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Survival of selected patients with ovarian cancer treated with fertility-sparing surgery

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KEY MESSAGE

This study supports the current recommendation to consider fertility-sparing surgery in young women with stage I epithelial ovarian cancer who wish to preserve their fertility.

A B S T R A C T

Research question: How many patients in Denmark were treated with fertility-sparing surgery (FSS) for epithelial ovarian cancer (EOC) and what was their prognosis compared with patients treated with radical surgery (RS)?

Design: This study was a retrospective Danish nationwide study, evaluating the effect of FSS compared with RS in patients with EOC, age ≤45 years and International Federation of Gynecology and Obstetrics (FIGO) stage ≤IC3 from 2005 to 2016.

Results: A total of 106 patients were included. Of these, 13 were treated with FSS and 93 were treated with RS. Median age was 27 versus 42 years ($P < 0.0001$). Overall survival did not differ significantly between the two groups. Overall survival rate in the FSS group was 100%, while the overall survival in the RS group was 87%. Disease-specific survival was 100% in the FSS group and 91% in the RS group.

Conclusions: This study shows that patients treated with FSS for FIGO stage I EOC do not have an impaired survival compared with patients treated with RS. Nevertheless, the conclusion must be interpreted with caution due to the limited number of patients and the retrospective nature of the study. Larger studies are needed before conclusions can be drawn.

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Introduction

Ovarian cancer is often a deadly disease, because most patients are diagnosed in an advanced stage. Only about a quarter of patients are detected in International Federation of Gynecology and Obstetrics (FIGO) stage I, where the 5-year survival is approximately 75–87% (Rosendahl et al., 2016).

Although ovarian cancer is primarily diagnosed in post-menopausal women, a significant minority afflicts women of childbearing age. Thus, roughly 10% of epithelial ovarian cancers (EOC) are diagnosed in women younger than 40 years of age (Duska et al., 1999). Due to current social trends, childbearing is increasingly postponed (Cooke et al., 2012) and the number of young women who present with EOC, and who have not yet completed their family building plans, may therefore increase. It is therefore relevant to consider preservation of fertility in these patients, depending on the desire of these women to have children.

Current international guidelines state that the surgical standard of care for patients with epithelial ovarian tumours is radical surgery (RS), which encompasses a bilateral salpingo-oophorectomy, hysterectomy, omentectomy, pelvic and para-aortic lymphadenectomy, removal of all visible peritoneal carcinomatosis as well as visceral metastases (Heintz et al., 2006; Redman et al., 2011). This approach is regarded as the most effective in ensuring radical tumour removal, and it is imperative in advanced disease. However, RS in women with stage I disease will also result in permanent sterility, and thus eliminate the possibility of future pregnancies.

Indeed, in women with EOC in FIGO stage I, who have a desire to preserve fertility, there is a possibility of fertility-sparing surgery (FSS). The procedure consists of a unilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, peritoneal biopsies and omentectomy, but leaves the contralateral ovarium and the uterus *in situ*, thereby preserving fertility (Bentivegna et al., 2015). In this selected group of women with stage I EOC it has previously been demonstrated that the less extensive surgical approach does not lead to an increase in mortality, poorer overall survival, or shorter disease-free survival (Ditto et al., 2015; Fruscio et al., 2016; Kajiyama et al., 2011; Wright et al., 2009).

In Denmark, the experience with FSS is limited, and it is not known whether the previously reported survival results apply to a Danish population. Also, there are no published reports revealing the number of patients that have been treated with FSS in Denmark. The aim of this study was therefore to review how many patients with EOC were treated with FSS, and whether these women had the same prognosis as women treated with RS in patients diagnosed with stage I EOC.

Materials and methods

Patients

All Danish women diagnosed with EOC from 2005 to 2013 were included. All surgical data were derived from the Danish Gynecological Cancer Database (DGCD), a nationwide cancer database that contains pre-, peri- and post-operative data on all Danish patients undergoing surgery for ovarian cancer. Pathology data were extracted from the Danish Pathology Register (PatoBank), and survival data were extracted from the National Patient Register (NPR) (Bjerregaard and Larsen, 2011; Lynge et al., 2011; Sorensen et al., 2016). Last day of follow-up was 14 August 2016. Data were provided from the DGCD, and approved on 10 February 2010 by the Danish Data Protection Agency (reference number: 2007-58-0014). As this was a retrospective cohort study based on data from a national database, it was not necessary under Danish law (NN) to obtain ethical approval.

Exclusion criteria were age >45 years and FIGO stage II–IV. Four patients were excluded due to synchronous cancers (one endometrial cancer, one pancreatic cancer and two breast cancer). The ovarian cancer was staged according to the 2013 FIGO classification (https://www.sgo.org/wp-content/uploads/2012/09/FIGO-Ovarian-Cancer-Staging_1.10.14.pdf).

FSS was defined as an operation that resulted in preservation of the uterus and the contralateral ovary. Patients who had undergone a prior hysterectomy and/or removal of the contralateral ovary were not included in the FSS group, and therefore included in the RS group.

According to the Danish national guidelines at the time of the study, adjuvant chemotherapy was offered to patients with stage IA–IB EOC with a grade 2 or 3 epithelial carcinoma, and all patients with FIGO stage IC, post-operatively (DGCG). The standard chemotherapy regimen at the time of treatment was 3–6 series of a carboplatin combined with a taxane.

Information regarding ovarian endocrine function and post-treatment fecundity was unavailable.

Statistical analysis

Statistical analyses were performed in SPSS (IBM SPSS Statistics for Windows, Version 22.0; Armonk, NY). To compare baseline characteristics between FSS and RS, the Pearson chi-squared test was used to evaluate categorical variables, and the Mann–Whitney *U*-test to compare the median age at diagnosis. To illustrate survival, Kaplan–Meier curves were constructed, and difference in survival was compared in a log-rank test. Five-year overall and disease-specific survival was derived from Kaplan–Meier life tables. Due to the low *number of events (deaths), it was not considered appropriate to perform a multivariate Cox regression analysis* (Peduzzi et al., 1996). *Overall survival was defined as time from diagnosis to death due to any cause. Patients who were alive at the last day of follow-up were censored at this date. Disease-specific survival was defined as time from diagnosis to death due to EOC. Patients were censored at the last day of follow-up or at the date of death from other causes than EOC.* A two-sided *P*-value <0.05 was considered statistically significant.

Results

Patients

From a total of 5365 patients diagnosed with EOC in Denmark from 2005 to 2013, 106 met the inclusion criteria (**Figure 1**). Of these 106 patients, 13 (12%) were treated with FSS and 93 (88%) with RS. Baseline characteristics of the women in the two groups are shown in **Table 1**. There were no significant differences in the baseline data between the two groups except for age; it was observed that patients undergoing FSS were younger than patients undergoing RS (**Table 1**). Median age at diagnosis for the FSS group was 27 years (range 13–44 years), while it was 42 years (range 15–45 years) in the RS group ($P < 0.0001$).

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