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PROSPECTIVE NATIONWIDE STUDIES ON THE ONCOLOGIC AND REPRODUCTIVE OUTCOME OF WOMEN TREATED WITH FERTILITY-SPARING SURGERY FOR OVARIAN CANCER AND BORDERLINE TUMORS

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We have recently reported the results of three prospective studies on the safety and efficacy of fertility-sparing surgery (FSS) in young women with ovarian cancers and borderline tumors in Sweden (1,2,3). The studies have been conducted using an epidemiological study design, which is feasible in the Nordic countries by using the data from population-based registries. In addition to Sweden and the remaining Nordic countries, there are only a few other countries in the world that have population-based registration of nationwide coverage, such as the U.K. or the Netherlands, where this kind of studies can be performed.

In our studies, the data from the Swedish National Quality Registry for Gynecological Cancer (SQRGC), which started in 2008 and collects data on all cases of gynecologic cancer from date of diagnosis in the whole country were accessed. The data are prospectively collected in the registry and include detailed information on the diagnostic methods applied, review of pathology reports, surgical techniques applied, individuals' treatment and relevant clinical outcomes of disease progression during follow-up. We could thus examine in this cohort if there is any difference in survival rates between women who receive fertility-sparing surgery (FSS), defined as the preservation of the uterus and at least part of one ovary, versus women who undergo radical surgery (RS), where the reproductive organs are removed completely.

Swedish citizens are also assigned a unique individual number at birth, which also allowed the linkage of individuals among additional population-based registries for this research. Hence, we could link our population of interest to their data collected in the Swedish Medical Birth Register, for detailed data on pregnancy and delivery, and to the Quality Registry for Assisted Reproductive Technology, ART, treatment (Q-IVF), for information on the use of ART after FSS. The first step was to identify in the SQRGC all women that were 18-40 years of age at time of diagnosis of early stage (stage 1) Epithelial Ovarian Cancer (EOC), Non-Epithelial Ovarian Cancer (NEOC) or Borderline Ovarian Tumors (BOT) between 2008 and 2015 in Sweden. The Swedish population has gone from 9 to 10 Million during the study period. In this context, the analytical cohort obtained was composed of 433 women with complete data, out of 493 identified in the SQRGC. The group that was excluded due to incomplete data did not differ from the analytical cohort with regards to age, tumor type or stage. Histologic reviews by a reference pathologist and a multidisciplinary conference including tumor surgeons, oncologists, radiologists, and pathologists were performed in 95% of patients with ovarian cancer and 88% of those with BOT.

Of the 83 women with EOCs, 43% underwent FSS. Women who underwent RS were significantly older, had higher parity, were more often diagnosed in stage IC (62% vs. 25%), had tumors of higher malignant potential, were more often surgically staged with lymph node dissections, and were more likely to receive chemotherapy. The full article is available with open access: (1)

Of the 73 patients with NEOCs, 78% underwent FSS. Women who underwent RS were older, had higher parity, and were more often surgically staged with lymph node dissections. The full article is available with open access: (2)

Of the 277 patients with BOTs, 77% underwent FSS. These women were younger compared to those who underwent RS. Of the 213 women with BOTs treated by FSS, 11 (5%) received a cystectomy (4 stage IA, 2 stage IB, 5 stage IC); the remaining 202 women (95%) had a unilateral salpingo-oophorectomy. The full article is available with open access: (3)

The 5-year overall survival (OS) rates among women treated for EOC, NEOC, and BOT, regardless of surgical procedure performed, were 92%, 98% and 99%, respectively. The 5-year progression-free survival (PFS) rates for EOC and NEOC, regardless of surgical procedure performed, were 88% and 96%, respectively. In general, recurrence rates were higher for high-grade tumors (14%) compared to low-grade tumors (7%), regardless of surgical approach. The highest recurrence rate was seen in high-grade tumors treated with RS, where 5 out of 26 recurred (19%); all 5 had also received adjuvant chemotherapy.

Regarding reproductive data, our analyses indicated that conception abilities were preserved by FSS and women presented with acceptable conception rates. The specific details on reproductive outcome according to diagnosis are available in the respective publications (1,2,3). Due to the lack of information on how many women attempted conception during the study period but did not achieve a live birth, we were not able to calculate a pregnancy rate. However, the data from the Q-IVF could be used as an infertility indicator for women in the cohort desiring pregnancy, due to the availability of fertility treatments in Sweden and the coverage of the Q-IVF. The use of ART in our cohort was unfrequent and most of these women had treatments performed with their own eggs. Of those who gave birth, very few received ART treatments.

Our nationwide, population-based cohort study found that the use of FSS in women of fertile age with early-stage ovarian cancer or borderline tumors who wished to preserve their fertility was not associated with poorer survival outcomes than those of women who underwent RS. The 5-year OS rates after FSS were 99%, 98%, and 92% for BOT, NEOC, and EOC, respectively. Relapses

were generally rare, but occurred more frequently in the RS group, suggesting that disease characteristics are more important for prognosis than surgical approach. The use of FSS was associated with preserved natural fertility in this cohort and the use of ART was relatively infrequent.

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