ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Appraisal of clinical complications after 23,827 oocyte retrievals in a large assisted reproductive technology program

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Objective: To assess complications encountered after transvaginal oocyte retrieval procedures.
Design: Retrospective analysis.
Setting: University hospital, fertility center.
Patient(s): A total of 23,827 consecutive transvaginal oocyte retrieval procedures in 12,615 patients.
Intervention(s): Oocyte retrieval procedures performed between June 1996 and October 2016.
Main Outcome Measure(s): All oocyte retrieval complications. Those requiring hospital admission for at least 24 hours were considered severe.
Result(s): A total of 96 patients (0.76 %) suffered complications, with hospital admission necessary for 71 patients (0.56 %). When calculated per retrieval, the overall complication rate was 0.4%, whereas 0.29% was the admission rate, with an average duration of hospital stay of 2.77 ± 2.5 days. A surgical procedure was necessary for 24 patients (0.1% per retrieval and 0.19% per patient). Multivariate analysis showed a significant correlation between complications and women age, body mass index (BMI), the number oocyte retrieved, and the mean time to complete oocyte retrieval. The incidence of complications was significantly higher for physicians who had performed <250 retrievals compared with those who had completed >250 retrievals (odds ratio 0.63, 95% confidence interval 0.40–0.99).
Conclusion(s): Oocyte retrieval can be considered a safe procedure but is not without risks. The most important, identifiable, risk factors for the occurrence of complications are: [1] high number of oocytes retrieved, [2] a long duration of the procedure and mean time per oocyte retrieved, [3] inexperience of the surgeon, [4] younger patients with a lesser BMI, and [5] history of prior abdominal or pelvic surgery or pelvic inflammatory disease.
Clinical Trial Registration Number: NCT03282279. (Fertil Steril® 2018;■:■–■. Copyright ©2018 The Authors. Published by Elsevier Inc. on behalf of the American Society for Reproductive Medicine. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Key Words: Oocyte retrieval, complications, vaginal and peritoneal bleeding, pelvic sepsis

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Ultrasound-guided transvaginal route (US-TV) is the most common approach used to harvest oocytes during IVF cycles. Oocyte retrieval by US-TV was first performed in 1983 (1), and as it is relatively easy to learn and much less invasive compared with the laparoscopic or transabdominal routes, it has become the gold standard for collecting oocytes (2, 3). Several observational studies evaluating the rates of complications

Received November 4, 2017; revised January 22, 2018; accepted February 1, 2018.
P.E.L.-S. has nothing to disclose. F.C. has nothing to disclose. V.S. has nothing to disclose. E.M. has nothing to disclose. F.H. has nothing to disclose. D.G. has nothing to disclose. E.Z. has nothing to disclose. P.P. has nothing to disclose.
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Fertility and Sterility® Vol. ■, No. ■, ■ 2018 0015-0282

https://doi.org/10.1016/j.fertnstert.2018.02.002

associated with this procedure have shown that it is safe, with very low rates of serious adverse events. However, the risks associated with US-TV should not be underestimated because some complications, although rare, may be life-threatening (2 deaths were reported in 2010) (4). More frequent complications are vaginal and peritoneal bleeding (5–8). Dessole et al. (9) found that 230 mL was the usual estimated blood loss about 24 hours after oocyte retrieval. Rarely, ovarian bleeding may lead to severe hemoperitoneum (10) and the symptoms may appear either early or late ($\leq$28 hours) after oocyte retrieval procedures. Other complications after retrieval are pelvic sepsis or abscess (5, 6, 11). A retrospective analysis (12) suggested that particularly in patients with ovarian endometriomas, complications, such as tubo-ovarian abscess, can occur even long after the completion of the assisted reproductive technology (ART) cycle, indicating that women with endometriosis are prone to develop infectious complications. Other rarer complications, described as case reports, are ureterovaginal fistulas (13), pseudoaneurysm of the iliac artery (14, 15), ureteral injury (11, 16, 17), bladder injury with hematuria (18–20), ovarian torsion (6), and ovarian abscess (21). All of these adverse events are iatrogenic, caused by the trauma of the aspiration needle on the pelvic organs. Because most IVF centers perform oocyte retrieval procedures either under general anesthesia or with deep sedation, complications from the anesthetic agents should also be considered. In general, the rates of complications associated with oocyte retrieval procedures are not easily available unless individual programs collect these data as indicators for their own quality performance. Most ART registries focus on cycle outcomes in terms of pregnancy and live birth, but neglect to collect information about the rate of complications during oocyte retrieval procedures. In addition, as complications often occur days to weeks after the oocyte retrieval procedure, the reporting of these complications to the registry may be suboptimal. The aim of the present study was to report complication rates after oocyte retrieval in one of the largest case studies analysis conducted in a single ART program. This information is valuable for counseling and informing patients undergoing US-TV about the treatment-related complications and risks.

MATERIALS AND METHODS

All oocyte retrieval procedures performed at the Fertility Center Humanitas Research Hospital (Rozzano, Milan, Italy) between June 1996 and October 2016 were included. All cycles consisted of controlled ovarian hyperstimulation (COH) with standard protocols (using either agonist or antagonist), with ultrasound and hormonal monitoring (17-beta-E_2 and P) beginning on day 5 of stimulation and continuing until follicles had a suitable diameter and hormone levels were acceptable. Final follicle maturation was triggered with hCG (urinary or recombinant) or, lately, with GnRH analogue to decrease the risk of ovarian hyperstimulation syndrome (OHSS). Per the protocol of the unit, routine preoperative assessment included a complete blood count with coagulation panel, fasting blood sugar, electrocardiogram, and an anesthesiologist evaluation. Specific to our unit's protocol, the day before retrieval patients were instructed to do a vaginal douching with iodopovidone 10% (Meda Pharma S.p.A), to insert a vaginal capsule of chloramphenicol (250 mg), and to do a light enema. The transvaginal ultrasound-guided oocyte retrieval procedure was performed 34–36 hours after hCG administration, in a dedicated surgical suite using either a single or double-lumen (17 G) aspiration needle (35 cm) (22), depending on the number of follicles and at a pressure of $<$150 mm Hg (23). Before retrieval, the operator scrubbed and wore powder-free sterile gloves, rinsed the vagina with isotonic saline solution, and covered the patient with sterile surgical drapes. A rotating team of gynecologists with different levels of experience performed the oocyte retrieval procedures and the times of each procedure were recorded. The oocyte retrieval procedures were performed under deep sedation using intravenous propofol (at a dose weight-related) + fentanyl (50γ), plus propofol drip (5 mg/kg/hour), IV paracetamol 1,000 mg, as well as assisted mask ventilation with oxygen. Antibiotic prophylaxis was not routinely used except in presence of risk factors, such as history of hydrosalpinx, ovarian endometrioma, pelvic inflammatory disease (PID), or when the estimated blood loss was $>$200 mL. At the end of each oocyte retrieval procedure, patients were observed for 2.5 hours and then discharged home with an emergency contact number. All data were collected using an exclusive internal web-based database. Such database allows for storage, organization, and ease in retrieving information about any patient. It also manages care processes versus time: from outpatient services to follow-up treatments, and includes tracking the details of any surgery or hospitalization. Patients' data are safeguarded by an advanced threat prevention, enterprise-class encryption, and authentication for any user with periodical need of password renewal. Patients had consented in writing that their medical records could be used for research purposes, as long as their anonymity was protected and medical record confidentiality assured. Because both conditions were met, this study had expedited review and approval (IRB number 17/17). The study protocol was registered in Clinicaltrial.com before full variable extraction and statistical analyses.

Primary outcome was the incidence of complications necessitating hospitalization or outpatient management. Cases of OHSS were not included.

Parameters considered for the statistical analyses were body mass index (BMI), patient age, duration of infertility, number of oocytes collected, time to complete the retrieval, mean time per oocyte (i.e., total time to complete the retrieval divided by the number of oocytes retrieved), and surgeon experience. Single versus double lumen needle and number of follicles at trigger were not included in the analyses for the nonindependency of the variables.

History of endometriosis, prior abdominal or pelvic surgery, PID, or hematologic disease were collected in all patients. Our internal protocol requires 50 US-TV procedures performed under supervision of a senior attending before granting privileges to junior colleagues, based on an external audit quality performance and the maintenance program was introduced in 2013. This system generates a report for all clinicians every