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Fertility-sparing surgery for treatment of non-epithelial ovarian cancer: Oncological and reproductive outcomes in a prospective nationwide population-based cohort study

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HIGHLIGHTS

- Overall survival rate for women of reproductive age with early-stage non-epithelial ovarian cancer is excellent.
- Outcomes after fertility-sparing surgery appear equivalent to radical surgery in Stage I non-epithelial ovarian cancer.
- Natural fertility is maintained after fertility-sparing surgery for early-stage non-epithelial ovarian cancer.
- The obstetrical outcome is not affected in women undergoing fertility-sparing surgery for non-epithelial ovarian cancer.

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ABSTRACT

Objective: To compare the oncologic outcome of women who underwent fertility-sparing surgery (FSS) vs. radical surgery (RS) for treatment of NEOC in a prospective, nationwide, population-based study and report on the reproductive outcomes in women after FSS.

Methods: Using the Swedish Quality Register for Gynecological Cancer, we identified all women ages 18–40 treated with either FSS or RS for stage I NEOC between 2008 and 2015. Progression-free survival (PFS) and overall survival (OS) rates were compared using the Kaplan-Meier method. Data on use of assisted reproductive technology (ART) treatments and obstetrical outcomes after FSS were extracted from the National Quality Register for Assisted Reproduction (Q-IVF) and the Swedish Medical Birth Register.

Results: During the study period, 73 women ages 18–40 received a stage I NEOC diagnosis. The majority, 78% ($n = 57$), underwent FSS. The 5-year OS rate, regardless of surgical approach, was 98%. There were no statistical differences between OS and PFS rates in women treated with FSS, compared to RS. Recurrences were more common after RS than FSS: 12.5% (2/16) vs. 3.5% (2/57), respectively. Following FSS, 11 women gave birth to 13 healthy children (all conceived naturally). Additionally, 12% of the women in the cohort developed infertility and received ART treatment ($n = 7$).

Conclusion: FSS is not associated with worse oncologic outcomes than RS in young women with early stage NEOC. The prognosis was excellent in both groups, with an OS of 98%. Natural fertility was maintained in women treated with FSS, only 12% required ART treatment.

1. Introduction

Non-epithelial ovarian cancer (NEOC), including sex cord stromal tumors (SCSTs) and germ cell tumors (GCTs), is often diagnosed in girls and young women of fertile age. Fertility preservation is recognized as an important aspect of quality of life of women of

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reproductive age treated for cancer [1], and fertility-sparing surgery (FSS) is the current standard of care in early stages of NEOC.

In GCTs, which are usually unilateral [2] and primarily affect children and very young women, FSS is the current standard even at advanced stages. This is supported by the fact that GCTs are highly chemo-sensitive, and the prognosis is generally good [2–7]. Additionally, adjuvant chemotherapy for GCTs has a recognized, low gonadotoxic effect, and women maintain menstrual cycles in 90–97% of cases [8–10]. The reported conception rate is heterogeneous and varies from 16 to 59% [6,7,9,11,12], while the reported pregnancy rate varies from 67 to 100% [6,7,9,11,12].

Regarding SCSTs, FSS is considered safe for treatment of early stage tumors [5,13] in selected and well-informed patients [14], but it is not recommended in advanced stages of the disease [5]. Adjuvant chemotherapy for SCSTs is controversial [2] and may not improve the prognosis [13,14]. Data on reproductive and obstetrical outcomes after treatment of SCSTs are sparse, with small patient volumes and lack of multicenter studies [8].

To date, there are no prospective studies published in this field. In general, in previous studies, no control group of women undergoing RS has been used for investigation of oncologic outcomes, and detailed information on procedures for surgical staging, tumor grade, and histological subtype has not been provided. Additionally, there are few reports on the use of assisted reproductive technology (ART) treatment.

Sweden has nationwide mandatory cancer registration and prospective population-based quality registries for gynecologic cancer, a medical birth registry and a national registry for ART, with detailed collected data. Using those registries we conducted a nationwide, population-based cohort study to investigate the oncological outcomes of women who have undergone FSS or RS for early stage NEOC. In women who have undergone FSS we also investigated the reproductive outcomes and performance of ART treatment.

2. Patients and methods

2.1. Patients and study design

The study includes all women 18–40 years old who were registered in the Swedish Quality Register for Gynecological Cancer (SQRGC) between 2008 and 2015 after a confirmed diagnosis of stage I NEOC. The SQRGC was initiated in 2008 and contains information on clinical, surgical, and oncological variables, pathology review, outcomes, and follow-up, together with mortality data, all prospectively and consecutively collected. In Sweden, it is compulsory to report every incidence of cancer to the National Swedish Cancer Register, which covers 98% of all malignant tumors [15]. The SQRGC has a 94% coverage rate; the validity of recorded data has been assessed, and the agreement of variables is close to 100% [15].

We used the 10-digit personal identification number assigned to all Swedish citizens and linked individuals to the National Death Register, to ensure lifelong follow-up and date of death, and to the Swedish Medical Birth Register, to obtain obstetrical data. The Swedish Medical Birth Register was founded in 1973 and includes data on all deliveries in Sweden. It is compulsory to report births to the register, and information from standardized prenatal, delivery, and neonatal care is collected from the medical records. For information on ART treatment, such as use of in vitro fertilization (IVF), linkage to Q-IVF was performed. Q-IVF was founded in 2007 and includes data on all assisted reproductive treatment given in Sweden with a coverage of 100% of treatments [16]. In Sweden, fertility treatments are provided within the health care system, free of charge to all citizens, up to the woman's age of 40. However, women without a partner could not apply for fertility treatment in Sweden before 2017.

Tumor classification was performed according to the World Health Organization criteria [17], the updated classification system was used after 2014. Tumor stage was determined using the FIGO system [18], and stage IC tumors were further classified as IC1 (surgical spillage), IC2 (capsule rupture before surgery or presence of tumor on the ovarian surface), or IC3 (positive cytology). All women were staged according to the 2014 classification. Data on procedures for staging including intraoperative findings were extracted from the SQRGC. According to the Swedish National Healthcare program for management of NEOC, the preoperative investigations include a thorax-abdominal CT scan [18].

FSS was defined as the preservation of the uterus and at least a part of one ovary. RS was defined as the performance of bilateral oophorectomy and hysterectomy. Patients known to be alive were censored at the time of data retrieval (July 27, 2017). Overall survival (OS) was calculated from the date of diagnosis to the date of death from any cause or the date of data retrieval. Progression-free survival (PFS) was defined as the time from diagnosis to the first appearance of relapse or the date of death from any cause. Patients known to be free of relapse were censored at the time of data retrieval. Medical records were reviewed when patient registration records were incomplete. For detailed data concerning relapses, all medical records were reviewed. The ethical review board at Karolinska University approved the study (Dnr 2016/1161–31/2).

2.2. Statistical analysis

The Student's *t*-test and ANOVA were used for comparison of continuous variables. Categorical variables were evaluated using Fisher's exact test, as appropriate for each category size. All comparisons were 2-sided, and a 5% level of significance was used. Statistical analysis was performed using Stata statistical software (Macintosh version 13.1) [19]. Estimation of relative survival was performed using R statistics software (Macintosh version 3.4.3) with the “survival” package (2.41.3). PFS and OS were analyzed using the Kaplan-Meier method.

3. Results

3.1. Patients

The study encompassed 73 women with complete data identified in the SQRGC. The patient flow chart is shown in Fig. 1. The 10 patients who were excluded due to incomplete data did not differ from the study cohort regarding age, histopathological type, or stage. Histologic reviews by a pathologist with expertise in gynecologic oncology and a multidisciplinary conference that included tumor surgeons, oncologists, radiologists, and pathologists were performed for 92% (67/73) of the patients.

Of the 73 patients, 78% ($n = 57$) underwent FSS. The 16 women who underwent RS were older, had significantly higher parity (previous children, $p < 0.001$), had more often undergone open surgery and re-staging surgery, and were more often surgically staged with lymph node dissections. The histopathological types reported in the RS and FSS groups are shown in Table 1. Women who had undergone RS had a longer follow-up, compared to the women who underwent FSS: 72 months (ranging from 21 to 111 months) and 65 months (ranging from 20 to 111 months), respectively (Table 1).

3.2. Oncological outcomes

The 5-year OS rate, for the total cohort, was 98% (Fig. 2a). A comparison of the 5-year OS rates is shown in Fig. 2b; the 5-year OS rates were 100% and 92% after FSS and RS, respectively. The 5-year PFS rate, regardless of surgical procedure performed, was 96% (Fig. 2c). Fig. 2d shows the 5-year PFS rates after FSS (98%) and RS (87%), and Fig. 2e compares this data according to tumor stage. The 5-year PFS rates were 100%, 92%, 82%, and 100% for FSS stage IA, FSS stage IC, RS stage IA, and RS stage IC, respectively.

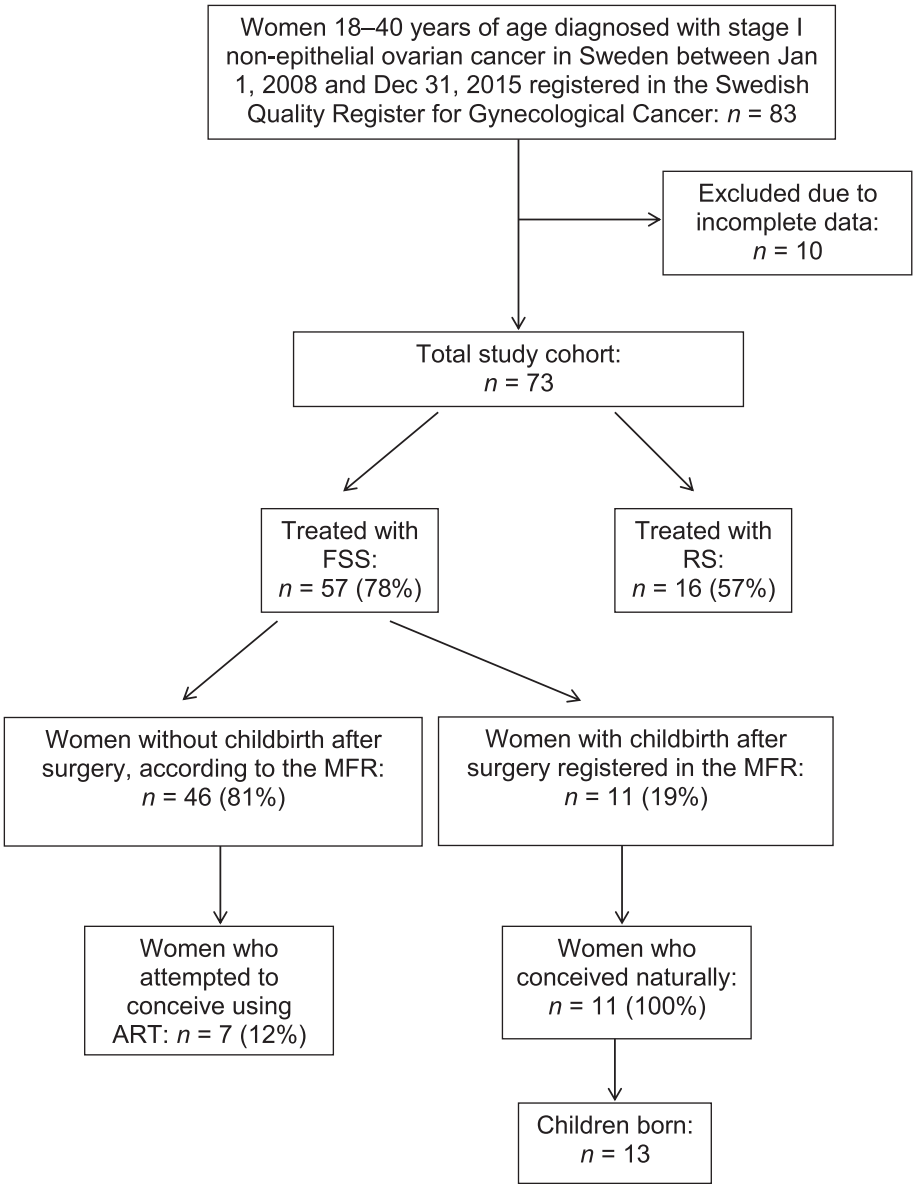

Fig. 1. The patient flow chart. FSS: fertility-sparing surgery; RS: radical surgery; MFR: Swedish Medical Birth Register; ART: assisted reproductive technology.

Recurrences were diagnosed in four women (5%); 3.5% (2/57) had a recurrence after FSS, and 12.5% (2/16) had a recurrence after RS (Table 2). None of the women who had recurrences had received adjuvant chemotherapy. Of the two women who underwent FSS and experienced a recurrence, one had a granulosa cell tumor stage IC1 and was diagnosed with both local (in the spared ovary and uterus) and distant metastasis 30 months after primary treatment. She was treated with surgery and six cycles of carboplatin and paclitaxel but was diagnosed with liver metastasis 26 months later. She was alive, with the disease, at the time of data analysis. The other woman was treated for an immature teratoma; she recurred with peritoneal carcinomatosis, which was successfully treated with four cycles of bleomycin, etoposide, and cisplatin (BEP). The two women who underwent RS and experienced a recurrence had GCTs. One was treated successfully with surgery and four cycles of BEP. The second woman did not respond to chemotherapy and died of the disease 18 months later—42 months after primary treatment (Table 2). Another woman died during the study period, due to a malignant melanoma diagnosed 59 months after RS for a granulosa cell tumor.

3.3. Reproductive outcomes

Of the 57 women who underwent FSS, 19% ($n = 11$) gave birth after surgery, at a mean age of 31.8 years and with a mean follow-up time after cancer treatment of 42 months (ranging from 10 to 79 months). There was no difference in mean age between those who had given birth after FSS and those who had not. Women who had given birth had a significantly longer follow-up than women who had not given birth after surgery: 84 months (ranging from 34 to 111 months) and 61 months (ranging from 20 to 105 months), respectively (Table 3). In the total cohort of 57 women who underwent FSS, 12% ($n = 7$) were registered to have received ART treatment; none of them had given birth.

3.4. Obstetrical outcomes

A total of 13 children were born to 11 women. No congenital malformations were registered, and all deliveries were full-term. Information on obstetrical outcomes is shown in Table 4.

Table 1
Demographics, clinical and tumor characteristics at diagnosis, surgical data, and oncological treatment and outcomes for women 18–40 years old diagnosed with non-epithelial ovarian cancer in Sweden 2008–2015.

	Treated with FSS	Treated with RS	*P*-value
N (%)	57 (78)	16 (22)	
Mean age, years (range)	29 (19–40)	34 (19–40)	0.0016
Previous parity, n (%)			<0.001
0	43 (75)	4 (25)	
1	8 (14)	0	
2	6 (11)	5 (31)	
≥3	0	6 (38)	
FIGO stage, n (%)			0.537
IA	41 (72)	13 (81)	
IB	–	–	
IC	16 (28)	3 (19)	
IC1	*9*	*1*	
IC2	*3*	*1*	
IC3	*3*	*1*	
IC unspecified	*1*	*0*	
Histologic type, n (%)			
Immature Teratoma	16 (28)	3 (19)	
Grade 1	5	*2*	
Grade 2	4	*0*	
Grade 3	3	*0*	
Dysgerminoma	7 (12)	3 (19)	
Granulosa cell	19 (33)	6 (38)	
Yolk sac	3 (5)	1 (6)	
Sertoli-Leydig	7 (12)	2 (13)	
Grade 1	*3*	*1*	
Grade 2	*3*	*0*	
Grade 3	*0*	*1*	
Carcinoma Struma Ovarii	3 (5)	0	
Other [a]	*2 (4)*	1 (6)	
Surgical mode,[b] n (%)			0.002
Open	38 (67)	15 (94)	
Laparoscopy	19 (33)	0	
Robot	0	1 (6)	
Type of surgery, n (%)			0.004
Primary	45 (79)	6 (38)	
Re-staging	12 (21)	10 (62)	
Type of staging procedure, n (%)			
Cytology	42 (74)	14 (88)	
Peritoneal biopsies	34 (60)	14 (88)	
Omental biopsy	33 (58)	15 (94)	
LN pelvic	7 (12)	6 (38)	
LN paraaortic	6 (11)	5 (31)	
Adjuvant chemotherapy, n (%)	18 (32)	5 (31)	1.00
Histologic review,[c] n (%)	54 (95)	13 (81)	0.115
Recurrence, n (%)	2 (4)	2 (13)	
Died of disease, n (%)	0	1 (6)	
Follow-up, months, mean (range)	65 (20–111)	72 (21–111)	0.132

[a]Small cell carcinoma, embryonal carcinoma, neuroendocrine tumor; [b]If primary surgery is laparoscopic and re-staging laparotomy, patient is classified as laparotomy; [c]Histologic review by a pathologist with expertise in gynecologic oncology; FSS: fertility-sparing surgery; RS: radical surgery; LN: lymph node.

4. Discussion

This is the first prospective study reporting on both the safety and efficacy of FSS for treatment of stage I NEOC, a rare disease. Sweden has a population that has grown from 9.3 to 9.9 million between 2008 and 2015 [20]. Using a population-based registry, we were able to identify 73 young women with complete data during that period of time. The 98% OS rate in the total cohort should be considered acceptable and within the expected range. The 5-year PFS rate was 96%, with a total recurrence rate of 5% (4/73). Even with this small sample size, the recurrence rate was lower after FSS (3.5%, 2/57) than after RS (12.5%, 2/16), indicating that the patients' prognoses are not impaired by FSS when patient selection is performed. There were no significant differences found between patients who underwent FSS, compared to RS, regarding the proportion of tumors with high malignancy potential, more advanced stages (such as IC), or the use of adjuvant chemotherapy that could explain this difference. Three out of four recurrences were diagnosed in patients with stage IA GCTs treated with surgery alone as the primary treatment. The Swedish national guidelines for NEOC [21] do not recommend adjuvant chemotherapy, either for treatment of stage IA dysgerminoma or stage IA, grade 1 immature teratoma. One of the patients with a recurrence had an immature teratoma grade 3 and should have received adjuvant chemotherapy, according to the national guidelines. Her recurrence was successfully treated with BEP, supporting the use of adjuvant chemotherapy in these tumors [5]. There was only one local recurrence in the uterus and the spared ovary diagnosed in a woman who underwent FSS for a stage IC1 granulosa cell tumor. Unfortunately, she had a second recurrence after surgery and chemotherapy. The response rate after chemotherapy for recurrent SCSTs varies in different studies [13]. Colombo et al. stated that >70% of patients with recurrent granulosa cell tumors will die of the disease [13]. The recurrence rate for granulosa cell tumors in our cohort of women undergoing FSS was 5% (1/19). Adjuvant chemotherapy is not recommended in stage I granulosa cell tumors, according to the national guidelines [21]. In a review by Iavazzo et al. of FSS for granulosa cell tumors, they recommended FSS only in well-selected patients after informed consent. RS is suggested after completion of family planning [14]. However, Iavazzo et al. stated that their data is based on a small number of retrospective studies and requested data from better-organized studies, in order to raise safe conclusions [14]. Little information exists about reproductive outcomes after FSS in granulosa cell tumors [14].

Our data indicate that the ability to conceive is preserved by using FSS, which supports the feasibility of FSS for treatment of young women with stage I NEOC. In our cohort, 19% ($n = 11$) of the women undergoing FSS conceived. All conceptions were natural, and all deliveries occurred at full-term. Importantly, the obstetrical outcomes were not affected, regardless of whether the women had received adjuvant chemotherapy (36%). Due to the lack of information on how many women had tried to conceive during the study period but did not achieve a pregnancy, we were not able to calculate the pregnancy rate in the cohort. However, the data from Q-IVF might be considered and used as an indicator for infertility in the cohort, since in Sweden, fertility treatments are provided within the health care system, free of charge to all women below an age limit of 40 years. Although, women without a partner could not apply for fertility treatment in Sweden before 2017. The use of ART treatment in our cohort was 12% ($n = 7$), which could be considered comparable to a normal population. There are only a few cases reported in the literature on the use of ART treatment after FSS for NEOC [8].

The studies of women conceiving after FSS for treatment of GCTs are heterogeneous, and reported rates vary between 16 and 59% [6,11,12]. Pregnancy rates are reported as between 67 and 100% [7,9,11,12]. A retrospective study by Zanetta et al. reported that 22% of women who underwent FSS without adjuvant chemotherapy tried to conceive, with a pregnancy rate of 100%. Of the women who underwent FSS and had received adjuvant chemotherapy, 27% tried to conceive; 80% succeeded [7]. Similarly, de La Motte Rouge et al. reported a pregnancy rate of 75% in 16 women trying to conceive after FSS and adjuvant chemotherapy for yolk sac tumors [9]. In a retrospective study by Tangir et al., the conception rate was a bit higher (59%), which could be explained by the long follow-up period, with a mean of 122 months. The pregnancy rate (76%) was similar to the other studies [12].

In our prospective cohort study, the follow-up time was significantly (23 months) longer in women who gave birth after FSS, compared to those who did not (84 vs. 61 months, respectively; $p \leq 0.001$). A possible explanation for this might be that, in many cases, women delay childbearing, due to fear of recurrence, or perhaps this is related to a non-active desire for pregnancy. The

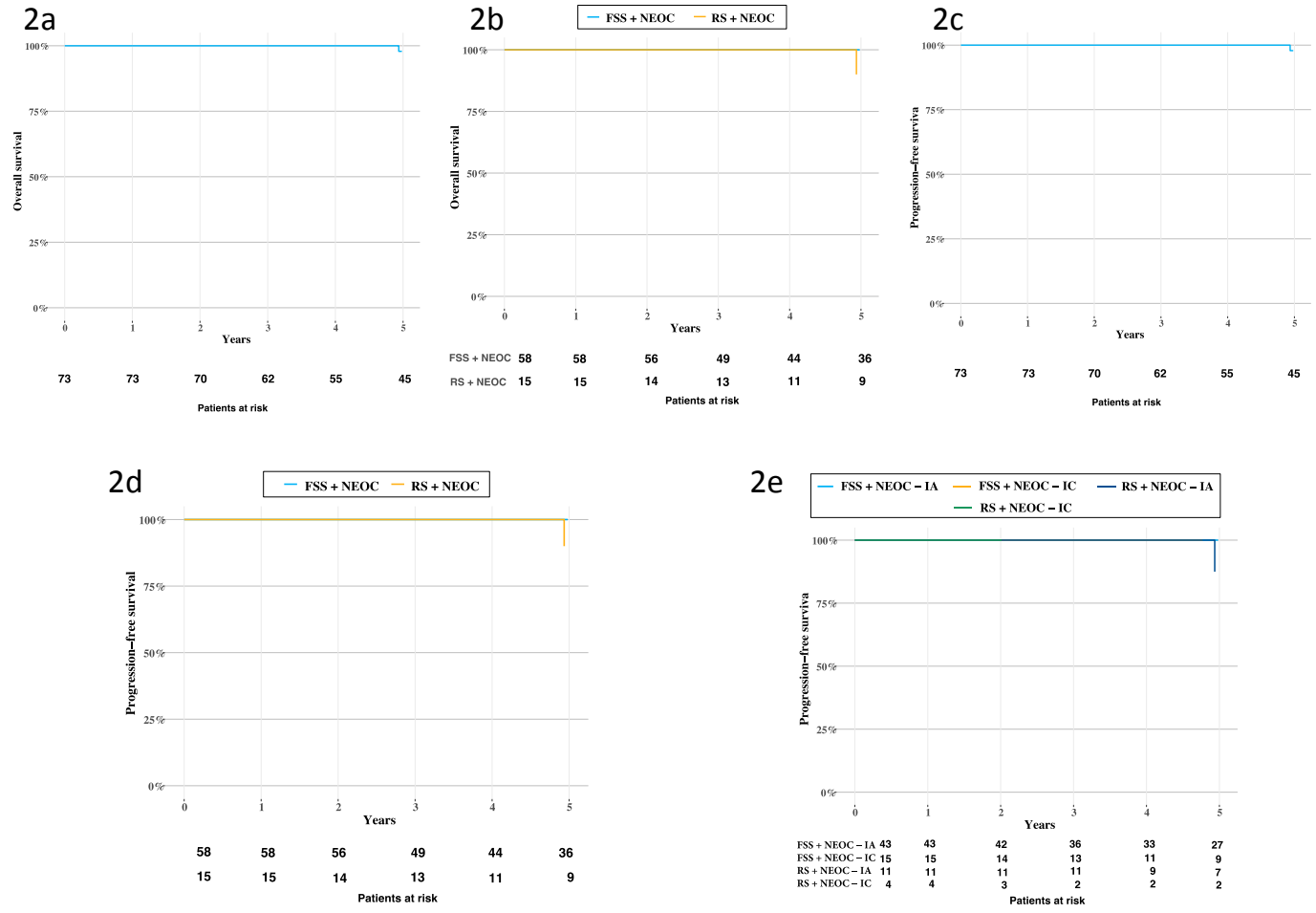

Fig. 2a. ive-year overall survival (OS) rate for women 18–40 years old with stage I non-epithelial ovarian cancer (NEOC). The 5-year OS rate was 98%. Patients at risk are shown under the curve. **Fig. 2b**. Five-year overall survival (OS) rates for women 18–40 years old with stage I non-epithelial ovarian cancer (NEOC) treated with fertility-sparing surgery (FSS) and radical surgery (RS). The 5-year OS rates are 100% for FSS and 92% for RS. Patients at risk are shown under the curve. **Fig. 2c**. Five-year progression-free survival (PFS) rates for women 18–40 years old with stage I non-epithelial ovarian cancer (NEOC). The 5-year PFS rate is 96%. Patients at risk are shown under the curve. **Fig. 2d**. Five-year progression-free survival (PFS) rates for women 18–40 years old with stage I non-epithelial ovarian cancer (NEOC) treated with FSS and RS. The 5-year PFS rates are 98% for FSS and 87% for RS. Patients at risk are shown under the curve. **Fig. 2e.** Five-year progression-free survival (PFS) rates for women 18–40 years old treated with FSS and RS for FIGO stages IA and IC non-epithelial ovarian cancer (NEOC). The 5-year PFS rates are as follows: FSS IA–100%; FSS IC–92%; RS IA–82%; and RS IC–100%. Patients at risk are shown under the curve.

Table 2
Details on recurrences and cause of death in women 18–40 years of age, diagnosed with stage I non-epithelial ovarian cancer between 2008 and 2015.

#	Age	FIGO stage	Histology	Grade	FSS	Adjuvant chemo	Recurrence	Time to recur. (months)	Site of recurrence	Treatment at recur.	Follow-up after recur. (months)	Status	Time from treatment to death (months)	Cause of death
1	37	IC1	Granulosa cell	–	Yes	No	Yes	30	Peritoneal & pelvic cavity	Surgery + chemo	34	AWD	–	
2	20	IA	Immature teratoma	3	Yes	No	Yes	6	Peritoneal	Chemo	68	NED	–	
3	39	IA	Dysgerminoma	–	No	No	Yes	22	Abdominal wall & pelvic LN	Surgery + chemo	22	NED	–	
4	39	IA	Immature teratoma	–	No	No	Yes	22	Liver, bone, paraaortic & sub-clavicular LN	Chemo	18	DOD	42	DOD
5	39	IA	Granulosa Cell	–	No	No	No	–	–	–	–	DEAD	59	Malignant melanoma
Total, mean (range)	35 (20–39)	IA (80%) IC (20%)						20 (6–30)			36 (18–68)		51 (42–59)	

FSS: fertility-sparing surgery; RS: radical surgery; LN: lymph node; NED: no evidence of disease; AWD: alive with disease; DOD: died of disease.

Table 3
Demographics, clinical and tumor characteristics at diagnosis, surgical data, and oncological outcomes for women 18–40 years old who either had or had not given birth after undergoing FSS for non-epithelial ovarian cancers in Sweden 2008–2015.

	Given birth after FSS	Not given birth after FSS	*P*-value
N (%)	11 (19)	46 (81)	
Mean age, years (range)	28 (20–37)	29 (19–40)	0.749
Previous parity, n (%)			
0	11 (100)	32 (70)	0.174
1	0	8 (17)	
2	0	6 (13)	
FIGO stage, n (%)			1.00
IA	8 (73)	33 (72)	
IB	0	0	
IC	3 (27)	13 (28)	
IC1	*2*	*7*	
IC2	*0*	*3*	
IC3	*1*	*2*	
IC unspecified	*0*	*1*	
Histologic type, n (%)			
Immature Teratoma	2 (18)	14 (30)	
Grade 1		*5*	
Grade 2		*4*	
Grade 3		*3*	
Dysgerminoma	1 (9)	6 (13)	
Granulosa cell	3 (27)	16 (35)	
Yolk sac	0	3 (7)	
Sertoli-Leydig	2 (18)	5 (11)	
Grade 1	*1*	*2*	
Grade 2	*1*	*2*	
Grade 3	*0*		
Carcinoma Struma Ovarii	2 (18)	1 (2)	
Other[a]	1 (9)	1 (2)	
Surgical mode,[b] n (%)	8 (73)	30 (65)	0.735
Open	3 (27)	16 (35)	
Laparoscopy			
Type of surgery, n (%)	11 (100)	34 (74)	0.097
Primary	0	12 (26)	
Re-staging			
Type of staging procedure, n (%)			
Cytology	8 (73)	34 (74)	
Peritoneal biopsies	6 (55)	28 (61)	
Omental biopsy	4 (36)	29 (63)	
LN pelvic	2 (18)	5 (11)	
LN paraaortic	2 (18)	4 (9)	
Adjuvant chemotherapy, n (%)	4 (36)	14 (30)	0.728
Histologic review,[c] n (%)	11 (100)	43 (93)	1.00
Recurrence, n (%)	0	2 (4)	
Follow-up, months, mean (range)	84 (34–111)	61 (20–105)	0.012

[a]Small cell carcinoma, embryonal carcinoma; [b]If primary surgery is laparoscopic and re-staging laparotomy, patient is classified as laparotomy; [c]Histologic review by a pathologist with expertise in gynecologic oncology; FSS: fertility-sparing surgery; RS: radical surgery; LN: lymph-node.

mean time from cancer treatment to pregnancy was 42 months (ranging from 10 to 79 months). The time to pregnancy has not been reported in other studies.

A major strength of our study is the use of a nationwide, population-based cohort with high-quality, prospectively gathered data and cross-linkage with additional population-based registries, including the National Death Registry, to ensure lifelong follow-up. Information on important prognostic variables—such as tumor stage (substage IC), grade, and surgical procedure—was nearly 100% complete. Our study also benefited from the presence of a comparison group who underwent RS. Although some may argue that these groups are not comparable, we believe that comparing these groups give valuable information. Future studies should also try to compare comprehensive surgical staged patients in different histological subtypes since our cohort is to small to make such an analysis with outcome associations. Perhaps conducting future meta-analysis studies with details on surgery may add further valuable information how to treat young women with NEOC. In addition, the mean follow-up time of 65 months (ranging from 19 to 114 months) reduced the risk of underestimating recurrence or OS rates. The median time to recurrence and death was 20 months (ranging from 6 to 30 months) and 50 months (ranging from 41 to 59 months), respectively. Although, late recurrences are seen in granulosa cell tumors [13,14]. We also presented detailed information on obstetrical outcomes and the use of ART treatment after FSS and adjuvant chemotherapy.

Table 4
Obstetrical outcomes for women who underwent FSS for treatment of stage I non-epithelial ovarian cancer in Sweden 2008–2015.

	Number of patients	Children born
N	11	13
Age at time of delivery, mean (range)		31 (21–40)
Delivery mode, n (%)		
Vaginal		12 (92)
Planned CS[a]		0
Unplanned CS		1 (8)
Induced delivery[b]		2 (15)
Birth, n (%)		
Singleton		12 (100)
Twin		0
Gestational age at birth, mean (range)		39 + 6 (37 + 2 −42 + 1)
Child weight at birth, g, mean (range)		3431 (2390–4525)
Child length at birth, cm, mean (range)		50.5 (47–54)
Apgar score, mean (range)		
1 min		9 (9–9)
5 min		9.9 (9–10)
10 min		10 (10–10)

[a]Cesarean section; [b]Ended in vaginal delivery, n = 1; unplanned CS, *n* = 1.

5. Conclusions

This nationwide, prospective, population-based study found that the use of FSS for treatment of stage I NEOC in women of fertile age was not associated with poorer survival outcomes than the use of RS. The 5-year OS rate after FSS was 98%. Recurrences were generally rare, but occurred more frequently in the RS group and in patients who had not received adjuvant chemotherapy. GCTs generally respond well to chemotherapy, and the treatment does not seem to affect the fertility outcome. Therefore adjuvant chemotherapy should be carefully considered and discussed at a multidisciplinary conference. FSS may be indicated for women of fertile age with early-stage NEOC and a future fertility wish.

Author contributions

Conception and design: Kenny A. Rodriguez-Wallberg, Pernilla Dahm-Kähler, and Gry Johansen. Provision of study materials or patients: Gry Johansen, Christian Staf, and Pernilla Dahm-Kähler. Collecting and assembling data: Gry Johansen and Christian Staf. Financial and administrative support: Kenny A. Rodriguez-Wallberg. Data analysis and interpretation: all authors. Manuscript writing: all authors. Final approval of manuscript: all authors. Accountable for all aspects of the work: all authors.

Declaration of competing interest

The authors have nothing to disclose.

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