For ovarian malignancies, oocyte retrieval is better out of the body

Each year, nearly 100,000 women in the United States are diagnosed with gynecologic malignancies. According to Surveillance, Epidemiology and End Results (SEER) statistics, approximately 12% of ovarian malignancies affect reproductive-age women (1). Although fertility-sparing surgery is an option for women with ovarian cancer with early-stage disease confined to one ovary, the standard treatment typically includes hysterectomy, bilateral salpingo-oophorectomy, staging with pelvic and para-aortic lymphadenectomy, and adjuvant chemotherapy in most cases (2). For young women who desire future fertility, the most common fertility preservation modalities include embryo or oocyte cryopreservation. However, in cases of ovarian malignancy, conventional controlled ovarian hyperstimulation followed by transvaginal follicular aspiration presents the risk of introducing cancer cells into the peritoneal cavity, potentially upstaging the disease and negatively impacting treatment and prognosis.

The video case report and review by Pereira et al. (3) demonstrates a novel technique to circumvent the obvious risks involved with oocyte aspiration in patients with presumed ovarian malignancies (3). The video shows that ex vivo (also referred to as extracorporeal) retrieval of mature oocytes after oophorectomy can be used with malignant ovarian tumors in cases when follicular puncture by traditional transvaginal oocyte retrieval techniques may cause iatrogenic tumor seeding and upstaging. In the case, a 37-year-old nulliparous woman with a known *BRCA1* mutation, a complex right adnexal mass, and an elevated CA-125 level undergoes luteal phase controlled ovarian hyperstimulation with gonadotropins and letrozole. Ovarian stimulation was initiated 12 days before the scheduled surgical staging procedure with the ovulatory trigger timed 34 hours before the planned surgical start time. Exploratory laparotomy with bilateral oophorectomy was performed, the ovaries were placed in dishes with warm saline, and oocyte retrieval was performed with a 30-cm, 16-gauge oocyte aspiration needle connected to wall suction. Enlarged follicles were punctured and aspirated under direct visualization. Follicular fluid, collected in six oocyte collection tubes, was then placed on a heating block and transferred to the embryology lab. The authors report a maximum time from oophorectomy to ex vivo oocyte retrieval start of 18 minutes, procedure time of 22 minutes, and transport time to the laboratory of 13 minutes. A total of seven mature oocytes were retrieved and vitrified. The patient, who had been counseled regarding the need for a gestational carrier in the future, also underwent total hysterectomy and surgical staging by gynecologic oncology.

While this is not the first reported case of ex vivo oocyte retrieval, this case is noteworthy as this is the first video describing the technique. Fatemi et al. (2010) first reported ex vivo retrieval of mature oocytes after controlled ovarian hyperstimulation in a patient who underwent oophorectomy and laparotomy. The case involved a patient with a history of borderline adenocarcinoma of the ovary status after a prior unilateral oophorectomy with ultrasound showing recurrent disease (4). Bocca et al. (2011) then reported an extracorporeal mature oocyte harvest after a laparoscopic oophorectomy in a patient with recurrent borderline tumor in a previously conserved ovary (5). In clinical scenarios of ovarian malignancy, the benefits of fertility preservation must be balanced with the risks of potential spread of malignancy. Extracorporeal oocyte retrieval offers the benefit of eliminating the risk of cancer cell spillage associated with standard transvaginal oocyte retrieval.

The authors highlight the fact that conservative fertility-sparing surgery is increasingly being used for women with ovarian malignancies of reproductive age who desire future fertility. Fertility-sparing surgery is limited to women with malignancy localized to one ovary at an early stage. Unfortunately, at the time of diagnosis of an adnexal mass on imaging, it is difficult to determine with certainty whether a woman will be a candidate for fertility-sparing surgery. Given the risks of seeding the peritoneal cavity with malignant cells and subsequent upstaging, oocyte retrieval on a woman with an adnexal mass presents risks that can be averted by an ex vivo oocyte retrieval technique. For the patient described in the case presentation, conservative surgery was not a reasonable option given her *BRCA1* mutation and increased likelihood of invasive malignancy. Aside from patients with *BRCA* mutations, other candidates for extracorporeal oocyte retrieval include those with a history of a prior ovarian malignancy status post conservative surgery with a new adnexal mass on the remaining ovary. Additionally, any woman with a suspicious ovarian mass should be considered for ex vivo oocyte retrieval given the unknown risk of whether the contralateral ovary is involved.

Unfortunately, for most patients with suspected ovarian malignancies, fertility centers are likely not equipped to easily perform extracorporeal oocyte retrieval. Despite the benefits of extracorporeal oocyte retrieval in terms of safety, moving forward with extracorporeal oocyte retrieval after oophorectomy is fraught with multiple logistical obstacles at most centers. Challenges include the timing, procedural aspects, location, and transport. Timing of an ex vivo oocyte retrieval will depend on when the surgical case is scheduled. While transvaginal oocyte retrievals are typically scheduled 2 days in advance when follicular size is optimal, that is usually not an option at hospital-based surgical centers where gynecologic oncology surgeries are performed. Therefore, time of the surgery and the retrieval must be carefully coordinated. Since it is not possible to perfectly predict the day of the trigger, the retrieval may occur a day sooner or later than would be performed under conventional circumstances. The oocyte aspiration technique requires careful planning regarding where and how the procedure will be performed. Many reproductive specialists may be inexperienced with the technique required to aspirate follicles ex vivo under direct visualization. If the oophorectomy is performed in a hospital and the lab is in a satellite location, the retrieval

will need to take place in the hospital. As gynecologic oncologists often require frozen pathology sections during this case, this must be taken into consideration as well. Performing the oocyte retrieval in a timely manner and transporting the follicular fluid to the embryology lab are also key. With many embryology labs located outside the hospital setting, there may be additional time delay in transport.

Regardless of logistical challenges, extracorporeal oocyte retrieval is the safest option currently available to allow for oocyte or embryo cryopreservation for women with suspected ovarian malignancies. The inconvenience of these challenges is outweighed by avoiding risk introduced by follicular puncture in terms of seeding cancer cells into the peritoneal cavity. Fertility centers that manage fertility preservation patients with suspected ovarian malignancies should use this video as a motivation to prioritize making ex vivo oocyte retrieval available for suitable patients.

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REFERENCES

1. National Cancer Institute. SEER cancer statistics review, 1975–2014. Bethesda, MD: National Cancer Institute. 2017. Available at: https://seer.cancer.gov/csr/1975_2014/. Accessed May 30, 2017.
2. Chan JL, Wang ET. Oncofertility for women with gynecologic malignancies. Gynecol Oncol 2017;144:631–6.
3. Pereira N, Hubschmann AG, Lekovich JP, Schattman GL, Rosenwaks Z. Ex vivo retrieval and cryopreservation of oocytes for fertility preservation in a *BRCA1* mutation carrier with ovarian cancer. Fertil Steril 2017;108:357–60.
4. Fatemi HM, Kyrou D, Al-Azemi M, Stoop D, De Sutter P, Bourgain C, et al. Ex-vivo oocyte retrieval for fertility preservation. Fertil Steril 2011;95:1787.e15–7.
5. Bocca S, Dedmond D, Jones E, Stadtmauer L, Oehninger S. Successful extracorporeal mature oocyte harvesting after laparoscopic oophorectomy following controlled ovarian hyperstimulation for the purpose of fertility preservation in a patient with borderline ovarian tumor. J Assist Reprod Genet 2011;28:771–2.