Gynecologic Oncology 141 (2016) 461–465

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Laparoscopic fertility-sparing surgery for early ovarian epithelial cancer: A multi-institutional experience

Fabio Ghezzi [a,*], Antonella Cromi [a], Francesco Fanfani [b], Mario Malzoni [c], Antonino Ditto [d], Pierandrea De Iaco [e], Stefano Uccella [a], Valerio Gallotta [f], Francesco Raspagliesi [d], Giovanni Scambia [f]

[a] Department of Gynecology and Obstetrics, University of Insubria, Varese, Italy
[b] Gynecologic Oncology Department of Medicine and Aging Sciences, University G. d'Annunzio of Chieti, Pescara, Italy
[c] Advanced Gynecological Endoscopy Center, Malzoni Medical Center, Avellino, Italy
[d] Department of Gynecologic Oncology, IRCCS Foundation, National Cancer Institute, Milan, Italy
[e] Minimally Invasive Gynaecological Surgery Unit, S. Orsola Hospital, University of Bologna, Bologna, Italy
[f] Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Catholic University of the Sacred Heart, Rome, Italy

HIGHLIGHTS

- Laparoscopic fertility-sparing treatment of early ovarian cancer shows *encouraging* survival outcomes.
- After conservative treatment, 64.8% woman reported pregnancy intent and 60% of these conceived spontaneously.

ARTICLE INFO

Article history:
Received 16 February 2016
Received in revised form 20 March 2016
Accepted 21 March 2016
Available online 13 April 2016

Keywords:
Early ovarian cancer
Laparoscopy
Surgical staging
Survival
Gynecologic oncology

ABSTRACT

Objective. There is as yet limited evidence about fertility-sparing surgery for early ovarian cancer (EOC) carried out laparoscopically. We sought to investigate the safety, adequacy and fertility outcome of ovarian cancer patients who underwent fertility-saving laparoscopic surgical staging using a multi-institutional sample.

Methods. Prospectively collected data in five gynecologic oncology service databases were searched for epithelial EOC patients undergoing laparoscopic fertility-preserving surgery. Surgical, pathologic, oncologic and reproductive outcome data were analysed.

Results. The study cohort consisted of 65 women. Median age of the patients was 33 (range: 21–42) years. In this cohort 36 (55.4%) and 29 (44.6%) patients were at low risk (FIGO stage IA G1–2) and high-risk (FIGO stage IA G3 or more), respectively. The disease was reclassified to a higher stage in 4 (6.1%) women. After a median follow up period of 38 months (range: 2–144), the overall survival was 95.4% and recurrence-free survival 84.6%. Overall, there were 23 pregnancies in 22 women. After ovarian cancer treatment, 64.8% women reported pregnancy intent and 60% of these conceived spontaneously.

Conclusions. Laparoscopic staging may represent a viable option for premenopausal women seeking fertility preservation in the setting of early ovarian cancer. More research is needed to determine whether laparoscopy may offer reproductive benefits to this particular population.

1. Introduction

In recent decades, there has been an increased emphasis on tailoring treatment for patients with gynecological malignancy to provide fertility-sparing options without compromising oncologic outcomes.

Ovarian cancer is the most lethal of all malignancies of the female genital tract and for a long time the primary goal of cancer therapy -survival- tended to overshadow survivorship considerations. However, approximately 11% of invasive ovarian cancers are diagnosed in women aged 20–45 years, with more than half of these being early-stage cancers. [1–2] Because young women with early stage disease have an excellent prognosis [3], issues affecting long-term survivors, including fertility preservation, have received growing attention and are now more widely recognized.

When the disease seems to be confined to one ovary, preservation of the uterus and contralateral ovary is increasingly being offered to women who wish to retain their childbearing ability. Laparoscopic staging has been indicated as preferable to open surgery for fertility-sparing surgeries due to the potential for minimizing adhesion formation and avoidance of laparotomy, known to decrease fecundity. [4] However,

* Corresponding author at: Department of Gynecology and Obstetrics, University of Insubria, Del Ponte Hospital, Piazza Biroldi 1, 21100 Varese, Italy.
E-mail address: fabio.ghezzi@uninsubria.it (F. Ghezzi).

http://dx.doi.org/10.1016/j.ygyno.2016.03.030
0090-8258/

previous studies on fertility-sparing laparoscopic surgery in the setting of a ovary-confined ovarian malignancy are based on single institution experiences and owing to the low prevalence of young women diagnosed with invasive ovarian cancer, these studies have been limited by a small number of patients and inclusion of low malignant potential tumors, germ cell or sex cord stromal tumors. [5–10] Moreover, in several series spanning over a very long period of time, the more recent laparoscopic cases and historical open cases were analyzed together, [11,12] thus preventing any evaluation of oncologic safety and reproductive outcome of a minimally invasive approach in this specialized population.

Preservation of the low recurrence rates and high overall survival observed for stage I ovarian cancers are of utmost importance when considering laparoscopic conservative treatment of early stage disease in reproductive-age women. As more research is needed to determine whether the clearly defined benefits of minimally invasive surgery can be extrapolated to include patients undergoing fertility-sparing staging for early ovarian cancer without assuming unacceptable risk, we decided to conduct a multi-institutional study including consecutive patients who underwent fertility-sparing laparoscopic treatment of early stage ovarian carcinoma (EOC) at five Italian high-volume centers.

2. Methods

This study is a multi-institutional, cohort study of consecutive women diagnosed with an apparent stage I ovarian cancer who underwent fertility-sparing surgery by laparoscopy. The study involved patients from 5 institutions: Gynecologic Oncology Unit of University of Insubria, Gynecologic Oncology Unit of Catholic University of Rome, Advanced Gynecological Endoscopy Center of Malzoni Medical Center, IRCCS National Cancer Institute, Milan and Oncologic Gynecology Unit, University Hospital S·Orsola-Malpighi, Bologna. In all the participating centers, more than 20 ovarian cancer surgeries are performed annually. Prospectively collected data in the five gynecologic oncology service databases were analyzed retrospectively. These research-quality data sets contain information concerning the surgical procedures, intra- and postoperative details as well as follow-up evaluations and are updated at each institution on a regular basis.

At each institution the option of conservative treatment of EOC with retention of the uterus and contralateral ovary has been offered to women aged 42 years or less who had not yet completed childbearing. A complete obstetric and gynecological history was obtained to identify patients with underlying potential infertility problems. Infertility work-up to document fertility potential was not required prior to the procedure, however patients with no realistic probabilities of achieving conception based on their age, history, and previous infertility evaluations were not considered candidates for fertility-sparing procedures. Women who were in the late 30s or early 40s were made aware that their fertility potential was obviously less.

For the purposes of this study, EOC was defined as an ovarian tumor grossly limited to one ovary, with no evidence of intraperitoneal disease. Gross evidence of spread of the disease beyond one ovary was regarded as exclusion criterion. Only women who had epithelial ovarian cancer (tumors classified as serous carcinomas, endometrioid carcinomas, mucinous tumors, and clear cell carcinomas) were included. The procedures were performed by surgeons with extensive training and experience in gynecologic oncology and in advanced minimally invasive surgery. At each institution, once laparoscopic surgery has been incorporated in the management of EOC from that moment onwards this approach was offered to each patient presenting with that condition, unless specific contraindications existed, such as a documented significant cardiopulmonary disease, atrial septal defect, etc. Since the largest endoscopic bags available in our operating rooms have a diameter of 12 cm, we have considered this tumor size as cut-off to offer minimally invasive approach. No patient was refused laparoscopic surgery for reasons of obesity, prior surgical history, anticipated difficulty of resection. Detailed description of the surgical technique used for laparoscopic staging of EOC has been reported elsewhere [13] and we ascertained no substantial differences in the technique between centers or surgeons.

A very thorough and extensive counseling has been given to the patient and partner, and immediate family members, highlighting the risks potentially inherent in non-standard care, before the decision to proceed with a fertility sparing surgery. At each hospital involved in the study specific consent forms have been developed aimed at maximizing patient understanding of the non-standard nature of the fertility preserving treatment, forcing patients to weigh the risks and benefits associated with each treatment option. As the optimal timing of pregnancy after conclusion of cancer treatment is uncertain, we did not suggest waiting a specific time period before attempting conception. In all participating centers research activities involving the collection or study of existing data are exempt from the requirement of IRB approval.

Intraoperative mass rupture was defined as any rupture, intentional or unintentional, that resulted in spill of cyst contents into the peritoneal cavity. If a mass was drained intentionally within a collection bag to facilitate removal without a resulting peritoneal spill, the mass was not considered ruptured. Operative times were defined as 'skin-to-skin' time. Postoperative complications were defined as adverse events occurring within 30 days of surgery as a result of the procedure. Hospital stay was counted from the first postoperative day.

Statistical analysis was performed with GraphPad version 5.00 for Windows (GraphPad Software, San Diego CA). Normality testing (D'Agostino and Pearson test) was performed to determine whether data were sampled from a Gaussian distribution. Disease-free and overall survivals were estimated using the Kaplan–Meier method; survival curves of two groups were compared using the log rank test. In survival analysis patients lost to follow-up were classified as censored.

3. Results

The study cohort consisted of 65 women undergoing laparoscopic fertility-preserving surgery for apparent early-stage ovarian cancer. Median age of the patients was 33 (range: 21–42) years, with 23 (35.4%) patients who were referred for restaging following cystectomy or salpingo-oophorectomy with findings of invasive disease on final pathology and 42 (64.6%) who had their malignancies diagnosed on frozen-section analysis at the time of laparoscopic surgery, with subsequent, immediate comprehensive surgical staging. The mean BMI in this study group was 22.2 ± 4.4 kg/m^2 and 8 (12.3%) women had a history of abdominal surgery.

Table 1
Hystologic types, tumor grading and stage after comprehensive surgical staging.

	Study cohort ($N = 65$)
Histotype	
Endometrioid	21 (32.3%)
Serous	15 (23.1%)
Mucinous	25 (38.4%)
Clear cell	3 (4.6%)
Small cell carcinoma	1 (1.5%)
Grading	
G1	38 (58.5%)
G2	19 (29.2%)
G3	8 (12.3%)
Final stage	
Ia	42 (64.6%)
Ib	1 (1.5%)
Ic	18 (27.7%)
IIb	1 (1.5%)
IIIc	3 (4.6%)

Data are expressed as number (%).