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Impact of Ovarian Transplantation Site on Reproductive Outcomes: A Comprehensive Systematic Review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202390008

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 September 2023 and was last updated on 04 September 2023.

INTRODUCTION

Review question / Objective Is there a difference in reproductive outcomes from ovarian transplantation based on the site of the transplant?

Rationale At present, there is no consensus on different ovarian transplantation sites. Which site has the highest pregnancy rate after ovarian transplantation? This issue needs to be further explored.

Condition being studied For many young women with malignant disease, a consequence of the high doses of cytotoxic treatment used to eradicate their cancer is loss of fertility. Providing this additional information at a difficult time can cause distress, but there is now an increasing awareness of the importance of the discussion of fertility preservation options at this time. Fertility preservation options involving oocyte and ovarian tissue cryopreservation are now acceptable techniques, with many countries establishing routine fertility preservation services and some receiving government funding for these services. Ovarian tissue cryopreservation (OTC) has major benefits over oocyte cryopreservation, as it avoids delays to treatment and is the only available option for prepubertal girls. In addition, tissue can be collected in conjunction with other surgical procedures and, in young women, it has offered the possibility of more than one birth from a single cryopreservation procedure and subsequent transplantation. Transplantation of cryopreserved ovarian tissue where unequivocal evidence that oocytes recovered have originated from cryopreserved tissue was first reported by Poirot at 2006. The oocytes retrieved from the subcutaneous (SC) abdominal transplant resulted in fertilization and embryo development but did not proceed to transfer. Births have resulted following bilateral oophorectomy and transplantation of cryopreserved ovarian tissue into the pelvic region,

using each of the above cryoprotectants . These provide proof of principle that primordial follicles can be preserved with these cryopreservation procedures and that full developmental potential is possible. They also indicate that there is no requirement for the full ovarian structure and milieu but the 1mm thick ovarian cortex alone with neovascularization is sufficient for full follicular development. However, there is no consensus on the specific site of ovarian tissue transplantation. Different studies have reported that different transplant sites have significantly different effects on the postoperative pregnancy rate. Therefore, more in-depth studies and more data are urgently needed to conduct research on this topic.

METHODS

Search strategy Search: ((ovarian transplantation[Title/Abstract]) OR (ovarian tissue transplantation[Title/Abstract])) AND ((((((((Pregnancy Outcome[Title/Abstract]) OR (Pregnancy Outcomes[Title/Abstract])) OR (Outcome, Pregnancy[Title/Abstract])) OR (Outcomes, Pregnancy[Title/Abstract])) OR (reproductive outcome[Title/Abstract])) OR ((((((((((pregnancy rate[Title/Abstract]) OR (Rates, Pregnancy[Title/Abstract])) OR (Pregnancy Rates[Title/Abstract])) OR (Rate, Pregnancy[Title/Abstract])) OR (Pregnancy Rate, Live-Birth[Title/Abstract])) OR (Live-Birth Pregnancy Rates[Title/Abstract])) OR (Pregnancy Rate, Live Birth[Title/Abstract])) OR (Pregnancy Rates, Live-Birth[Title/Abstract])) OR (Rate, Live-Birth Pregnancy[Title/Abstract])) OR (Rates, Live-Birth Pregnancy[Title/Abstract])) OR (Live-Birth Pregnancy Rate[Title/Abstract])) OR (Live Birth Pregnancy Rate[Title/Abstract]))) OR ((((((((((((((((((((((delivery rate[Title/Abstract]) OR (Perfusion Pumps, Implantable[Title/Abstract])) OR (Implantable Perfusion Pump[Title/Abstract])) OR (Implantable Perfusion Pumps[Title/Abstract])) OR (Perfusion Pump, Implantable[Title/Abstract])) OR (Pump, Implantable Perfusion[Title/Abstract])) OR (Pumps, Implantable Perfusion[Title/Abstract])) OR (Drug Delivery Systems, Implantable[Title/Abstract])) OR (Implantable Infusion Pumps[Title/Abstract])) OR (Implantable Infusion Pump[Title/Abstract])) OR (Infusion Pump, Implantable[Title/Abstract])) OR (Pump, Implantable Infusion[Title/Abstract])) OR (Pumps, Implantable Infusion[Title/Abstract])) OR (Medication Systems, Programmable Implantable[Title/Abstract])) OR (Programmable Implantable Medication Systems[Title/Abstract])) OR (Systems, Programmable Implantable Medication[Title/Abstract])) OR (Implantable Medication Systems, Programmable[Title/Abstract])) OR (Peristaltic Pumps, Implantable[Title/Abstract])) OR (Implantable Peristaltic Pump[Title/Abstract])) OR (Implantable Peristaltic Pumps[Title/Abstract])) OR (Peristaltic Pump, Implantable[Title/Abstract])) OR (Pump, Implantable Peristaltic[Title/Abstract])) OR (Pumps, Implantable Peristaltic[Title/Abstract]))) OR ((reproductive outcome[Title/Abstract]) OR (Reproductive outcomes[Title/Abstract]))) OR (((Pregnancy[Title/Abstract]) OR (Pregnancies[Title/Abstract])) OR(Gestation[Title/Abstract]))).

Participant or population Women/young girls with cancer or those requiring fertility preservation measures.

Intervention Ovarian transplantation.

Comparator Sites of the transplants.

Study designs to be included Randomised trials, cohort studies, case series, or systematic reviews of these study designs. Studies in languages otherthan English will only be translated if they represent a higher level of evidence than that available in the English languageevidence-base.

Eligibility criteria 1. Patients with ovarian transplantation and fertility intention; 2. Report the transplant site in detail; 3. Report specific pregnancy outcomes.

Information sources The following databases will be searched from inception to September 2023: PubMed/MEDLINE, EMBASE, Cohcrane Central Register of Controlled Trials (CENTRAL), Systematic reviews conducted on the topic will be reviewed. In addition, reference checking of reviews and selected articles will be performed. There will be no restriction on language or publication period.

Main outcome(s) pregnancy (confirmed by urinary or serum beta-hCG), clinical pregnancy (confirmed by ultrasonography), live birth and miscarriage.

Data management We intend to perform an individual patient data meta-analysis if the data allows. Studies that have reported on participant level will be analysed using individual patient data (IPD) analysis. Each reproductive outcome (pregnancy, live birth and miscarriage) will be reported individually.

Quality assessment / Risk of bias analysis Risk of bias assessment will be done in duplicate by two reviewers. For randomised control trials the 'Cochrane risk of bias tool' will be used whereas

for controlled studies, a modified Newcastle-Ottawa scale will be used.

Strategy of data synthesis We intend to perform an individual patient data meta-analysis if the data allows. Studies that have reported on participant level will be analysed using individual patient data (IPD) analysis. Each reproductive outcome (pregnancy, live birth and miscarriage) will be reported individually. Any discrepancies will be resolved using a researcher with expertise in methodology and statistics (BW).

Subgroup analysis Subgroup analysis will be performed based on variables that are likely to influence the outcome and will include:
1. IVF vs spontaneous pregnancy
2. Patients with or without premature ovarian insufficiency at the time of transplant
3. Amount of tissue transplanted
4. Frozen/thawed tissue vs. fresh transplant.
5. Orthotopic vs. Heterotopic site for graft transplant
6. Age at ovarian tissue retrieval
7. Age at transplantation
8. Slow freezing vs. Vitrification vs. other techniques
9. Type of gonadotoxic treatment (e.g. radiotherapy vs. chemotherapy)
10. Size and nature of the ovarian graft transplanted
11. Residual ovary vs. graft alone
12. Pre-retrieval ovarian reserve
13. Transplantation technique.

Sensitivity analysis If necessary, use other analysis methods and change the assumptions to analyze the data again to see if the results have changed.

Language restriction English.

Country(ies) involved China.

Keywords ovarian transplantation; Pregnancy Outcome; reproductive outcome; pregnancy rate.

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