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New Horizons in Ovarian Tissue Cryopreservation: From Clinical Evidence to Research Perspectives

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Abstract: Fertility preservation in patients undergoing gonadotoxic treatments, particularly those with cancer, has become a major priority in reproductive health over the past two decades. Ovarian tissue cryopreservation (OTC), as a relatively novel yet rapidly expanding technique, offers distinct advantages compared to oocyte or embryo cryopreservation. These include its immediate applicability without the need for ovarian stimulation, feasibility in patients requiring urgent treatment or in prepubertal girls, and the possibility of simultaneous restoration of endocrine function following tissue transplantation. Recent reviews indicate that more than 200 live births have been reported worldwide after ovarian tissue transplantation (OTT), highlighting its genuine clinical efficacy [1,2].

Keywords: Ovarian Tissue Cryopreservation; Clinical application; fertility.

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Letter to the Editor

Fertility preservation in patients undergoing gonadotoxic treatments, particularly those with cancer, has become a major priority in reproductive health over the past two decades. Ovarian tissue cryopreservation (OTC), as a relatively novel yet rapidly expanding technique, offers distinct advantages compared to oocyte or embryo cryopreservation. These include its immediate applicability without the need for ovarian stimulation, feasibility in patients requiring urgent treatment or in prepubertal girls, and the possibility of simultaneous restoration of endocrine function following tissue transplantation. Recent reviews indicate that more than 200 live births have been reported worldwide after ovarian tissue transplantation (OTT), highlighting its genuine clinical efficacy [1,2].

Multicenter studies and systematic reviews have demonstrated that transplantation of cryopreserved ovarian tissue often leads to the recovery of ovarian endocrine function, and in a considerable proportion of patients, to pregnancy and live birth. Meta-analyses confirm high rates of endocrine recovery (resumption of menstruation and hormone production) and variable, yet encouraging, pregnancy outcomes in selected populations [3].

Key clinical applications of OTC include its role in emergency settings and for children and adolescents, since it does not require ovarian stimulation and can be performed rapidly. For prepubertal girls who are not eligible for oocyte cryopreservation, OTC represents the only viable fertility-preserving option [4]. Furthermore, the restoration of endocrine activity is another important benefit; ovarian tissue transplantation can resume estrogen/progesterone production and mitigate symptoms of premature ovarian insufficiency [5,6].

Nonetheless, safety challenges and concerns remain. The most critical issue is the risk of reintroducing malignant cells, particularly in cases of leukemia or certain sarcomas, where the transplanted tissue may harbor minimal residual disease (MRD) leading to cancer recurrence. Molecular diagnostics, flow cytometry, and xenograft models have been recommended to reduce this risk, though standardized protocols and long-term evidence are still required [7].

Despite successful outcomes, the actual utilization of OTC remains limited in many centers, and incomplete national/international registries hinder systematic follow-up and reporting [8].

Recent technical and research advances in this field have been noteworthy. Two cryopreservation techniques, slow freezing and vitrification have been evaluated in recent studies. While meta-analyses suggest that vitrification may offer certain advantages, especially in preserving stromal cell integrity, findings remain inconsistent and no universal consensus has been reached. Rigorous randomized controlled trials and real-world fertility outcome data are still needed [9].

In addition, tissue engineering and follicle culture are emerging as promising innovations. Advances in three-dimensional follicle culture, biomaterial scaffolding, and stem cell applications may eventually provide alternatives that circumvent the need for autologous tissue transplantation, thereby eliminating the risk of reintroducing malignant cells. However, these approaches are currently confined to experimental research [10].

For the advancement of clinical practice and research in OTC at the national level, the following strategies are recommended: 1- Establishment of a national registry for OTC and OTT outcomes to allow long-term monitoring of fertility and safety. 2- Development of standardized MRD screening protocols for high-risk cancer patients prior to tissue transplantation. 3- Investment in training programs for laparoscopic ovarian tissue retrieval, establishment of tissue banks, and comparative local studies of vitrification versus slow freezing. 4- Strengthening multidisciplinary collaboration among oncologists, reproductive specialists, and pathologists to support individualized patient-centered decision-making.

Conclusion

Ovarian tissue cryopreservation represents a powerful and expanding clinical tool for fertility preservation, with robust evidence of live births and restored hormonal function. Nevertheless, safety concerns (particularly in certain malignancies), inadequate outcome reporting, and technical heterogeneity highlight the need for further research and the development of local policies. Coordinated expansion of this technology in specialized centers could improve patient access and enhance the quality of fertility preservation care.

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