial insertion of the needle. As shown in Table 2, for 121 patients most of these procedures failed, and a transabdominal access was attempted by moving the transabdominal ultrasound probe over abdomen in correspondence to the ovary location and subsequent insertion of the needle coupled with a needle guide through the abdomen. In 113 cases of the full cohort of patients, namely those grouped in A, all the above-mentioned procedures were unable to facilitate the eggs' recovery, thus making necessary the needle passage through the myometrium.

Table 2
Sequence of maneuvers carried out for oocyte pick up in patients with inaccessible ovaries.

	1st maneuver	2nd maneuver	3rd maneuver	4th maneuver	5th maneuver
Bimanual examination/abdominal pressure	337	6	17	121	113
or probe pressure					
Trandelenburg position					
Cervical clamp traction					
Transabdominal pick-up					
Transmyometrial pick-up					

Therefore, in order to evaluate the reproductive outcomes and the potential complications of this alternative procedure, the Group A were compared to Group B including 113 women from the full cohort of 594 original patients for whom the above-mentioned procedures had been effective and resulted productive by the standard OPU.

Both groups were first investigated on mostly frequent reasons of infertility as showed in Table 3 and then compared for patient age, mean estradiol level, number of collected follicles, stimulation days, eggs and embryos obtained, ongoing pregnancy and spontaneous abortion rates.

Table 3
Infertility causes in transmyometrial oocyte retrievals (GroupA) and controls (Group B).

Diagnosis	Group A (113)	Group B (113)	P value
Male factor	32	36	NS
Tubal factor	19	6	NS
Unexplained	20	20	NS
Oligo/anovulation	4	23	NS
Endometriosis	27	19	NS
Polycystic ovary	1	4	NS
Uterine	1	0	NS
Other	9	5	NS

However, Table 4 shows that no significant differences of those parameters between both groups were found ($P > 0.05$ in all instances).

Table 4
Outcomes of IVF cycles in transmyometrial oocyte retrievals (Group A) and controls (Group B).

IVF outcome	Group A (n = 113)	Group B (n = 113)	P value
Age	36.9 ± 0.9	36.9 ± 0.9	NS
Attempt number	2 ± 0.3	2 ± 0.3	NS
Estradiol level on day hCG	1678 ± 207	1873 ± 176	NS
No. of follicles on day of hCG	11.4 ± 0.8	12 ± 0.7	NS
No. of stimulation days	11.6 ± 0.4	11.5 ± 0.3	NS
Total eggs	10 ± 1.6	10.5 ± 1.3	NS
No. of mature eggs injected	5.1 ± 0.3	5.8 ± 0.2	NS
No. of embryos	4 ± 0.6	4.2 ± 0.7	NS
No. of embryo transferred	2 ± 0.3	2 ± 0.2	NS
Average cell no. of embryos	6.4 ± 0.3	6.3 ± 0.1	NS
Ongoing pregnancy	30	37	NS
Not pregnant	59	53	NS
Spontaneous abortion	7	8	NS
Chemical pregnancy	11	14	NS
Ectopic pregnancy	3	1	NS

Furthermore, to evaluate both safety and potential complications related to the trans-myometrial oocyte retrieval, we noticed that after 4 h and 24 h from the surgical procedure, no cases of peritoneal or endometrial bleeding were reported in Group A (Table 5).

Table 5 Color-Doppler ultrasound evaluation of blood loss on the posterior uterine wall in correspondence with the needle exit point in Group A.

Blood loss	Not	Yes
After 2 hours	86	17
After 4 hours	113	0
After 24 hours	113	0

Finally, as reported in Table 6, further analysis was devoted to investigate the safety of trans-myometrial procedure in 24 patients in whom the needle was passed through the endometrium, namely the trans-myometrial/endometrial retrieval, with respect to the remaining 89 patients underwent to trans-myometrial needle passage.

Table 6
Outcomes of transmyometrial IVF cycles in patients where the needle was passed through the endometrium (transendometrial) compared to women where the needle was not passed through the endometrium (not transendometrial).

IVF outcome	Transendometrial (n = 24)	Not transendometrial (n = 89)	P value
Ongoing pregnancy	6	24	NS
Not pregnant	13	50	NS
Spontaneous abortion	2	5	NS
Chemical pregnancy	3	7	NS
Ectopic pregnancy	0	3	NS

However, although including small number of patients in both groups, their comparison revealed that both procedures were safe and that the transmyometrial/endometrial insertion of the needle was unable to affect the endometrial nesting of eggs neither to influence the evolution of pregnancy or spontaneous abortion. In fact, no significant difference was found between both groups.

Discussion

The oocyte retrieval is generally performed by a TVUS-guided follicular aspiration [22, 23], which has replaced the laparoscopic and transabdominal conventional techniques [24], since studies have proven its safety, efficacy and simplicity of use. Therefore, to this regard, several Authors have tried to compare these different oocyte recovery strategies, in term of time required, invasiveness and safety [25].

Barton SE and Coworkers have reported in their study that the TVUS follicular aspiration was preferable as procedure requiring less time and invasiveness, compared to the TAUS which could be considered a safer

and useful technique for oocyte retrieval in cases of inaccessible ovaries by the transvaginal approach [26]. In fact, literature data report that the TAUS approach is able to maximize the number of oocytes retrieved, mainly in women with radical hysterectomies, transposed ovaries [27, 28], Müllerian agenesis [29] as well as in cases of increased body mass index (BMI) for which the poor ultrasound image quality, make the ovaries unreachable [30, 31]. However, despite the feasibility of this approach, the TAUS retrieval, often requiring multiple punctures for each ovary impacting on patients' discomfort and the infectious risk [17], makes preferable the transvaginal approach. Thus, in order to avoid conditions of inaccessible ovaries which recur in approximately 2% of females undergoing OPU, several management options including the urinary bladder emptying, the vaginal scan probe manipulation with abdominal pressure, or a transvaginal transmyometrial oocyte retrieval, become necessary [32].

Generally, the passage of the needle through the endometrium, that happens during a transmyometrial oocyte retrieval, is considered not a conventional procedure since some oocytes are not recruitable in addition to possible interference with the next embryo implantation. However, the real effects of the transmyometrial retrieval on reproductive outcomes and the complications deriving from this practice are still poorly explored.

Davis and Colleagues, in their study showed that the trans-myometrial retrieval did not significantly affect the pregnancy outcome on a cohort of 85 infertile women, when compared to the same number of patients undergone a standard transvaginal OPU, thus suggesting the need for a larger study to find a statistically significant difference [33]. To date, however, no one has still assessed the possible vascular risks and the reproductive outcome correlated with the trans-myometrial retrieval.

Therefore, our study (Fig. 1) is aimed to evaluate the reproductive outcome and the potential complications deriving from the execution of a transvaginal transmyometrial oocyte retrieval (Fig. 2, 3) compared to the standard transvaginal oocyte retrieval on a cohort of infertile patients.

Moreover, a further objective of the study has also been to evaluate the complications and the reproductive outcomes of 24 cases of transmyometrial/endometrial recruitment. The absence of any complications related procedure, cases of peritoneal or endometrial bleeding, allowed us to prove that this further invasive procedure is apparently safe for the endometrium and the IVF outcome, thus giving further support to our study.

Conclusion

Data presented in our study suggest that the transmyometrial oocyte retrieval, might be considered a safe approach in IVF programs, to achieve exclusively in case of inaccessible ovary even unreachable by alternative medical maneuvers, which does not seem to be associated with a reduction of oocyte yield or a decrease in pregnancy rate.

Declarations

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The authors thank all of the participants involved in this study.

Authors' contributions

The authors contributed in the following ways: Domenico Baldini: data collection, data analysis, study design; Lavopa Cristina: data collection; Vizziello Giovanni: data collection, data analysis; Todaro Pasquale: data collection; Malvasi Antonio: data collection, drafting; Ferri Daniele: technical support, drafting; Erica Silvestris: drafting, critical revision and final approval of the manuscript. All the authors read and approved the final manuscript.

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Availability of data and materials

The dataset supporting the conclusions of this article is included within the article.

Ethics approval and consent to participate

The study was approved by the local Ethical Committee (code n. 0612) and each enrolled patient signed an informed consent in line with standard criteria of the study.

Consent for publication

All of the authors have agreed to publish this article in your journal if it should be accepted.

Competing interests

The authors declare that they have no competing interests.

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Figures

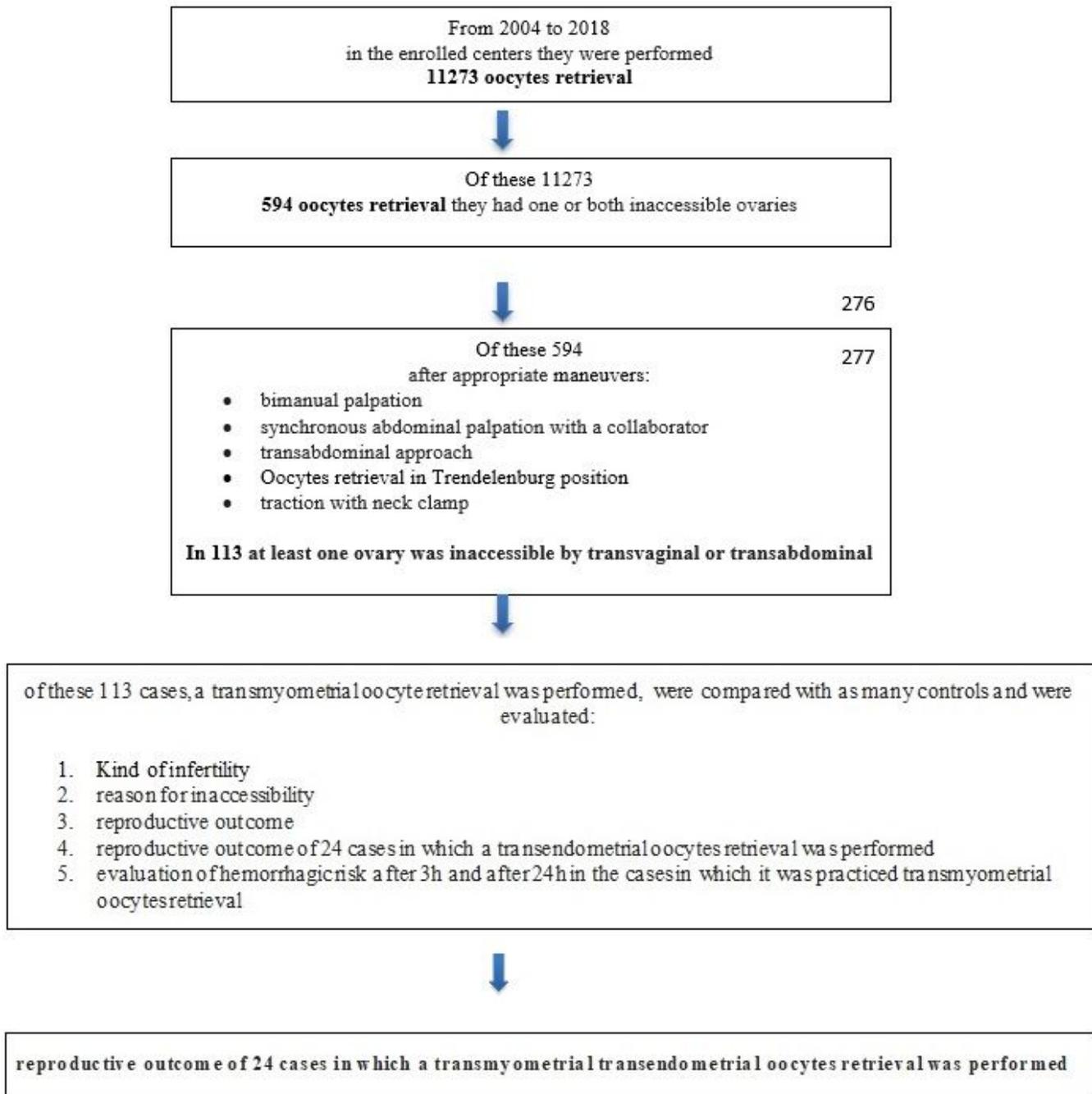


Figure 1

Draw of a Multicenter retrospective study: (Enrolled IVF Center Momò FertiLIFE – Bisceglie ,Italy and Clinica Santa Maria – Bari, Italy).

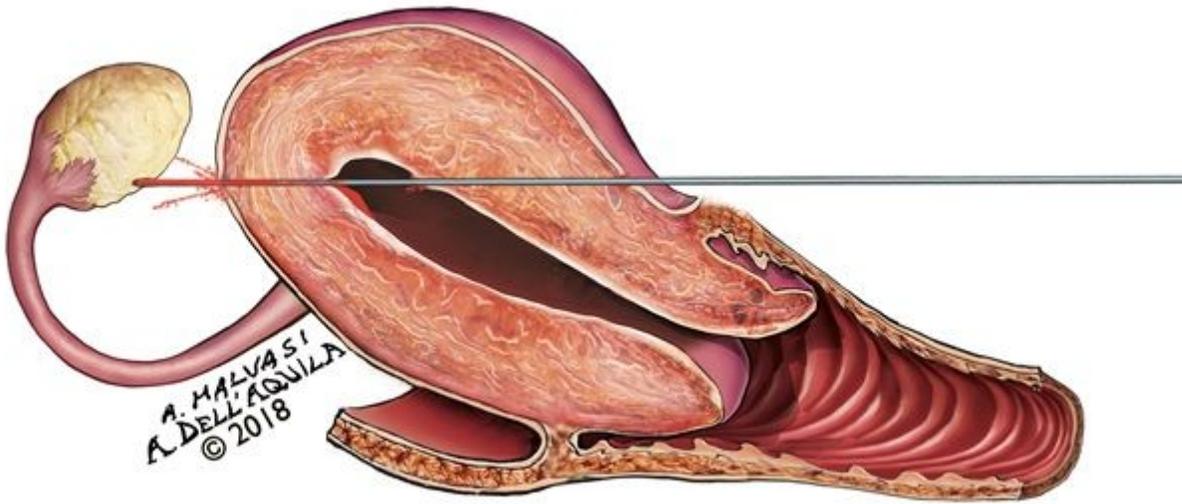


Figure 2

Schematic representation of trans-myometrial/endometrial oocytes retrieval performed in 24 cases of the Group A.

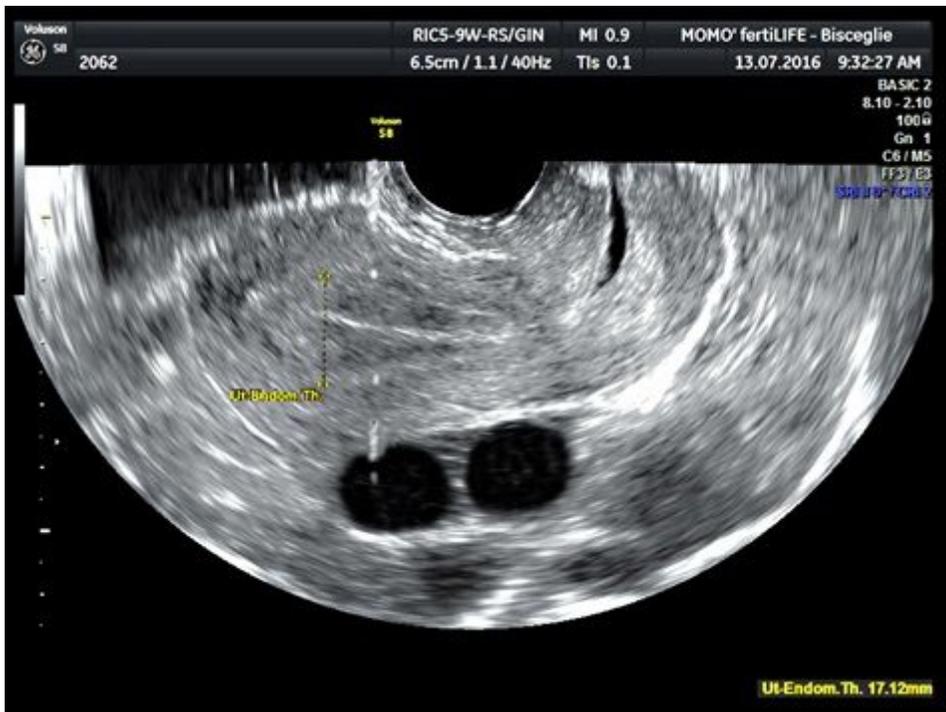


Figure 3

Ultrasound findings of trans-myometrial/endometrial oocytes retrieval performed in 24 cases of the Group A.