INPLASY

Enhancement of angiogenesis and follicular survival using growth factors during ovarian tissue transplantation — a systematic review

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 June 2025 and was last updated on 8 June 2025.

INTRODUCTION

Review question / Objective P: Female mice with bilateral ovaries surgically removed. I: Growth factors are added during ovarian tissue transplantation. C:Blank control. O:Ovarian histomorphological evaluation, vascular density count, recovery of ovarian function, and tissue fibrosis. S:Randomized controlled trials.

Rationale Ovarian tissue cryopreservation transplantation (OTCT) is a procedure in which a portion of the ovarian tissue is surgically removed before the onset of severe impairment in ovarian function. The tissue is then processed into standard thickness sections, cryopreserved using cryobiological methods, and stored for future use. In cases where the patient's condition is suitable, the frozen ovarian tissues are resuscitated and transplanted back into the body. This procedure is intended to restore the reproductive and endocrine functions of the ovaries. It is also effective in preventing and controlling drug-induced premature ovarian insufficiency (POI). However, because ovarian tissue transplantation is a non-vascular, anastomotic-free graft. The growth and development of the transplanted ovary are contingent on the re-establishment of the circulatory system, and more than 50% loss of primordial follicles is observed before neovascularisation of the tissue is established after transplantation. Therefore, there is a need to improve and accelerate graft angiogenesis and reduce follicle loss. The regulation of angiogenesis is a complex process involving a variety of vasoactive and angiogenic factors. The application of angiogenic factors (e.g., erythropoietin, vascular endothelial growth factor, and basic fibroblast growth factor) to ovarian tissue grafts has been shown to have a positive effect on angiogenesis and follicular survival. No systematic review of

growth factor applications in ovarian tissue grafts has been conducted.

Condition being studied In recent years, the incidence of female malignant tumors has been growing globally, and the latest statistics show that there will be nearly 9 million new cases of female cancer in 2022. With the continuous advancement of cancer prevention, diagnosis, and treatment technologies, the mortality rate of cancer patients has gradually declined, and, in particular, the 5-year survival rate of adolescents and young adults with cancer has risen to more than 85%. Unfortunately, drugs such as the alkylating agent cyclophosphamide used in cancer therapy are gonadotoxic. They induce double-stranded DNA breaks that lead to apoptosis, causing irreversible damage to germ cells. Secondly, during radiotherapy, the exposure of the ovaries to radiation damages the germ cells by destroying the DNA, either directly or by brief junction. The gonadal toxicity of anticancer therapy can cause irreversible damage to the ovarian function of patients, leading to a decrease or even loss of female fertility and triggering symptoms of early menopause and systemic estrogen reduction, which significantly increases the risk of osteoporosis, cardiovascular disease, neurodegenerative disease and a series of other diseases, and seriously affects the health and life expectancy of women throughout the entire life cycle. Therefore, for individuals of childbearing age or younger who require anticancer treatment, the option of fertility preservation should be considered while improving survival rates, prolonging survival time, and improving the quality of patient survival, which remains a key clinical issue to be addressed at this stage.

METHODS

Search strategy As of 1 December 2024, Embase and PubMed databases were searched. The following search criteria were applied: ((ovari*) OR (overi* tissue) OR (ovari* cortex)) AND ((cryopreserv*) OR (bank*) OR (vitrificat*) OR (freez*)) AND ((growth factors*) OR (vascular endothelial growth factor*) OR (VEGF) OR (basic fibroblast growth factor*) OR (bFGF*) OR (erythropoietinl*) OR (EPO*)). No search filters or text analysis tools were used, and all articles were evaluated from when the database was created to when the search was performed.

Participant or population Female mice with bilateral ovaries surgically removed.

Intervention Growth factors are used during ovarian tissue transplantation.

Comparator No planned.

Study designs to be included Randomized controlled trials.

Eligibility criteria Weincluded randomized controlled trials using mouse or human ovarian tissue for transplantation in combination with growth factors that considered outcomes that indirectly assessed the effects of ischemia after transplantation. The results of studies that performed systematic and qualitative evaluations included histological analyses of ovarian tissues. These immunohistochemical assays provided information about angiogenesis promotion, follicular growth, and indicators of endocrine function in the ovary.

Information sources Electronic databases.

Main outcome(s) It can directly or indirectly reflect the indicators of follicular survival and angiogenesis.

Quality assessment / Risk of bias analysis We considered the risk of bias using the Cochrane Risk of Bias Tool for Randomised Trials (RoB 2) version 2.

Strategy of data synthesis Experimental analysis, outcome measures, and interpretation of reports were performed in the included studies.

Subgroup analysis No plan.

Sensitivity analysis No plan.

Country(ies) involved China.

Keywords ovarian tissue, transplantation, growth factors, angiogenesis, follicular survival.

Contributions of each author

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