Long-term risk of ovarian tumours after assisted reproductive technology

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Study question:

Does assisted reproductive technology (ART) increase the risk of invasive and borderline ovarian tumours?

Summary answer:

After a median follow-up of 22 years, the risk of invasive ovarian cancer is not increased.

What is known already:

Despite the large number of women treated with ART every year, evidence about the long-term risk of ovarian tumours after ART is lacking. Previous studies, with a median follow-up of 4 to 17 years, showed inconsistent results with respect to invasive ovarian cancer, while for borderline ovarian tumours an increased risk was found in several reports.

Study design, size, duration:

Long-term risk of ovarian tumours was assessed in the OMEGA study, a nationwide historical cohort with prospective follow-up. The cohort includes 30,636 women who received ovarian stimulation for ART (ART group) between 1983 and 2001 in one of the 12 Dutch IVF centers and 9,969 women who underwent subfertility treatments other than ART (non-ART group) between 1980 and 2001. Median follow-up amounted to 22 years.

Participants/materials, setting, methods:

Detailed information on subfertility cause and treatment was collected from the medical records. Data on reproductive and lifestyle factors were obtained from the women through a questionnaire. Cancer incidence was ascertained through linkage with the Netherlands Cancer Registry (1989-July 2018). Ovarian cancer risk in the cohort was compared between the ART group and non-ART group using multivariable time-dependent Cox regression analyses.

Main results and the role of chance:

After a median follow-up of 22 years 143 invasive ovarian cancers were observed in the entire cohort, 108 in the ART group (36/10,000) and 35 in the non-ART group (35/10,000). The risk of ovarian cancer in ART-treated women was not increased (hazard ratio (HR): 1.03, 95% confidence interval (CI) 0.70-1.52) compared with the non-ART group. In addition, no trend emerged with a higher number of ART cycles (1-2 cycles HR:1.23, 95% CI 0.79-1.91, 3-4 cycles HR:0.82, 95% CI 0.51-1.32, 5-6 cycles HR:0.77, 95% CI 0.40-1.50, >7 cycles HR: 1.50, 95% CI 0.80-2.80). The risk did also not increase after long follow-up (>25 years: HR: 1.03, 95% CI 0.37-2.88).

As expected, parous women had a reduced risk of ovarian cancer (HR: 0.57, 95% CI 0.41-0.80) compared with nulliparous women. Although there was no significant interaction between parity and ART, ovarian cancer risk tended to be slightly increased in parous women treated with ART compared to parous women not treated with ART (HR: 1.40, 95% CI 0.50-1.51), while among nulliparous women ART-treatment did not increase ovarian cancer risk (HR:0.87, 95% CI 0.80-2.42).

Limitations, reasons for caution:

Risk of borderline tumours could not yet be analysed because data collection through the nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA) is currently being completed. The final results, including the risk of borderline ovarian tumours, will be available for presentation at the ESHRE conference.

Wider implications of the findings:

This large study, with an internal comparison group of subfertile women not treated with ART, importantly contributes to knowledge of the long-term risks of ART. The reassuring results with respect to invasive ovarian cancer can be used to inform couples who are contemplating to start or continue with ART.

Trial registration number:

not applicable