O-178 Reproductive and endocrine outcomes after fresh and frozen-thawed ovarian tissue transplantation based on age and anti-cancer therapy: A systematic review and individual patient data meta-analysis

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Study question: Do reproductive and endocrine outcomes from fresh and frozen-thawed ovarian transplants differ based on age and anti-cancer therapy before cryopreservation?

Summary answer: There was a significant difference in reproductive outcomes of women who have their tissue cryopreserved before or at the age of 35 years.

What is known already: Ovarian tissue cryopreservation (OTC) and transplantation is emerging as a new fertility preservation method. Despite being available for two decades, there is a marked variation in the delivery of this procedure worldwide. Most of the data are based on case reports from specialised centres with expertise in providing this procedure, but there are many unreported cases. Through this review, we aim to collate reproductive and endocrine outcomes from ovarian tissue transplantation. In particular the outcomes in women based on age at cryopreservation and whether they had anti-cancer therapy before cryopreservation were explored.

Study design, size, duration: This study was a systematic review and individual participant level meta-analysis to synthesize the existing evidence on the use of fresh and cryopreserved ovarian tissue transplantation. The review protocol was registered with PROSPERO (CRD42018115233) in November 2018 and the review was concluded in December 2020, including 87 studies (768 women).

Participants/materials, setting, methods: Literature search was performed using MEDLINE, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials from inception to October 2020. After screening 20,566 abstracts, 87 studies (768 women) were included in the review. Patient-level data was extracted for 388 women and study-level data for 380 women. Authors were also contacted for data if relevant outcomes were not reported in published manuscripts. Meta-analysis was performed using inverse-variance weighting to calculate summary estimates using a fixed-effects model.

Main results and the role of chance: Age at cryopreservation was provided for 319 out of 388 (82%) women at participant level data. Of these, 283 (88.7%) had ovarian tissue retrieved at ≤35 years of age. A subgroup of four studies that reported data on participants age at cryopreservation and transplantation were included in meta-analysis. Pregnancy rates were higher in participants at ≤35 years of age at cryopreservation, with results being statistically significant (OR, 0.35; 95% CI: 0.13 to 0.92; z = 2.13; P 0.03, I^2 = 0%). Return of hormonal function shown as a decrease in FSH (IU/L) was also lower in this group (MD, 4.38; 95% CI: -4.29 to 13.05; z = 0.99; P 0.32, I^2 = 0%. Whether a participant had received chemotherapy before cryopreservation was explicitly reported in 122 out of 388 (31%) participants and 56 of them (46%) had received anti-cancer treatment before OTC. Thirty-five pregnancies and twenty-four live births were reported in these women. A further meta-analysis from 5 studies showed that although the results were not statistically significant for return of endocrine function, a decrease in FSH, an increase in oestrogen and increased pregnancy rates were noted in participants who did not receive anti-cancer therapy before cryopreservation.

Limitations, reasons for caution: Although we gathered 768 cases of ovarian transplants published in the literature, most were case reports and therefore not included in the meta-analysis. Of the studies included in the meta-analysis, information such as age and anti-cancer therapy were not always provided for individual participants but as an aggregate.

Wider implications of the findings: There was no difference in reproductive and endocrine outcomes for anti-cancer therapy before OTC. Previous

chemotherapy alone should therefore not be a deterrent in offering young girls and women OTC. Furthermore, the ideal age to achieve higher pregnancy and live birth rates from OTC is less than 35 years.

Trial registration number: PROSPERO (CRD42018115233)