

Ovarian tissue cryopreservation – not just fertility preservation

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Ovarian tissue cryopreservation is now an increasingly prevalent method of preserving fertility among patients across the globe. The first ever ovarian tissue transplant was performed in 1999 to restore endocrinological functions in a patient with premature menopause.^[1]

The first successful case of pregnancy following a transplant was reported in 2004.^[2,3] Following which, it took another 16 years, in March 2020, for the experimental tag to be removed by the American Society of Reproductive medicine.

Since then, this has been the method of choice for pre- and peripubertal girls for onco-fertility preservation. This is a method that can be utilized for women in the reproductive age group, who do not have the stipulated time of approximately 2 weeks for oocyte or embryo cryopreservation before they proceed with gonadotoxic therapy.

The ovarian cortex contains upto 90% of the primordial follicles encompassing the ovarian reserve. In young pre- and peri-pubertal girls, the only option for fertility preservation is surgical removal of the ovarian cortex followed by cryopreservation and reimplantation at a later


date when the patient is free of the disease. In younger patients, one of the ovaries is excised and frozen rather than the cortical tissue since the size is small.

The procedure involves laparoscopic removal of either the ovarian cortical tissue or, in some cases, even the entire ovary may be removed.

The ovarian tissue is initially activated in the Lebowhitz medium. This tissue is then processed and fashioned to form strips of $1 \times 2 \times 2$ cm³ approximately. Once the strips are ready, they are frozen, most commonly using the slow freezing method.

If done meticulously by the slow freezing method, post thawing the ovarian tissue regains almost 95% of its endocrine function, which would be evident both clinically with the resumption of the menstrual cycle and on the ultrasound.

Among the 50% of patients who have a conception following ovarian transplantation, almost half of the patients who undergo this procedure would even conceive spontaneously, and other half would do so with the ART procedures.

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The transplant can be performed at orthotopic or heterotopic sites. The commonest and one of the most successful was over the ovarian medulla, from which the cortical tissue had been excised. The heterotopic sites are commonly used in cases of cell-based HRT. The anterior abdominal wall and even the wrist are sites that have been reportedly used for reimplantation of the tissue.

In the current era, the spectrum of ovarian tissue cryopreservation has extended beyond the indications of onco fertility preservation.

CELL/TISSUE BASED HRT

The incidence of premature ovarian failure, which represents cessation of ovarian function before 40 years of age, is rising across the world. Although, in most of the cases it is idiopathic, there are a subset of patients for whom there can be certain predisposing factors.

Ovarian tissue cryopreservation followed by transplantation is the only method of natural hormone replacement therapy and has been an indication of ovarian tissue cryopreservation.

As already mentioned, post-transplant endocrine function of the ovary resumes in almost 95% of the patients.^[4] This can be utilized as a hormone replacement therapy in patients with a high risk of premature ovarian failure, as in cases of mosaic Turner's syndrome or Fragile X syndrome carriers, etc. Post-transplantation the thawed ovarian tissue, takes 4 to 5 months for the resumption of ovarian function.

In pre-pubertal premature ovarian failure patients, cell/tissue-based HRT can act as an effective method for inducing pubertal changes. Isolated case reports of patients in the pre-pubertal age being treated with ovarian tissue-based HRT have shown encouraging results.^[5,6]

POST-MENOPAUSAL WOMEN AND HRT

Estrogen and progesterone have been widely studied as a form of hormonal replacement therapy for post-menopausal women. It is beneficial for some of the symptoms of the menopausal age group. However, careful evaluation and risk benefit analysis need to be performed before patients are put on these medications for the shortest possible duration. Cell-based hormone replacement therapy can be the main stay of therapy for

these women, which is very safe and efficacious even for long term. Once transplanted, the tissue can survive for many years, depending on the age of the patients and the amount and age at which the ovarian tissue was cryopreserved.

INDUCTION OF PUBERTY

In patients with high risk of premature ovarian failure due to genetic predisposition, for example, fragile X syndrome and turners, an option for induction of natural puberty would be ovarian tissue preservation followed by transplantation at a later date and time. A few strips can be laparoscopically re-implanted at the site to promote the endocrine functions of the ovary. It takes as early as 15 to 20 weeks for the endocrine function to initiate and subsequently establish the hormonal effects of ovarian function.

SOCIAL EGG FREEZING

In the current era of career-oriented women, freezing oocytes to utilize them at a later time and age is an upcoming indication of fertility preservation. Apart from the usual advantages of oocyte freezing, the advantage of ovarian tissue in such females would be the increased chance of natural conception in up to 50% of patients. Secondly, the main reason would be the added benefits of ovarian endocrine function and allaying the menopausal features until a later age among this group of patients.

FUTURE PERSPECTIVES

These treatments include in vitro follicle development utilizing stem cells from post-menopausal ovaries.^[7]

Artificial ovary, which consists of transplanting the ovary in the artificially created scaffold, has also been reported. Robotic-Assistance and Neovascularizing Human Extracellular Tissue Matrix Scaffold to improve ovarian auto-transplantation outcome and improved vascularization and decreased primordial follicular loss immediately. Post-transplant is a relatively new technique to improve the outcome as compared to the conventional methodology.^[8]

CONCLUSION

Fertility preservation has an increasing application in current society. The newer innovations in the techniques of oocyte cryopreservation would further

enhance the applications of the technique and improve its efficiency.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Oktay K, Karlikaya G. Ovarian function after transplantation of frozen, banked autologous ovarian tissue. *N Engl J Med* 2000;342:1919.
2. Donnez J, Dolmans MM, Demylle D, *et al.* Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. *Lancet*. 2004; 364:1405–10.
3. Marin L, Bedoschi G, Kawahara T, Oktay KH. History, evolution and current state of ovarian tissue auto-transplantation with cryopreserved tissue: a successful translational research journey from 1999 to 2020. *Reprod Sci* 2020;27:955-62.
4. Gellert SE, Pors SE, Kristensen SG, Bay-Bjorn AM, Ernst E, Yding AC. Transplantation of frozen-thawed ovarian tissue: an update on worldwide activity published in peer-reviewed papers and on the Danish cohort. *J Assist Reprod Genet* 2018;35:561–70.
5. Ernst E, Kjærsgaard M, Birkebæk NH, Clausen N, Andersen CY. Stimulation of puberty in a girl with chemo- and radiation therapy induced ovarian failure by transplantation of a small part of her frozen/thawed ovarian tissue. *Eur J Cancer* 2013;49: 911–4.
6. Anderson RA, Hindmarsh PC, Wallace WH. Letter to the editor: induction of puberty by autograft of cryopreserved ovarian tissue in a patient previously treated for Ewing sarcoma. *Eur J Cancer* 2013;49:2960–1.
7. Oqani RK, So S, Lee Y, Ko JJ, Kang E. Artificial oocyte: development and potential application. *Cells* 2022;11:1135.
8. Oktay K, Bedoschi G, Pacheco F, Turan V, Emirdar V. First pregnancies, live birth, and in vitro fertilization outcomes after transplantation of frozen-banked ovarian tissue with a human extracellular matrix scaffold using robot-assisted minimally invasive surgery. *Am J Obstet Gynecol* 2016;214:94.