Review Article

Role of laparoscopic oocyte retrieval in modern practice

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Abstract

Since the advent of assisted reproductive technology (ART) using laparoscopy for egg collection, significant clinical and technological evolution has paved the way for simpler and safer techniques of egg recovery. Although transvaginal ultrasound-guided oocyte retrieval is the mainstay of modern ART practice, the use of laparoscopy in select indications continues to be relevant and often imperative. An extensive literature search was accomplished using Cochrane, Embase, and Medline searches and relevant literature was reviewed. The surgical technique of laparoscopic oocyte retrieval has evolved through the years in the hands of different groups of clinicians across the world and the authors have discussed their own experience. Although surgical safety checks and complications have improved, laparoscopy nevertheless is more cumbersome when compared to the vaginal procedure. However, the role of laparoscopic egg retrieval in modern practice is invaluable in certain cases, including in prepubertal and adolescent girls diagnosed with cancer requiring fertility preservation, in women with Mullerian agenesis with malpositioned ovaries, in those with cervical cancer with a risk of dissemination, and occasionally in those who need concomitant laparoscopy for diagnosis of pelvic pathology. The authors' experience in laparoscopic oocyte retrieval in a tertiary hospital in the UK showed good results but had several drawbacks. Although there is a paucity of studies stating the extent of use or incidence of laparoscopic oocyte retrieval in any ART program, this technique should be considered as an effective and safe alternative to difficult transvaginal recovery and may enable patients with specific clinical backgrounds to achieve pregnancy.

Keywords: laparoscopy, oocyte, retrieval

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INTRODUCTION

The world saw the dawn of a new era with the advent of assisted reproductive technology (ART) in the seventh and eighth decades of the last century–the culmination of a fusion between the science and research of gamete handling, and the surgical expertise of laparoscopy. Although laparoscopy enabled oocyte retrieval in the initial years, it was effectively replaced by transvaginal ultrasound (USG) guidance as a safer, simpler, and more efficient technique by the late 1980s. However, with the recent surge in fertility preservation and Mullerian agenesis patients contemplating pregnancy, laparoscopic oocyte retrieval appears to be an alternative option in selected cases of *in-vitro* fertilization (IVF) as highlighted

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in this review article, and therefore continues to be relevant in contemporary fertility practice.

History

In 1978, the world's first baby was born via IVF as a result of the work of Patrick Steptoe, a pioneering laparoscopic surgeon and Robert Edwards, a scientist.[1,2] When IVF was first established, oocytes were retrieved laparoscopically through follicular puncture under direct vision.[1,3] In subsequent years, ovarian follicular changes were monitored using USG and with this technology, US-guided collection was employed through transabdominal or transvesical routes.[4-6] Wikland *et al.* (1983) demonstrated that US-guided transvesical oocyte retrieval was as effective as laparoscopic retrieval. It could be used in all patients but particularly in those with adhesions whose ovaries were inaccessible via laparoscopy.[7] This technique was then developed further, and US-guided transvaginal retrieval was introduced.[3] Comparing the above methods, laparoscopy was not found to support a higher oocyte retrieval or pregnancy rate compared to US-guided transvesical or transvaginal retrieval.[3]

Laparoscopy requires hospital admission, an operating theatre, and general anesthesia. General anesthetic causes a significant increase in prolactin levels which although decrease after 2 hours, remain elevated until the following day.[8] This can disturb the ovulatory cycle which may have consequences in ART.[8] Carbon dioxide is used to inflate the abdominal cavity during laparoscopy which decreases the pH of the follicular fluid and may affect oocyte quality.[9] However, Dor *et al.* (1990) concluded that oocytes may be resistant to short-term exposure to decreases in pH caused by carbon dioxide and laparoscopy did not cause a negative effect on the oocyte in ART.[10]

The transvaginal approach provides a shorter distance of the ovaries to the transducer, a better view of the ovaries, higher recovery rate of good-quality oocytes, less need for general anesthesia, reduced risk of bowel injury, has a quicker recovery time postprocedure, has a decreased cost, and a quicker learning curve compared to transabdominal or laparoscopic retrieval.[11] For these reasons, almost all oocyte retrievals are now performed transvaginally.

Surgical Considerations

The original technique and equipment for laparoscopic oocyte retrieval have evolved over the years, however, the principle remains the same. The procedure usually involves three ports of entry into the abdomen for a camera, a grasper to stabilize the ovary, and a third port for puncture by the egg collection needle. Additional modifications have included the use of double lumen needles to aid follicular flushing using suction pressure and varying diameter of the puncture needle, the use of a human chorionic gonadotrophin trigger to aid in scheduling the surgery within convenient hours for the operating team, and the addition of a preprocedure laparoscopic adhesiolysis to help in ovarian access in indicated cases.[12]

Laparoscopy carries risks. The risk of serious complications from diagnostic laparoscopy is 2 in 1000.[13] This includes damage to bowel, bladder, uterus, ureters, or major blood vessels which would require repair by laparoscopy or laparotomy. Other serious complications include failure to enter the abdominal cavity, entry-site hernia, thromboembolic complications, and death. Frequent risks include bruising, shoulder-tip pain, wound gaping, and infection.[13]

On a similar note, although less common, there are risks with US-guided transvaginal oocyte retrieval as well. Severe complications may include development of an acute abdomen due to ruptured tubo-ovarian abscesses, ruptured endometriomas, or hemoperitoneum.[14] These complications may present as a surgical emergency and require urgent laparoscopy or laparotomy to establish the cause and treat.[14]

Apart from surgical risks, anesthetic complications from sedation or general anesthesia can occur in both techniques. These include asphyxia, apnea, hypotension and pulmonary aspiration of gastric contents.[15]

Indications for Laparoscopic Oocyte Retrieval

There are a few indications of laparoscopic egg collection described in literature. These are in women with Mullerian anomalies, cervical cancer, and in young adolescents undergoing fertility preservation, where laparoscopic access was found to be technically easier and clinically safer. However, laparoscopic egg collection by a suitably trained person can be considered in any scenario where ovarian access either by transabdominal or transvaginal guidance is deemed difficult, as discussed later in a study conducted by the authors.

Mayer-Rokitansky-Küster-Hauser syndrome (MRKHS) is a congenital disorder characterized by the absence of Mullerian structures including the fallopian tubes,

uterus, and the internal portion of the vagina.[16] Patients with this condition provide a challenge in oocyte retrieval.[16] Some patients have a surgically created vagina, so an US-guided transvaginal approach may be considered first. Sometimes due to the absence of vaginal elasticity and relaxation in the neovagina and high lateral location of the ovaries, this approach may be technically difficult.[17] The second option is transabdominal US-guided oocyte retrieval. This is limited in patients with central obesity and poor visibility of ovaries due to overlying bowel loops.[18] A further option for oocyte retrieval in such cases is laparoscopy.

Management of patients with MRKHS includes vaginoplasty as well as discussion of fertility options. Laparoscopic oocyte collection and vaginoplasty may be combined into a single procedure to minimize surgical invasiveness.[18] This procedure is particularly useful in patients where transvaginal egg retrieval would be technically challenging when the ovaries are located laterally in the pelvis or in those with pelvic kidneys or ectopic ovaries.[18] Early cryopreservation of oocytes in patients diagnosed with MRKHS may reduce some of the psychological distress compared with delaying retrieval.[18]

In patients with cervical cancer, transvaginal egg collection provides a challenge due to the risk of bleeding and intra-abdominal seeding of cancer cells. It is likely that laparoscopic oocyte retrieval reduces this risk by preventing the egg collection needle from traversing malignant tissue.[19,20]

As a result of improved cancer survival rates, there is an increased need to think about the long-term complications including impacts of treatment on fertility. In young cancer patients, more are reaching child-bearing age. Both chemotherapy and radiotherapy can destroy ovarian tissue, increasing the risk of premature ovarian insufficiency.[21,22] Radiation can also cause uterine adhesions which can impair fertility.[22] It has been estimated that 25% of cancer survivors are women of reproductive age who may wish to conceive.[23] There are various options for fertility preservation including embryo or oocyte cryopreservation and ovarian transposition. Embryo cryopreservation is not ethical in minors and as many are prepubertal, ovarian cryopreservation through collection of ovarian tissue at laparoscopy is the only option for fertility preservation in young adults.[21,23] It can be carried out at any point in a cycle and therefore does not delay cancer treatment.

Diagnostic laparoscopy is an important step in the investigation of some infertile women. Previously, this was done in all women but is now only recommended in women with comorbidities such as pelvic inflammatory disease, previous ectopic pregnancy, or endometriosis.[24] Laparoscopic oocyte retrieval combined with diagnostic laparoscopy allowed investigation of the cause of infertility, and often treatment at laparoscopy to improve conception rate in the current as well as subsequent cycles.[25] This was particularly relevant in optimizing the pelvic anatomy and tubal health, for example, fulguration of endometriosis or adhesiolysis, in relation to treatments like GIFT (gamete intrafallopian transfer) or ZIFT (zygote intrafallopian transfer) in the nineties' decade.[26] It has also been shown that the pregnancy rate achieved with a combined diagnostic laparoscopy and oocyte retrieval was similar to that of patients whose procedures were carried out separately.[27] However, this approach was criticized by other authors who felt that there was insufficient evidence and significant risk in combining IVF with a diagnostic laparoscopic assessment.[28] Laparoscopic oocyte retrieval and ovarian electrocautery for polycystic ovary syndrome (PCOS) have been reported during a single procedure, providing treatment and ART.[29] In modern clinical practice, with IVF as a strong answer to almost every infertility question, the role of laparoscopic surgery itself is limited to certain strict indications.[30] Therefore, diagnostic laparoscopy is indeed a rarity in combination with laparoscopic oocyte retrieval.

Review of Laparoscopic Egg Retrieval in the Literature

An extensive literature search for this article was accomplished, using Cochrane, Embase, and Medline searches to extract relevant articles dating back to 1978, the year of birth of the first IVF baby in the world. The authors then selected articles relevant to the specific areas covered in this review article.

Wood *et al.* (1999) aimed to find out the best method of oocyte retrieval in patients with MRKHS.[17] Twelve patients underwent a total of 49 treatment cycles. In nine of these cycles, laparoscopy was required for egg retrieval which included seven cycles in those who had undergone surgical neovagina construction. They found a statistically significant reduction in ability to conduct transvaginal egg retrieval in patients with a neovagina.[17] Raju *et al.* (2006) describe a patient with Mullerian agenesis and primary infertility who underwent laparoscopic oocyte retrieval and subsequent IVF.[16]

Eleven oocytes were retrieved by laparoscopy and 2 weeks after embryo transfer into a gestational carrier, a live pregnancy was confirmed.[16] Eleven patients underwent combined laparoscopic oocyte collection and vaginoplasty for MRKHS without complication.[18] A mean of 8.8 mature oocytes were retrieved and cryopreserved. This combined procedure reduced total operating time, invasiveness, and the need for patients to undergo future egg collection.[18]

Nakagawa *et al.* (2009) discussed a patient with ovarian malposition causing primary infertility.[31] The ovaries could not be detected via transvaginal USG and were confirmed to be in the upper pelvic cavity, attached to the area containing the common iliac vessels. Due to the dangerous position of the ovaries, neither transvaginal nor transabdominal US-guided retrieval could be conducted, so laparoscopic-assisted transabdominal retrieval was performed. Following the third oocyte retrieval, a pregnancy was achieved.[31]

Nagele *et al.* (2002) reported a case of a patient with clomiphene-resistant PCOS who underwent oocyte collection and ovarian electrocautery.[30] Sixteen immature oocytes were retrieved, seven fertilized and three embryos transferred, resulting in a singleton pregnancy and birth. If pregnancy was not achieved via IVF, as electrocautery was conducted at laparoscopy, this provided a chance of natural conception in later cycles.[27]

Ghourab and Lavery (2016) evaluated the outcomes of 15 patients with cervical cancer who underwent 16 cycles of oocyte and/or embryo cryopreservation.[32] Five patients had laparoscopic oocyte retrieval (mean number of oocytes collected = 6) and 10 patients had transvaginal oocyte retrieval (mean number of oocytes collected = 15) including three with a cervical mass (a novel procedure). They reported that transvaginal oocyte retrieval in the presence of a cervical mass could be performed safely with a higher number of oocytes retrieved compared to laparoscopy. However, sample size was small and no conclusions could be made.

Lotz *et al.* (2020) conducted a study of 53 prepubertal and adolescent girls who underwent ovarian tissue cryopreservation due to malignancy or benign disease with a high risk of causing premature ovarian insufficiency.[33] Forty-five patients underwent this during laparoscopy and eight during laparotomy. In 52 cases, removal was without complication. However, in one case a further laparoscopy was needed due to postoperative bleeding.

Authors' Experience of Laparoscopic Oocyte Retrieval

In a retrospective case series, in a tertiary university hospital in the UK, between 2015 and 2018, six women had seven laparoscopic oocyte retrievals, among a total of 4925 IVF cycles performed in the same time period.[34] Indications for the laparoscopic technique included fertility preservation in those with myelodysplasia with an intact hymen and cervical cancer. Other indications were transvaginally inaccessible ovaries caused by MRKHS, fibroids, and unicornuate uterus.

Out of these seven women, except for a lady with multiple fibroid uterus, all others had follicular monitoring by transvaginal USG. When these women were assessed preprocedure, ovarian access and visibility by transabdominal USG was deemed difficult for egg collection and therefore decided for laparoscopy. The two women with Mullerian anomalies (one had MRKH syndrome and the other had unicornuate uterus) had high ovaries above the pelvis; the teenager undergoing fertility preservation for myelodysplasia had an intact hymen. There were two women with cervical cancer, one with a 4 cm cervical mass at Stage IIB with significant risk of disease dissemination, and other lady had only one ovary which responded to stimulation, very high in the pelvis, with poor visualization on scan. Finally, there was a patient with multiple fibroid uterus who had had a previous US-guided transmyometrial difficult oocyte retrieval with poor yield, who then underwent transvaginal follicular monitoring but had a laparoscopic egg collection with adhesiolysis, to enable easier access to the ovaries, and went on to have a live birth.

Oocyte recovery was successful in all seven cases with a mean of 5.57 oocytes retrieved and an 80% fertilization rate in the three patients who had subsequent IVF/intracytoplasmic sperm injection. Three of these women fell pregnant, among which, two had successful live births.[31]

These cases were performed in the Main Gynecology Theatres at Saint Mary's Hospital, Manchester, located in a different building of the IVF unit within the same campus. This necessitated transportation of oocytes in follicular fluid to the IVF lab, in compliance with the HFEA (Human Fertilization and Embryology Authority, UK) regulations. Depending on the surgeon's choice, standard laparoscopic entry techniques were employed, varying between open (Hassan's technique) and closed

techniques, through an intraumbilical incision. A single side port was placed along the left midclavicular line below the level of the umbilicus, using conventional techniques, for stabilizing the ovary with an atraumatic grasper. A third smaller incision was done suprapubically or along the right midclavicular line close to the ovaries for allowing entry of the oocyte retrieval needle. A standard 17–18G Wallace single lumen needle was directly introduced into the peritoneal cavity under vision and connected to test tubes under suction pressures of 110–120 mm Hg. Follicles were aspirated under direct vision and the fluid in individual test tubes was placed in a portable incubator maintained at 37^0C before transporting them to the IVF lab by an embryologist attending the theatre. The eggs were then retrieved from the follicular fluid under the laminar flow and microscope in the IVF lab. This lag between the egg retrieval procedure and confirmation of the final egg count was one of the main disadvantages of the procedure, as felt by the authors, as it was not possible to know whether the number of follicles aspirated corresponded to the oocyte numbers, till much later. Additional drawbacks of this technique were difficulty in assessing deeper follicles within the ovaries at risk of inadvertent puncture or incomplete drainage, as well as difficulty in estimating when a follicle was completely drained, due to the lack of precise ultrasonographic cross-sectional view and depth perception.

CONCLUSIONS AND WIDER IMPLICATIONS

In summary, although there is a paucity of studies stating the extent of use or incidence of laparoscopic oocyte retrieval in any ART program, this technique should be considered as an effective and safe alternative to difficult transvaginal recovery and may enable patients with specific clinical backgrounds to achieve pregnancy. The indications for this method of egg collection include those with Mullerian agenesis, ovarian malposition, severe cervical disease including cancer, in those undergoing diagnostic or therapeutic laparoscopy and wanting fertility treatment, and in those wishing for fertility preservation including tissue cryopreservation in prepubertal and adolescent females. There are risks of laparoscopic surgery and these should be weighed against the benefits, and clear information about the advantages and disadvantages of laparoscopy in the specific context of each patient's unique clinical scenario should be discussed in detail. Larger, prospectively designed randomized controlled studies are required to support this technique as a standard alternative to transvaginal ultrasonography.

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COMMENTARY

Reinventing laparoscopic oocyte retrieval: Need of the day

The technique of *in vitro* fertilization started with laparoscopic oocyte pick-up (L-OPU) and was almost completely replaced by the transvaginal ultrasound–guided ovum retrieval (TUR). The historic scientific papers from the 1980s are full of papers comparing the L-OPU and TUR, clearly demonstrating the superiority of TUR. The authors have raised a very important issue regarding the role of L-OPU in modern practice. Now is the time to find instead of competitive the complementary role of L-OPU and other unconventional methods which may be required today. OPU from ovaries that are inaccessible through transvaginal route, such as in Mullerian agenesis, after ovarian transposition, at time of cancer surgery, after ovarian tissue cryopreservation, congenital high position of ovaries, and similar such situations, the only

option remains L-OPU or transabdominal ultrasound (TAUSG)-guided procedure.

The paucity of the cases requiring L-OPU makes this procedure an "out of reach option" for many, and lack of knowledge of technique, need to improvise the laparoscopy operation theaters for L-OPU, and safe transport of aspirated follicular fluid in optimal conditions to IVF laboratory are some of the reasons. Besides other technical reasons, specific case-related difficulties at L-OPU may be there, e.g., adhesions making ovaries inaccessible even at laparoscopy. In comparative studies published in the 1980s, the overall fertilization and success rates were lower with L-OPU. These factors need to be considered before a final decision for L-OPU is taken.

There is an urgent need of reporting with detailed methodology of such cases in the literature to give more confidence to modern generation of fertility specialists.

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