REVIEW

Surgical complications of in vitro fertilization

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ABSTRACT

The incidence of complications arising from in vitro fertilization and oocyte retrieval is relatively low. Infections, bleeding, and ovarian torsion are the main complications discussed in this review. Physicians and patients need to be aware of these complications at all times during the treatment process. Early diagnosis and proper medical or surgical interventions will lead to a successful resolution in the majority of cases.

Keywords: Complications, surgery, in vitro fertilization.

INTRODUCTION

In vitro fertilization (IVF) has been established as a widespread treatment of infertility throughout the world. It is indicated as primary treatment in cases with male factor infertility, severe tubal disease, and moderate to severe endometriosis. It is also a treatment option for patients with advanced maternal age (>35 years), poor ovarian reserve, unexplained infertility, and anovulation that is resistant to simpler treatment modalities.

The major risks and complications from IVF include ovarian hyperstimulation syndrome, multiple pregnancy, and ectopic and heterotopic pregnancies. There are other risks and complications that mainly arise from the ultrasound guided transvaginal oocyte retrieval (TVOR) procedure, and the ovarian stimulation process. These risks include infection, bleeding, and ovarian torsion and will be the focus of this article. Although these complications may be rare, both the fertility specialist and the general obstetrician and gynecologist need to be aware of them so that they can counsel their patients better, and be able to provide proper treatment as well.

Infection

Pelvic infection during IVF is a complication mainly resulting from the transvaginal oocyte retrieval (TVOR). Infection has been reported with
an incidence as low as 0.02% by the 2000 registry of the European Society of Human Reproduction and Embryology (1). Other reports have included a slightly higher incidence ranging from 0.3-1.5% (2) with the majority of studies revolving more specifically around the 0.3-0.6% range. Although pelvic infection overall may be considered a very low risk of IVF, it must be recognized and managed appropriately to avoid serious consequences such as an acute abdomen or pelvic abscess.

Iatrogenic inoculation of the peritoneal cavity with bacterial flora from the vagina during TVOR is the most obvious, logical explanation for pelvic infections during IVF (3). Patients undergoing ovulation induction alone without other interventions have an extremely rare incidence of infection which supports the idea that the oocyte retrieval itself is the culprit (4). Not only is there the possibility of introducing bacteria into the peritoneal cavity, but also fungal organisms, which can often be present in the vagina. Other, more rare, possible mechanisms for pelvic infection includes reactivation of latent pelvic inflammatory disease, or direct colonic injury (5).

Different preventative methods have been studied to decrease the incidence of pelvic infections. Although some may still be controversial, they are important factors to keep in mind during the technique of oocyte retrieval. The most well established and accepted technique to decrease the risk of pelvic infection is using the fewest possible vaginal punctures (6, 7). Serour et al. emphasized the importance of the fact that most patients in their study had a maximum of only two vaginal punctures (7).

Other preventative measures, however, such as using vaginal disinfectants and prophylactic oral antibiotics are more controversial. Both the significance of their benefit and the exact protocol for their use are unresolved issues. Van Os et al. reported that vaginal disinfection with 1% solution of povidone-iodine was associated with a lower pregnancy rate secondary to the possible embryotoxic effects of the disinfectants (8). Rinsing the vagina with saline, instead, did not cause a significant risk of infection, but it did have a much higher pregnancy rate of 30% compared to only 17% in the disinfectant group (8). More recent studies have shown that preparing the vagina with povidone-iodine followed by thorough saline irrigation prior to the punctures helps prevent pelvic infection without compromising pregnancy outcome (7, 9).

Prophylactic antibiotics and even antifungal agents may also help decrease the risk of pelvic infection, although vaginal microbes can still be introduced into the ovaries despite such prophylaxis. Older studies tend to question their use given the low incidence of pelvic infections (6, 10, 11). Other investigators, however, do advocate using prophylactic antibiotics as a general rule (7, 12, 13). Although there is no consensus on the type and protocol for antibiotic use, doxycycline and metronidazole are the common ones. First generation cephalosporins, which are routinely used as prophylactic antibiotics preoperatively, are another class of antimicrobials that have been used before TVOR (5). Serour et al. even used fluconazole, an antifungal agent, as part of their protocol prior to oocyte retrieval (7). Although antifungal prophylaxis may seem excessive, an interesting report by Ibara et al. discussed two cases of systemic candida glabrata infections diagnosed at 34 and 22 weeks gestation following IVF (14). The yeast was isolated from both the mothers and their babies. Another approach can also be to reserve prophylactic antibiotics to high risk patients such as those with history of pelvic inflammatory disease or endometriosis.

A particularly concerning consequence of pelvic infection is the formation of a pelvic abscess, especially when pregnancy is achieved. The time of presentation of symptoms secondary to pelvic abscess after TVOR can be highly variable, which can make their diagnosis even that much more challenging. This should always be in the differential diagnosis of patients with abdominal pain, fever, and/or leukocytosis after TVOR, even if prophylactic antibiotics or vaginal disinfection were used.

While direct inoculation of vaginal flora into the ovary during TVOR is thought to be the primary mechanism leading to abscess formation, the presence of endometriomas may further increase that risk by providing a rich culture medium for bacteria. Endometriosis has been associated with an increased risk of pelvic...
inflammatory disease after oocyte retrieval through multiple reports, and pelvic abscess can be one manifestation of that infection (5, 15, 16).

Given that endometriosis leads to infertility in many women who may eventually seek IVF, this risk factor should always be acknowledged and those patients should be handled with more stringent protocols for prophylaxis whether that be antibiotics, and/or vaginal preparation. Also, great caution should be undertaken to avoid the puncture and aspiration of an endometrioma during TVOR, which is why a good ultrasound technique is essential during this procedure. Such an action could lead to the development of infected endometriotic cysts as presented by Yaron et al. in 1994 (18).

The organisms involved in pelvic abscesses are most commonly in the coliform family (E. coli, etc.). Enterococcus, Bacteroides, Peptostreptococcus, and other anaerobes can also be evident in these abscesses (5). Just as prophylactic antimicrobial therapy and/or vaginal disinfection are still controversial, the exact management of pelvic abscesses in this setting is also unclear. In general, peritonitis with acute abdomen associated with abscess rupture should be handled swiftly and surgically and may require oophorectomy in some cases. However, stable patients can be managed with medical therapy and/or abscess drainage. The timing of drainage, especially when a pregnancy is present, is not clear. It can be performed under either ultrasound or computerized tomography (CT) scan guidance.

Structures other than the ovary can also be affected by iatrogenic induced infection after TVOR. Although the incidence may be much rarer, it is possible. As an example, the frequency of iatrogenic vertebral osteomyelitis is trending upwards which may be associated with the increasing use of procedures such as TVOR. A case report of Streptococcus fecalis spondylodiscitis of L5-S1 after TVOR illustrates that point (19). Conservative management is generally followed, and surgical intervention may be required in some cases.

Bowel injury is yet another example of an extremely rare complication of TVOR involving damage to a structure other than the ovary which can lead to infection. Puncturing a hole in the bowel can lead to contamination of the pelvis and subsequent inflammation and infection. In 1992, Van Hoorde et al. presented the first case report of appendicitis caused by TVOR at which time holes were punctured into the appendix (20). It is important to be cognizant of peristaltic bowel on ultrasound while performing the aspiration to avoid such incidental bowel punctures.

**Bleeding**

Bleeding is another complication of IVF resulting from TVOR. Although insignificant bleeding from the vaginal vessels can be a common problem encountered with TVOR, the more concerning intraperitoneal bleeding is very rare but does occur. Intraperitoneal bleeding may originate from the ovarian vein, iliac or sacral vessels, or from the actual follicle puncture. Other sources of bleeding can be ovarian lacerations, and ruptured endometriomas. Major bleeding is reported in 0.03-0.5% of IVF cases (4, 6). A higher incidence was reported by the European registry (1) but they covered all bleeding complications, even minor ones not leading to hospitalization.

Guidelines for reducing the risk of bleeding include limiting the number of vaginal punctures, ultrasound visualization of peripheral follicles in a cross section before puncture, and using color Doppler whenever possible (7). However, color Doppler is not commonly used and not available in all IVF centers. Bleeding from incidental trauma to pelvic vessels which are misidentified as ovarian follicles may have occurred in older reports, but can be easily avoided now given the improved ultrasound equipment and technique (21). Structures should always be visualized in the longitudinal and transverse axis. Also, the pelvis should be inspected well during the procedure to ensure there is no significant fluid collection forming (17).

Both intraperitoneal and extraperitoneal hematomas may form secondary to the bleeding, and are best definitively diagnosed with CT scans. Hematomas should be suspected in patients with worsening lower abdominal pain, falling serial hematocrits, and anemia symptoms such as lightheadedness, weakness, shortness of breath, and/or palpitations. Peritoneal signs on physical
exam may help differentiate the location of the hematoma.

A case report of a rectus sheath hematoma extending from the space of Retzius (22) shows how large hematomas may form even in the extraperitoneal space. Therefore, the absence of significant physical or ultrasound findings in a patient with acute lower abdominal pain after TVOR may lead to a false sense of security if extraperitoneal pathology is not also ruled out via CT scan. Management of hematomas includes hospitalization with close monitoring. Hemodynamically stable patients without signs of deterioration can be managed conservatively. Many hematomas resorb without the need for evacuation and exploratory surgery.

Coagulation disorders should also be considered in patients with bleeding complications after TVOR. This is especially a concern for patients with massive bleeding, but no significant vascular injury.

Torsion

Superovulation protocols used in IVF lead to transiently enlarged, multicystic ovaries that are at risk for torsion. Gonadotropin stimulation followed by human chorionic gonadotropin can enlarge the ovaries to two to four times the normal size even after follicular aspiration (6). The risk rises even further for those patients who develop ovarian hyperstimulation syndrome (OHSS), and especially for those who become pregnant with this syndrome. A large series by Govaerts et al. in 1998 showed the incidence of torsion is approximately 0.1% overall (6). However, the numbers can rise significantly with IVF pregnant patients with OHSS. Mashiach et al. reported a 16% incidence of torsion in 75 pregnancies after gonadotropin therapy complicated by OHSS (23). The patients usually presented between six and thirteen weeks gestational age. However, when pregnancy was not achieved, the incidence of torsion was only 2.3% in those patients with OHSS.

Traditionally, untwisting was discouraged secondary to the concern for thrombosis and development of necrotic tissue. Salpingo-oophorectomy was considered the optimal treatment for the twisted ischemic ovary.

Currently, the gold standard has shifted to a more conservative approach which encourages laparoscopic untwisting of the ovary, especially in young infertile women. Early surgical intervention can allow for reperfusion and preservation of the affected ovary, especially if performed within six hours of the torsion.

Cohen et. al (2003) and Oelsner et al (2003) reviewed important results from their studies which evaluated patients receiving minimal surgery for ischemic ovaries (24, 25). Adnexal torsion occurred outside the setting of IVF for these patients. Laparoscopy or laparotomy was performed to achieve untwisting. Cohen et al reported that re-evaluation of 92 patients showed normal sized ovaries, with follicular development in at least 91% of them (24). Also, grossly normal ovaries were noted on all the 14 patients who underwent subsequent surgeries except for one in the laparotomy group. Furthermore, all six patients who underwent IVF at a later date had oocytes retrieved and fertilized from the previously torsed ovary. No pelvic or systemic thromboembolism was noted.

Oelsner et al. reported that 35 of 37 patients had normal sized, functional ovaries by ultrasound postoperatively (25). Two patients undergoing IVF had oocytes retrieved and fertilized from the untwisted ovary. The results from these studies not only reinforce that the current management approach of untwisting can save the ovary from necrosis, but also, that it can be achieved successfully by laparoscopy with subsequent functional preservation of that ovary.

A unique case of simultaneous bilateral ovarian torsion after gonadotropin ovulation induction by Kang et al. in 2006 was managed with laparoscopy, untwisting of both ovaries, and aspiration of cysts (26). The case illustrates that even though torsion is uncommon, it is a real and concerning risk of persistently enlarged ovaries. Furthermore, the management for the infertile patient should always attempt to be conservative and focused on ovarian preservation.

Another case report by Robson et al. (2000) discusses a patient with acute adnexal torsion immediately before scheduled oocyte retrieval (27). TVOR was still performed as a means of possibly returning the ovary to its normal position.
by aspirating the follicles. The patient required laparoscopy, though, within hours after TVOR. Untwisting was performed and resulted in the return to normal appearance of the ovary. The fertilization rate of the oocytes from the affected side was only 33% compared to 86% from the unaffected side. However, the luteal phase was unremarkable. The case report suggests that the occurrence of acute adnexal torsion before TVOR does not necessarily mean the IVF cycle must be cancelled. If adnexal necrosis occurs, which is unlikely in most cases, then embryo cryopreservation can be performed. Of note, pregnancy was not achieved in this case. If this approach is considered in any patient, the use of prophylactic antibiotics is warranted given that the needle can be passing through necrotic tissue.

Although the current conservative surgical management approach for adnexal torsion has been shown to be successful, it does not mean that adnexal necrosis can never occur. A case report by Pryor et al. effectively illustrates a rare example of this unfortunate outcome (28). The patient initially had untwisting performed of a torsed hyperstimulated ovary, but then required unilateral salpingo-oophorectomy two days later secondary to necrosis. While preserving the ovaries may be the primary goal in young women with torsion, it cannot be accomplished at the expense of the patient’s health.

Ureteral and nerve injury

Infection, bleeding, and torsion are the most commonly encountered surgical complications of IVF. Although much more rare, injury to surrounding structures is another possible risk of TVOR. Incidental puncture of bowel was discussed above in the context of infection since it leads to intra-abdominal contamination. Other reported targets of injury include the ureters and nerves, which are much smaller and almost impossible to identify ultrasonographically. Pelvic adhesions from endometriosis or infection can increase the risk of such injury secondary to distorted anatomy (29).

Ureteral obstruction post TVOR may occur secondary to extrinsic compression from a hematoma or abscess, or it may occur secondary to direct injury with subsequent scarring (30). The obstruction can present as hydronephrosis resulting in pelvic, abdominal, or flank pain with or without pyelonephritis. Management can be conservative with the placement of a ureteral stent or nephrostomy tube. However, in some cases, surgical repair may be necessary with simultaneous drainage of the hematoma or abscess if present (30). Given the close proximity of the ureter to the vagina and cervix, it is very likely that ureteral injury is much more common than is reported since it may go unrecognized (17). Furthermore, the timetable for the recognition of ureteral injury can be highly variable. The diagnosis of such an injury may occur acutely after TVOR or much later.

Similarly, nerve injury may result from compression due to a surrounding hematoma or abscess, or from direct injury with the needle (31). Presenting symptoms include paresis and paresthesias involving the lower extremity. Of note, anesthesia can also transiently cause such symptoms. In the case report by Van Eenige in 1997, the patient recovered completely within a short period of time with simple expectant management.

Limiting the number of needle punctures is again very important in decreasing the risk of injury to surrounding structures whether they are vessels, ureters, or nerves. In addition, ultrasound techniques have been continuously improving since the introduction of TVOR. Advancements such as three dimensional imaging and color Doppler can further aid in the accurate visualization of female pelvic anatomy.

CONCLUSION

IVF is a wonderful option for the infertile couple or patient which has gained more and more success and acceptance worldwide. The advent of ultrasound guided TVOR since 1985 as the gold standard for retrieval of oocytes has made the IVF process even more appealing by avoiding the need to undergo laparoscopy. In counseling and managing patients contemplating this elective treatment, however, the full extent of possible complications must be acknowledged and understood.
Table 1. List of IVF complications, incidence, and prevention/treatment

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<th>Complication</th>
<th>Incidence</th>
<th>Prevention / treatment</th>
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<tr>
<td>Infection</td>
<td>0.3-1.5%</td>
<td>• Limit the number of vaginal punctures, preferably only two.</td>
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<td>• Antibiotic and/or antifungal prophylaxis (controversial), but especially in high risk patients (history of pelvic inflammatory disease or endometriosis).</td>
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<td></td>
<td>• Vaginal disinfection with povidone iodine then irrigate with saline (controversial).</td>
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<td>• Be cognizant of peristaltic bowel on ultrasound to avoid bowel puncture and subsequent inflammation/infection.</td>
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<td>Major bleeding</td>
<td>0.03-0.5%</td>
<td>• Limit the number of vaginal punctures, preferably only two.</td>
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<td></td>
<td>• Visualize all structures by ultrasound in both the longitudinal and transverse axis before attempting puncture.</td>
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<td>• Inspect pelvis well to ensure that no significant fluid collection is forming.</td>
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<td>• Use color Doppler if available.</td>
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<td></td>
<td></td>
<td>• Hemodynamically unstable patients should be explored surgically and quickly.</td>
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<tr>
<td>Torsion</td>
<td>0.1%</td>
<td>• Aspirate all follicles to help decrease the size of the ovary.</td>
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<td>• Attempt early conservative management with laparoscopic untwisting of torsed adnexa.</td>
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<td>• Reserve salpingo-oophorectomy for cases of infarction.</td>
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Table 1 summarizes the incidence, prevention, and treatment recommendations for the complications of infection, major bleeding, and torsion.

Infection, bleeding, and ovarian torsion may be rare problems that arise after TVOR and the administration of super-ovulatory drugs, but when they occur they can have serious consequences. Given that most of these infertile patients are otherwise young, healthy women, these consequences can be very troubling for both the patient and physician involved. In all these complications, early recognition and appropriate management is key, which can only be accomplished if the physician keeps them in the differential diagnosis despite their rarity. Furthermore, staying up to date on different techniques to help minimize the risks for these complications is also important.

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