

Pregnancy with vitrified oocytes after fertility sparing surgery in a patient with fallopian tube cancer and a BRCA2 mutation: A case report and literature review

GUGLIELMO STABILE¹, STEFANIA CICOGNA², GABRIELLA ZITO², ANNA VIDO³,
ANDREA ROMANO⁴, ALESSANDRO MANGOGNA², LUIGI NAPPI¹ and GIUSEPPE RICCI^{2,3}

¹Department of Medical and Surgical Sciences, Institute of Obstetrics and Gynecology, University of Foggia, Foggia I-71121, Italy;

²Institute for Maternal and Child Health IRCCS (Institute of Scientific Hospitalization and Treatment) 'Burlo Garofolo',

Trieste I-34100, Italy; ³Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste I-34100, Italy;

⁴Unit of Anatomy and Histology Pathology, Trieste University Hospital (Giuliano Isontina University Health Authority), Trieste I-34129, Italy

Received June 2, 2025; Accepted September 16, 2025

DOI: 10.3892/ol.2025.15417

Abstract. High-grade carcinomas affecting the ovary or peritoneum may originate from the epithelium of the fallopian tubes. Whilst gynecological cancers are more frequent in post-menopausal patients, 12.1% of ovarian malignancies are diagnosed in patients of childbearing age, aged <45 years. There is not enough data to provide an accurate estimate on the incidence of relapse, the chance of pregnancy and outcomes of assisted reproduction and fertility-sparing surgery techniques in young patients with ovarian cancer. Moreover, there is currently a lack of data regarding fertility preservation techniques for patients with cancer of the fallopian tubes. To the best of our knowledge, the present report describes the first live newborn birth using vitrified oocytes retrieved before fertility-sparing surgery for primary fallopian tube cancer (stage IC1) in a patient with a BRCA2 mutation. Furthermore, a narrative review of literature from 2000-2024 from several online databases was performed to identify articles involving patients with fallopian tube cancer and BRCA mutations, who underwent fertility preservation with vitrified oocytes and fertility-sparing surgery. A total of 44 manuscripts were retrieved, with only two articles reporting data on pregnancy with vitrified oocytes after fertility-sparing surgery, and 3 cases included. Whilst more research is required for assisted reproductive technology and ovarian cancer, and for the elucidation of the role of BRCA mutations on fertility, the present report aims to provide impetus to further research in this field.

Introduction

Tube-ovarian cancer (OC) ranks eighth among malignant neoplasms affecting females overall; however, it is the fourth leading cancer in terms of mortality in patients of childbearing age of <44 years (1,2). Moreover, the incidence markedly increases in patients carrying BRCA1/2 mutations (BRCA1mut and BRCA2mut), in whom the lifetime breast cancer risk is >60%, with an OC risk of 40-60 and 15-30% for those with BRCA1mut and BRCA2mut, respectively (3-5). Inflammation has been implicated in ovarian carcinogenesis and a history of pelvic inflammatory disease or endometriosis is associated with an increased risk of epithelial OC (6-8).

Fertility-sparing surgery (FSS) can be proposed only for patients with selected histotypes of OC at initial stages apparently confined to the ovary, consisting of unilateral salpingo-oophorectomy and peritoneal and lymph-node surgical staging according to the histopathology of the primary tumor, and preferably with a minimally invasive surgical approach (9,10). However, it is unclear what the ideal FSS treatment is in case of primary fallopian tube carcinoma, as there are no data regarding ovarian preservation following salpingectomy, to the best of our knowledge. Furthermore, available data regarding fertility preservation (FP) in OC with oocytes retrieval are associated with borderline ovarian tumors (BOTs) and non-epithelial ovarian tumors, whilst there are no data regarding the safety of FP with oocyte retrieval in case of invasive tube-ovarian epithelial carcinoma (11). Additionally, the FP options available to patients with OC are dependent on staging, histological type, location and spread; and the options consist of oocytes or embryos cryopreservation. FSS should be an option in patients with early-stage OC, followed by close follow-up (1).

There are few retrospective studies and case reports regarding assisted reproductive techniques (ART) in young patients with OC (12,13). Moreover, there is not enough data to provide an accurate estimate on the incidence of relapse, the actual chance of pregnancy and its outcome. There is also currently no data regarding FP techniques for patients with Fallopian tubes cancer, to the best of our knowledge.

Correspondence to: Dr Guglielmo Stabile, Department of Medical and Surgical Sciences, Institute of Obstetrics and Gynecology, University of Foggia, 1 Viale Luigi Pinto, Foggia I-71121, Italy
E-mail: guglielmost@gmail.com

Key words: fallopian tube cancer, fertility sparing surgery, pregnancy, vitrified oocytes, BRCA mutation

The present report describes the first case, to the best of our knowledge, of a pregnancy with a healthy newborn using vitrified oocytes after FSS in a young patient with a BRCA-2 mutation and invasive Fallopian tube cancer [International Federation of Gynecology and Obstetrics (FIGO) stage IC1] (14).

Case report

In September 2019, a 32-year-old female patient was referred to Department of Obstetrics and Gynecology at the Institute for Maternal and Child Health IRCCS 'Burlo Garofolo' (Trieste, Italy) by an attending gynecologist due to suspected bilateral hydrosalpinx identified with vaginal ultrasound. The patient was actively seeking pregnancy and waiting to start ART. The patient was nulliparous and did not report a family history of gynecological cancers or other pathologies. The patient had no prior history of symptoms indicative of pelvic inflammatory disease or sexually transmitted infections, and denied experiencing dysmenorrhea, dyspareunia or chronic pelvic pain. The patient had a body mass index (BMI) of 30 kg/m² and was a smoker.

During pre-operative checks, a diagnostic work-up was performed, in which a second level transvaginal ultrasound confirmed the hypothesis of a left 22x47 mm hydrosalpinx. Ovarian tumor markers CA125, carcinoembryonic antigen, CA 19.9 and α -fetoprotein were negative. A total of 5 months later, the patient underwent a laparoscopic bilateral salpingectomy, in which laparoscopic exploration showed both tubes congested and enlarged, especially on the left side, attached to the ipsilateral ovarian fossa, the posterior wall of the uterus and the omentum. The right ovary showed an unilocular neof ormation of 2 cm, with a tight-elastic consistency. The left ovary was regular. There were no signs of peritoneal carcinomatosis or suspicious peritoneal nodularity. There was no pelvic or aortic lymph node enlargement. During mobilization, a surgical spillage of the left tube occurred, with the release of purulent, thick and brownish liquid that was promptly aspirated (data not shown).

Histological examination revealed a primary endometrioid carcinoma of the Fallopian tube, G2 (Fig. 1). Tissue samples were fixed in 4% formaldehyde at room temperature for 24 h, embedded in paraffin, sectioned at 4 μ m, and stained with hematoxylin and eosin (H&E) using the HistoCore SPECTRA ST automated stainer (Leica Biosystems) at room temperature, for ~1 h. Light microscopic evaluation was carried out with the Aperio AT2 system (Leica Biosystems).

Immunohistochemistry (IHC) demonstrated p53 positivity (Fig. 2) as well as positive staining for ER and PR receptors. Representative IHC images are not shown (the official pathology report is available upon request). Tissue preparation followed the same fixation and embedding protocol as aforementioned. All IHC procedures were performed using the BenchMark ULTRA system (Roche Tissue Diagnostics), strictly following the manufacturer's instructions. For p53 staining, the CONFIRM anti-p53 (DO-7) Primary Antibody (REF 800-2912, Ventana, Roche) was used together with the OptiView DAB IHC Detection Kit (REF 760-700, Ventana, Roche). Estrogen receptor (ER) expression was assessed using the CONFIRM anti-ER (SP1) Rabbit Monoclonal

Primary Antibody (REF 790-4324, Ventana, Roche), while progesterone receptor (PR) staining was performed with the CONFIRM anti-PR (1E2) Rabbit Monoclonal Primary Antibody (cat. no. 790-2223, Ventana, Roche). Detection of ER and PR was achieved using the ultraView Universal DAB Detection Kit (REF 760-500, Ventana, Roche).

(Immunohistochemistry images of positive estrogen and progesterone are not presented; however, an official report is available on request.)

After the diagnosis of Fallopian tube cancer, the patient was counselled about surgical restaging. Preoperative work-up included chest-abdomen-pelvis PET/CT that was normal, and a hysteroscopic endometrial biopsy that was negative for neoplasia.

Before surgical restaging, the patient was referred to an oncofertility consultant, considering the young age and the strong reproductive desire of the patient. The patient underwent oocyte preservation in July 2020. Anti-Müllerian hormone levels were 2.08 ng/ml and ovarian stimulation was performed with 5 mg/day letrozole + recombinant follicle-stimulating hormone (rFSH) from the second day of the menstrual cycle. On day 5 of rFSH stimulation, a gonadotropin-releasing hormone (GnRH) antagonist was administered to prevent a premature luteinizing hormone surge and discontinued on the day of the trigger, which was achieved using a GnRH agonist, triptorelin acetate (0.2 mg). After ovarian pick-up, 12 oocytes were cryopreserved.

In September 2020, the patient underwent laparoscopic surgical restaging with a bilateral ovariectomy, systematic pelvic lymphadenectomy, total omentectomy, multiple peritoneal biopsies and peritoneal washing. Histological examination of all the specimens was negative, and a cytological examination of peritoneal washing did not show any cells suggestive of malignancy. The final stage was IC1 (FIGO 2014). Furthermore, post-surgery genetic counseling and next-generation sequencing revealed a germinal BRCA-2 mutation in December 2020.

The present case was presented at a gynecological oncology multidisciplinary meeting, and based on the histopathological characteristics and tumor stage, two potential management options were proposed: Adjuvant chemotherapy or close surveillance. The patient expressed a strong preference against chemotherapy and opted for a closely monitored gynecological and breast follow-up approach. This included gynecological evaluation with pelvic ultrasonography performed every 4 months, in addition to an annual breast ultrasound examination.

After 3 years of negative clinical and radiological follow-up, the patient decided to undergo embryo transfer. In July 2023, an oocyte intra cytoplasmic sperm injection with partner semen was performed, and a single blastocyst was transferred into the uterus of the patient with success. Adequate endometrial preparation was performed with oral administration of estradiol valerate (4 mg administered on cycle days 1-3, then a dose increase to 6 mg per day on days 10-13). After ultrasound revealed a regular endometrium thickness, progesterone was orally administered for adequate luteal phase support. A total of 11 days after embryo transfer, a positive serum pregnancy test was achieved. Therefore, the patient was administered oral estradiol and progesterone until 12 weeks.

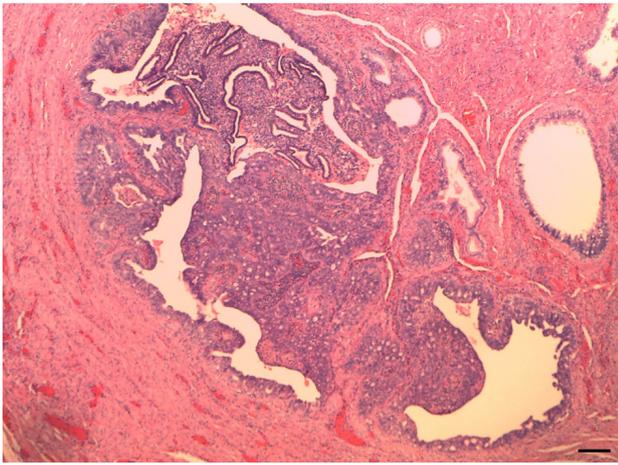


Figure 1. Histopathological image of the primary endometrioid carcinoma of the fallopian tube, grade 2, stained with hematoxylin and eosin. The neoplastic proliferation displays a predominantly glandular architecture with irregular, angulated glands and cribriform structures embedded in a moderately cellular stroma. There is focal glandular crowding and loss of normal tubal architecture, consistent with grade 2 differentiation. Magnification, x50. Scale bar, 200 μm .

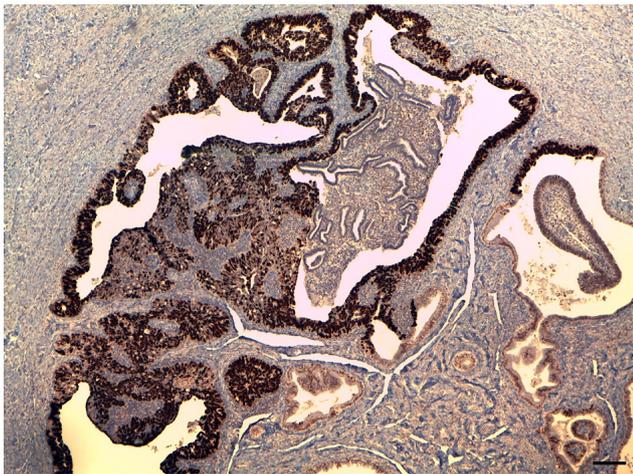


Figure 2. Immunohistochemical staining for p53 in the present case of primary endometrioid carcinoma of the fallopian tube. The carcinoma shows overexpression of p53 with intense staining in virtually all tumor cell nuclei, with internal control (stroma and normal endometrial glands) showing a nuclear wild-type pattern. Magnification, x50. Scale bar, 200 μm .

Pregnancy was complicated by early fetal growth restriction, for which the patient underwent amniocentesis. This was negative with a normal karyotype 46XY at 18 weeks of gestation. At 30 weeks of gestation, the patient developed preeclampsia and was hospitalized for close monitoring with ultrasound and cardiotocography. Due to a worsening of flowmetry, a caesarean section was performed at 33 weeks and 5 days, with the birth of a healthy male newborn of 1,152 g and Apgar of 5 and 8 at 1 and 5 min, respectively, an arterial pH of 7.33 and base excess, 5.4. The baby was hospitalized for 1 month in neonatal intensive care due to the gestational age and weight. The patient was discharged after 1 week with well-controlled blood pressure without puerperal complications.

Following delivery, the patient regularly continued gynecological and breast surveillance, consisting of clinical evaluation and pelvic ultrasound every 6 months, and an annual breast ultrasound. The most recent follow up was performed in February 2025, in which the patient was asymptomatic, the gynecological examination unremarkable and imaging studies were within normal limits. The patient also underwent a recent breast assessment, which was regular. The patient remains on a scheduled follow up.

Literature review

A narrative review was performed by searching the PubMed (pubmed.ncbi.nlm.nih.gov/), Scopus (scopus.com/), Web of Science (<https://www.webofscience.com/wos/>) and Google Scholar (<https://scholar.google.com/>) databases for articles published between 2000 to November 2024 involving patients with fallopian tubes cancer and BRCA mutations that underwent a FP with vitrified oocytes and FSS. Articles not relevant to the present review or not written in English were excluded, as well as cases with multiple tumors and those with patients who underwent *ex vivo* oocyte retrieval or other types of preservation techniques.

The following keywords were used for the search: ‘Fallopian tubes Cancer’, ‘BRCA mutation’, ‘Fertility sparing treatment’ and ‘Fertility preservation’. Different combinations of the terms were used. Due to the rarity of this pathology and procedure, numerous case reports or case series of patients with OC that underwent a fertility sparing treatment with vitrified oocytes were identified, but no cases of fallopian tube cancer. For this reason, the data is presented in a descriptive manner with the aim to delve deeper into the topic through parallels with OC.

A total of 44 articles were identified through the search of databases and references of the retrieved articles. However, only two articles reported data on pregnancy with vitrified oocytes after FSS, and they included 3 cases (15,16). These articles included a case report on a birth of a healthy newborn using vitrified-warmed oocytes in a young patient with invasive mucinous ovarian carcinoma (stage IC) and two cases in two patients with BOTs. All the pregnancies reached full term with healthy babies, without disease recurrence during pregnancy and in the immediate postpartum period (Table I).

In case 1, the 28-year-old patient underwent two cycles of ovarian stimulation, and 14 oocytes were vitrified before FSS. A total of 1 year later, a transfer of two embryos was performed, and 18 days after the transfer, the patient underwent a laparotomy as a right cornual ectopic pregnancy in the uterus was diagnosed. A wedge resection was performed, and an elective Caesarean section was performed at week 38 of gestation, resulting in the birth of a healthy male newborn, weighing 2,650 g.

In case 2, the two patients were 36 and 26 years old, respectively, with BOTs. A total of 15 and 16 oocytes were retrieved, respectively, and after 14 and 12 months, respectively, embryo transfer was performed with two embryos. However, in this article, the course of the pregnancies, the mode of delivery, and the sex and birth weight of the newborns were not reported.

Discussion

Pregnancy following gynecological cancer is an option that has only been considered and offered to patients in recent

Table I. Outcomes and characteristics of patients in the literature.

First author/s, year	Age at diag- nosis, years	Site	Histo- type	FIGO 2014 stage	BRCA mutation	Surgical treatment	Number of oocytes	ART technique	Number of embryos transferred	Age at pregnancy, years	Type of delivery	Gesta- tional age at delivery, weeks	Compli- cations (Refs.)
Alvarez <i>et al.</i> , 2014	28	Ovaries	Invasive mucinous ovarian carcinoma	IC	/	Bilateral salpingo- oophorec- tomy, appende- ctomy, pelvic and aortic lymphade- nectomy, and- omentectomy	14	ICSI	2	29	Elective Caesarian section	38	Cornual ectopic pregnancy of 1 embryo after 18 days (15)
Mayeur <i>et al.</i> , 2021	36	Ovaries	Borderline ovarian cancer	/	/	/	15	/	2	37	/	/	(16)
	26	Ovaries	Borderline ovarian cancer	/	/	/	16	/	2	27	/	/	/
Present case	32	Tubes	Endome- trioid G2	IC1	Yes	Bilateral salpingo- oophorec- tomy, omen- tectomy, bilateral pelvic lymphade- nectomy, peritoneal biopsy and peritoneal washing	12	ICSI	1	34	Urgent Caesarian section	33 + 5	Early FGR, precla- mpsia and flowmetry anomalies -

FIGO, International Federation of Gynecology and Obstetrics; ART, assisted reproductive techniques; ICSI, Intra Cytoplasmatic Sperm Injection; FGR, fetal growth restriction; /, not specified.

years (17). For this reason, very little data is available regarding ART after gynecological cancer, particularly after FSS for OC.

According to international guidelines on ovarian and fallopian tube cancer, conservative surgery can be proposed in selected patients who are strongly motivated to preserve fertility, and according to the histotype and stage disease (18,19). FSS is feasible in patients with BOTs, non-epithelial tumors and low-grade epithelial tumors (serous, endometrioid or mucinous expansile sub-type) stage IA and selected IC1 stages (20). Moreover, FSS in OC presents an acceptable overall recurrence rate of ~11%, comparable with patients treated with radical surgery at initial stages (21). Following surgery, spontaneous pregnancy seeking is recommended, although there is no established timing. The spontaneous pregnancy rate following FSS for OC is high at ~84% (22).

Conversely, data regarding ART in patients with OC are extremely limited. Adequate evidence does not currently exist to support the oncologic safety or harmfulness of ovarian stimulation by pituitary gonadotropins after FSS for OC (23). In particular, an increased rate of BOTs recurrence after stimulation is reported, ranging from 19.4-27.7%, but without an impact on mortality (24). Nevertheless, ovarian stimulation after FSS for BOTs could be contraindicated in certain high-risk cases, such as the presence of peritoneal implants, a micropapillary pattern, the presence of microinvasion and in cases of recurrence (25). Moreover, regarding ART after invasive epithelial OC, there is limited data from case reports and case series, which provide conflicting information (26,27).

In patients with cancer, options for preservation of fertility before gonadotoxic treatments include the following: Cryopreservation (oocytes or embryos), ovarian transposition (if pelvic irradiation is planned), pharmacological protection with GnRH analogous and ovarian tissue cryopreservation (OTC), and transplantation. OTC or ovarian tissue transposition (OTT) are options for patients with certain type of cancers (such as hematological cancers); however, OTT cannot be considered for patients with fallopian tube cancer (28-30). Moreover, oocyte/embryo cryopreservation is recommended in oncological patients if the initiation of chemotherapy can be delayed. Due to the fewer number of oocytes expected to be retrieved and limitations associated with preimplantation genetic diagnosis (31,32), two consecutive stimulations should be considered for those patients when feasible (31). However, for patients with cancer who require radical surgery and have limited time available for FP, controlled ovarian stimulation (COS) is not feasible. In these cases, immature oocyte collection without COS, followed by *in vitro* maturation (IVM) and oocyte freezing, represents an alternative option. This technique has been used in conjunction with ovarian tissue freezing. IVM is proposed as an additional strategy to enhance the effectiveness of ovarian tissue freezing. As antral follicles are devoid of cancer cell infiltration, oocytes retrieved from these follicles provide a reliable option for patients with cancer with a high risk of ovarian involvement or *in situ* OC. This method offers a potential strategy for FP in patients with recurrent disease, without the risk of cancer cell spillage associated with standard transvaginal oocyte retrieval (33).

Furthermore, there are issues associated with the fertility of patients with a BRCA2 mutation. According to certain studies, BRCA2 mutation-positive patients have lower levels of anti-Müllerian hormone compared with patients who

are BRCA-negative and BRCA1 mutation-positive (34-37). This may reflect a diminished oocyte reserve in these patients (34-37). Among the patients who tried to conceive, infertility was observed in 30.8% of those who were BRCA2 mutation-positive. Moreover, BRCA mutations result in defective DNA repair, leading to oocyte damage with apoptotic cell death (35,36). According to previous research, even if patients with a BRCA2 mutation have lower levels of anti-Müllerian hormone, this does not appear to have a negative impact on reproductive outcome (34). Therefore, this should be considered during onco-fertility counseling of these patients.

For the patient in the present case, after multidisciplinary consultation with the oncologist and the reproductive medicine consultant, adequate oncofertility counseling was performed. Considering the risk-benefit ratio of FSS, the low-grade histology of the tumor and the desire of the patient, it was decided in the present case to perform *in vivo* oocyte cryopreservation before restaging surgery. As there were no data regarding the safety of ovarian preservation in early-stage primary Fallopian tube carcinoma, the patient underwent bilateral oophorectomy, preserving the uterus exclusively.

In vitro fertilization for oocyte cryopreservation requires ovarian stimulation, which results in an increased estrogen environment. For other hormone-sensitive tumors, such as breast cancer, the safety of FP has now been established, and indeed, controlled hormonal stimulation does not impact progression free survival or overall survival (38).

COS protocols have been enhanced by the incorporation of aromatase inhibitors (39,40). In the present case, letrozole was administered during the stimulation phase to suppress the aromatization of androgens into estrogens, thereby reducing circulating estrogen levels. Beyond its role in limiting estrogen synthesis, letrozole also promotes an increase in androgen levels, which has been associated with improved ovarian responsiveness to stimulation (41).

Moreover, in the present case, all ultrasound examinations performed during ovarian stimulation appeared normal, with no evidence of cysts or suspicious areas. Before cryopreservation, a hysteroscopy was performed in consideration of the endometrial histotype of cancer. Rienzi *et al* (28) reported that, to achieve a successful live birth through cryopreserving oocytes, ≥ 8 oocytes are required for patients aged <38 years. In the present case, 12 oocytes were cryopreserved. Additionally, the laparoscopic approach has been described as a feasible technique by several authors (42-46). Considering the negative thoracic-abdominal PET-CT scans in the present case, complete laparoscopic surgical restaging with bilateral ovariectomy was performed.

Embryo transfer was performed following hormonal replacement therapy, initiated with oral estradiol (E2) on days 1-3 of the cycle to prepare the endometrium and inhibit spontaneous follicular development. Estradiol was administered either at a fixed daily dose (6 mg) or via a step-up regimen. Although no randomized controlled trials have directly compared these approaches, a large retrospective analysis of 8,254 oocyte donation cycles reported similar live birth rates after a fixed daily dose or after a step-up regimen (33.0 vs. 32.5%, respectively) (47). Furthermore, in the present case, vaginal micronized progesterone was administered (200 mg, x3/day) for adequate luteal phase support.

Regarding the fetal growth restriction and the development of early preeclampsia in the present case, these were complications associated with the BMI of the patient (30 kg/m²), nulliparity and smoking (48), as well as because it was >2 years since the cancer diagnosis and the patient had not undergone chemotherapy.

Pregnancies after gynecological cancer need to be managed by different medical specialties; therefore, it is desirable to have a close collaboration between consultants with an expertise in oncology, reproductive medicine and high-risk pregnancy in referral oncological centers.

The present case is the first case, to the best of our knowledge, of ART after FSS for a primary Fallopian tube cancer in a patient with BRCA2 mutation. However, there are certain reflections to be made: On the one hand, the present report presents the first case of the feasibility of FP with COS in case of diagnosis of low-grade primary Fallopian tube cancer at initial stage; whilst on the other hand, there was a fertility issue regarding a germline pathogenic variant in the BRCA1/2 gene. In fact, certain research suggests that the ovarian reserve of patients with the BRCA1/2 mutation may be reduced (34). Therefore, we hypothesize a practice-changing strategy: FP could be systematically offered to healthy patients carrying a BRCA mutation who have not yet completed the reproductive cycle, and then perform a risk-reducing bilateral salpingo-oophorectomy after 35 years.

In conclusion, due to the limited reproductive research in patients with Fallopian tube cancer, evaluating the safety, efficacy and feasibility of FP, and post-diagnosis pregnancy, should be considered a research priority. Reporting the first case in the literature of pregnancy after epithelial primary Fallopian tube cancer using conservative surgery and oocyte freezing, to the best of our knowledge, the present report aims to give impetus to further research in this field. Oocyte cryopreservation appears to be a feasible method to preserve fertility in selected cases of OC. FP by oocyte/embryo freezing employing specific ovarian stimulation protocols could represent a therapeutic option in young patients with BRCA1/BRCA2 mutations who have not completed their reproductive cycle within the 35 years, even if further evidence is needed for elucidation of the role of BRCA mutations on fertility.

Acknowledgements

Not applicable.

Funding

The present work was supported by the Ministry of Health (Rome, Italy), in collaboration with the Institute for Maternal and Child Health IRCCS ‘Burlo Garofolo’ (Trieste, Italy).

Availability of data and materials

The next-generation sequencing data are not publicly available as they contain information that could compromise the privacy of research participants; however, they may be requested from the corresponding author. All other data generated in the present study may be requested from the corresponding author.

Authors' contributions

GS, SC, AV, GZ and GR conceived and designed the study; AR and AM performed the experiments. GR, LN and AM performed the analysis and interpretation of data. GS, AV, AR, GZ, SC and AM wrote the manuscript. GS, AV, AR, AM, GZ and LN revised the manuscript. All authors read and approved the final manuscript. GS and AV confirm the authenticity of all the raw data.

Ethics approval and consent to participate

All procedures performed in the present study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The present study was approved by the Institutional Review Board of the Institute for Maternal and Child Health IRCCS ‘Burlo Garofolo’ (approval no. RC 08/2022; April 15, 2022).

Patient consent for publication

Written informed consent was obtained from the patient to publish the present paper.

Competing interests

The authors declare that they have no competing interests.

References

1. Santos ML, Pais AS and Almeida Santos T: Fertility preservation in ovarian cancer patients. *Gynecol Endocrinol* 37: 483-489, 2021.
2. International Agency for Research on Cancer, Global Cancer Observatory, Cancer Today Globocan 2022: Ovary factsheet. <https://gco.iarc.who.int/media/globocan/factsheets/cancers/25-ovary-fact-sheet.pdf>. Accessed February 8, 2024.
3. Taylan E and Oktay K: Fertility preservation in gynecologic cancers. *Gynecol Oncol* 155: 522-529, 2019.
4. National Comprehensive Cancer Network. Ovarian Cancer (Version 1.2017). https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed April 15, 2024.
5. Arcieri M, Tius V, Andretta C, Restaino S, Biasioli A, Poletto E, Damante G, Ercoli A, Driul L, Fagotti A, *et al.*: How BRCA and homologous recombination deficiency change therapeutic strategies in ovarian cancer: A review of literature. *Front Oncol* 14: 1335196, 2024.
6. Rasmussen CB, Kjaer SK, Albieri V, Bandera EV, Doherty JA, Høgdall E, Webb PM, Jordan SJ, Rossing MA, Wicklund KG, *et al.*: Pelvic inflammatory disease and the risk of ovarian cancer and borderline ovarian tumors: A pooled analysis of 13 Case-control studies. *Am J Epidemiol* 185: 8-20, 2017.
7. De Seta F, Banco R, Turrisi A, Airoud M, De Leo R, Stabile G, Ceccarello M, Restaino S and De Santo D: Pelvic inflammatory disease (PID) from Chlamydia trachomatis versus PID from Neisseria gonorrhoea: From clinical suspicion to therapy. *G Ital Dermatol Venereol* 147: 423-430, 2012.
8. Barnard ME, Farland LV, Yan B, Wang J, Trabert B, Doherty JA, Meeks HD, Madsen M, Guinto E, Collin LJ, *et al.*: Endometriosis typology and ovarian cancer risk. *JAMA* 332: 482-489, 2024.
9. Kim SY and Lee JR: Fertility preservation option in young women with ovarian cancer. *Future Oncol* 12: 1695-1698, 2016.
10. Lavoue V, Huchon C, Akladios C, Alfonsi P, Bakrin N, Ballester M, Bendifallah S, Bolze PA, Bonnet F, Bourgin C, *et al.*: Management of epithelial cancer of the ovary, fallopian tube, primary peritoneum. Long text of the joint French clinical practice guidelines issued by FRANCOGYN, CNGOF, SFOG, GINECO-ARCAGY, endorsed by INCa. (Part 2: Systemic, intraperitoneal treatment, elderly patients, fertility preservation, follow-up). *J Gynecol Obstet Hum Reprod* 48: 379-386, 2019.

11. Mangili G, Somigliana E, Giorgione V, Martinelli F, Filippi F, Petrella MC, Candiani M and Peccatori F: Fertility preservation in women with borderline ovarian tumours. *Cancer Treat Rev* 49: 13-24, 2016.
12. Tsonis O and Kopeika J: Fertility preservation in patients with gynecologic malignancy: Response to ovarian stimulation and long-term outcomes. *Eur J Obstet Gynecol Reprod Biol* 290: 93-100, 2023.
13. Akel RA, Guo XM, Moravek MB, Confino R, Smith KN, Lawson AK, Klock SC, Tanner III EJ and Pavone ME: Ovarian stimulation is safe and effective for patients with gynecologic cancer. *J Adolesc Young Adult Oncol* 9: 367-374, 2020.
14. Berek JS, Renz M, Kehoe S, Kumar L and Friedlander M: Cancer of the ovary, fallopian tube, and peritoneum: 2021 update. *Int J Gynaecol Obstet* 155 (Suppl 1): S61-S85, 2021.
15. Alvarez M, Solé M, Devesa M, Fábregas R, Boada M, Tur R, Coroleu B, Veiga A and Barri PN: Live birth using vitrified-warmed oocytes in invasive ovarian cancer: Case report and literature review. *Reprod Biomed Online* 28: 663-668, 2014.
16. Mayeur A, Puy V, Windal V, Hesters L, Gallot V, Benoit A, Grynberg M, Sonigo C and Frydman N: Live birth rate after use of cryopreserved oocytes or embryos at the time of cancer diagnosis in female survivors: A retrospective study of ten years of experience. *J Assist Reprod Genet* 38: 1767-1775, 2021.
17. Nitecki R, Clapp MA, Fu S, Lamiman K, Melamed A, Brady PC, Kaimal A, Del Carmen MG, Woodard TL, Meyer LA, *et al*: Outcomes of the first pregnancy after Fertility-sparing surgery for Early-stage ovarian cancer. *Obstet Gynecol* 137: 1109-1118, 2021.
18. Ledermann JA, Matias-Guiu X, Amant F, Concin N, Davidson B, Fotopoulou C, González-Martín A, Gourley C, Leary A, Lorusso D, *et al*: ESGO-ESMO-ESP consensus conference recommendations on ovarian cancer: Pathology and molecular biology and early, advanced and recurrent disease. *Ann Oncol* 35: 248-266, 2024.
19. NCCN Guidelines Version 1.2024 Ovarian Cancer/Fallopian Tube Cancer/Primary Perit.
20. Armstrong DK, Alvarez RD, Backes FJ, Bakkum-Gamez JN, Barroilhet L, Behbakht K, Berchuck A, Chen LM, Chitoyo VC, Cristea M, *et al*: NCCN Guidelines® Insights: Ovarian cancer, version 3.2022. *J Natl Compr Canc Netw* 20: 972-980, 2022.
21. Bentivegna E, Gouy S, Maulard A, Pautier P, Leary A, Colombo N and Morice P: Fertility-sparing surgery in epithelial ovarian cancer: A systematic review of oncological issues. *Ann Oncol* 27: 1994-2004, 2016.
22. Zapardiel I, Cruz M, Diestro MD, Requena A and Garcia-Velasco JA: Assisted reproductive techniques after fertility-sparing treatments in gynaecological cancers. *Hum Reprod Update* 22: 281-305, 2016.
23. Tomao F, Di Pinto A, Sassu CM, Bardhi E, Di Donato V, Muzii L, Petrella MC, Peccatori FA and Panici PB: Fertility preservation in ovarian tumours. *Ecancermedicalscience* 12: 885, 20185.
24. Darai E, Fauvet R, Uzan C, Gouy S, Duvillard P and Morice P: Fertility and borderline ovarian tumor: A systematic review of conservative management, risk of recurrence and alternative options. *Hum Reprod Update* 19: 151-166, 2013.
25. Poulain M, Vandame J, Tran C, Koutchinsky S, Pirtea P and Ayoubi JM: Fertility preservation in borderline ovarian tumor patients and survivors. *Horm Mol Biol Clin Investig* 43: 179-186, 2020.
26. Fortin A, Hazout A, Thoury A, Alvès K, Bats AS, Dhainaut C and Madelenat P: Assistance médicale à la procréation après traitement conservateur d'une tumeur de l'ovaire invasive ou à la limite de la malignité Assisted reproductive technologies after conservative management of borderline or invasive ovarian tumours. *Gynecol Obstet Fertil* 33: 488-4897, 2005.
27. Zaami S, Melcarne R, Patrone R, Gullo G, Negro F, Napoletano G, Monti M, Aceti V, Panarese A, Borcea MC, *et al*: Oncofertility and reproductive counseling in patients with breast cancer: A retrospective study. *J Clin Med* 11: 1311, 2022.
28. Rienzi L, Cobo A, Paffoni A, Scarduelli C, Capalbo A, Vajta G, Remohí J, Ragni G and Ubaldi FM: Consistent and predictable delivery rates after oocyte vitrification: An observational longitudinal cohort multicentric study. *Hum Reprod* 27: 1606-1612, 2012.
29. SHRE Guideline Group on Female Fertility Preservation; Anderson RA, Amant F, Braat D, D'Angelo A, Chua de Sousa Lopes SM, Demeestere I, Dwek S, Frith L, Lambertini M, *et al*: ESHRE guideline: Female fertility preservation. *Hum Reprod Open* 2020: hoaa052, 2020.
30. Gullo G, Perino A and Cucinella G: Open vs. closed vitrification system: Which one is safer? *Eur Rev Med Pharmacol Sci* 26: 1065-1067, 2022.
31. Peccatori FA, Mangili G, Bergamini A, Filippi F, Martinelli F, Ferrari F, Noli S, Rabaiotti E, Candiani M and Somigliana E: Fertility preservation in women harboring deleterious BRCA mutations: Ready for prime time? *Hum Reprod* 33: 181-187, 2018.
32. Gullo G, Basile G, Cucinella G, Greco ME, Perino A, Chiantera V and Marinelli S: Fresh vs. frozen embryo transfer in assisted reproductive techniques: A single center retrospective cohort study and Ethical-legal implications. *Eur Rev Med Pharmacol Sci* 27: 6809-6823, 2023.
33. Park CW, Lee SH, Yang KM, Lee IH, Lim KT, Lee KH and Kim TJ: Cryopreservation of in vitro matured oocytes after ex vivo oocyte retrieval from gynecologic cancer patients undergoing radical surgery. *Clin Exp Reprod Med* 43: 119-125, 2016.
34. Ponce J, Fernandez-Gonzalez S, Calvo I, Climent M, Peñafiel J, Feliubadaló L, Teulé A, Lázaro C, Brunet JM, Candás-Estébanez B and Durán Retamal M: Assessment of ovarian reserve and reproductive outcomes in BRCA1 or BRCA2 mutation carriers. *Int J Gynecol Cancer* 30: 83-88, 2020.
35. Oktay K, Kim JY, Barad D and Babayev SN: Association of BRCA1 mutations with occult primary ovarian insufficiency: A possible explanation for the link between infertility and breast/ovarian cancer risks. *J Clin Oncol* 28: 240-204, 2010.
36. Oktay K, Turan V, Titus S, Stobezki R and Liu L: BRCA mutations, DNA repair deficiency, and ovarian aging. *Biol Reprod* 93: 67, 2015.
37. Wang ET, Pisarska MD, Bresee C, Chen YD, Lester J, Afshar Y, Alexander C and Karlan BY: BRCA1 germline mutations may be associated with reduced ovarian reserve. *Fertil Steril* 102: 1723-1728, 2014.
38. Kufel-Grabowska J, Podolak A, Maliszewski D, Bartoszkiewicz M, Ramlau R and Lukaszuk K: Fertility counseling in BRCA1/2-mutated women with breast cancer and healthy individuals. *J Clin Med* 11: 3996, 2022.
39. Marklund A, Lekberg T, Hedayati E, Liljegren A, Bergh J, Lundberg FE and Rodriguez-Wallberg KA: Relapse rates and Disease-specific mortality following procedures for fertility preservation at time of breast cancer diagnosis. *JAMA Oncol* 8: 1438-1446, 2022.
40. Kim J, Turan V and Oktay K: Long-term safety of letrozole and gonadotropin stimulation for fertility preservation in women with breast cancer. *J Clin Endocrinol Metab* 101: 1364-1371, 2016.
41. Oktay K, Buyuk E, Libertella N, Akar M and Rosenwaks Z: Fertility preservation in breast cancer patients: A prospective controlled comparison of ovarian stimulation with tamoxifen and letrozole for embryo cryopreservation. *J Clin Oncol* 23: 4347-4353, 2005.
42. Dias Nunes J, Demeestere I and Devos M: BRCA mutations and fertility preservation. *Int J Mol Sci* 25: 204, 2023.
43. Tomao F, Peccatori F, Del Pup L, Franchi D, Zanagnolo V, Panici PB and Colombo N: Special issues in fertility preservation for gynecologic malignancies. *Crit Rev Oncol Hematol* 97: 206-219, 2016.
44. Martinez A, Poilblanc M, Ferron G, De Cuyper M, Jouve E and Querleu D: Fertility-preserving surgical procedures, techniques. *Best Pract Res Clin Obstet Gynaecol* 26: 407-424, 2012.
45. Bruno M, Ludovisi M, Ronsini C, Capanna G, Stabile G and Guido M: Tertiary cytoreduction for isolated lymphnode recurrence (ILNR) ovarian cancer in a BRCA2 mutated patient: Our experience and prevalence of BRCA 1 or 2 genes mutational status in ILNR. *Medicina (Kaunas)* 59: 606, 2023.
46. Restaino S, Finelli A, Pellicchia G, Biasoli A, Mauro J, Ronsini C, Martina MD, Arcieri M, Della Corte L, Sorrentino F, *et al*: Scar-free laparoscopy in BRCA-mutated women. *Medicina (Kaunas)* 58: 943, 2022.
47. Madero S, Rodriguez A, Vassena R and Vernaev V: Endometrial preparation: Effect of estrogen dose and administration route on reproductive outcomes in oocyte donation cycles with fresh embryo transfer. *Hum Reprod* 31: 1755-1764, 2016.
48. Bartsch E, Medcalf KE, Park AL and Ray JG: Clinical risk factors for pre-eclampsia determined in early pregnancy: Systematic review and Meta-analysis of large cohort studies. *BMJ* 353: i1753, 2016.

