

Laparoscopic management of early stage ovarian cancer: is it feasible, safe, and adequate? A retrospective study

G. Montanari, N. Di Donato, S. Del Forno, A. Benfenati,
V. Bertoldo, C. Vincenzi, P. Casadio, R. Seracchioli

Minimally Invasive Gynecological Surgery Unit, S. Orsola Hospital, University of Bologna, Bologna (Italy)

Summary

Introduction: Minimally invasive surgery to stage early ovarian cancer is still regarded as pioneering among gynecologic oncologists. Previous retrospective experiences demonstrated the safety and feasibility of laparoscopy in this field. **Aims:** To review the laparoscopic staging procedure in a series of patients with early ovarian cancer and compare results with the literature. **Materials and Methods:** From January 2004 to September 2011, 19 patients with apparent early stage ovarian/fallopian tube cancer Stage IA to IC underwent either primary treatment or completion staging by laparoscopy. Surgical, pathologic, and oncologic outcomes were analyzed. **Results:** The mean operative time was 212 ± 69 minutes. Three patients (16%) underwent fertility sparing surgery. The mean estimated blood loss was two \pm two g/dl. The mean number of pelvic and para-aortic lymph nodes collected was 17 (range 7-27) and 14 (range 8-21), respectively. The mean volume of ovarian/tubal tumor was 119 cm³ (range 1.5-500). The disease was reclassified to a higher stage in ten women (52%). One major intraoperative complication (five percent) occurred which required the conversion to laparotomy. The mean follow up period was 30 ± 16 months (range 10-74). Overall survival and disease-free survival were 100% and 84%, respectively. **Conclusions:** Laparoscopic staging of early ovarian cancer appears to be feasible and comprehensive when performed by gynecologic oncologists experienced with advanced laparoscopy.

Key words: Early ovarian cancer; Laparoscopy; Staging; Minimally invasive treatment.

Introduction

Laparoscopic management of gynecological cancers is increasing. A national practice survey in France showed that in 2005, five percent of patients underwent laparoscopic treatment for gynecological cancer in a referral Center [1]. Many advantages have been evidenced compared to laparotomic approach when performing a minimally invasive technique for the management of early stage gynecological cancer: less intraoperative blood loss, shorter hospital stay, faster recovery, and less damage to body image [2]. Recently, laparoscopy has showed to be feasible and associated with less morbidity in obese women with early stage endometrial cancer [3] and in older patients with early stage gynecological malignancies [4].

While minimally invasive approach has been largely demonstrated as safe and feasible for early stage endometrial and cervical cancer, laparoscopic staging and management of early stage ovarian/tubal cancer is still under debate due to the concern about its feasibility and adequacy [2]. Nonetheless, early stage ovarian/tubal cancer is rare compared to advanced stage and it has numerous potential sites of occult metastatic disease [5]. Previous retrospective experiences of laparoscopic management of early ovarian cancer (EOC) demonstrated the safety and feasibility of laparoscopy in this field, however this approach is still not recommended by the guidelines [2].

Materials and Methods

From January 2004 to September 2011, 19 patients with apparent early stage ovarian/fallopian tube cancer Stage IA to IC underwent either primary treatment or completion staging by laparoscopy.

Laparoscopic staging protocol fulfilled oncological standards and adhered to FIGO recommendations. Gross evidence of spread of the disease beyond the ovaries was regarded as an exclusion criterion. A conservative approach was used when patient desired to maintain fertility and with apparent Stage IA, with preservation of the uterus and contralateral ovary. The study was approved by the ethical committees of Sant'Orsola Malpighi Hospital and patients gave informed consent to the chart review of their reports.

Laparoscopic technique

Patients were placed in lithotomic position. After pneumoperitoneum was created, a 10-mm 0° operative laparoscope was introduced at the umbilical site. Under direct vision, three ancillary trocars were inserted, one ten-mm laterally to the epigastric artery and two of five-mm placed suprapubically and laterally to the epigastric artery. First, sterile saline solution was instilled for peritoneal washing and the liquid aspirated was sent for cytologic examination. Parietal and visceral peritoneal surfaces were carefully inspected, including diaphragm, liver, gallbladder, small bowel and mesentery, recto-sigmoid colon, pouch of Douglas, paracolic gutters, and abdominal wall. Subsequently, in those women not referred for restaging, the ovary with the suspicious mass was removed and retrieved via an endobag to avoid contact with the port sites and it was submitted for frozen section assessment. The surgical specimens were removed through the trocar. In case of large cystic tumors, puncture of the mass and aspiration were performed within the retrieval bag. When

* These authors contributed equally to this work

solid components were encountered, they were removed by morcellation (while in the bag) using Kocher clamps or curved Mayo clamps.

Once the mass was removed in its entirety along with the bag, endobag integrity was verified and surgeons' gloves were changed. After the diagnosis of malignancy, multiple random peritoneal biopsies were performed. Patient underwent hysterectomy with adnexectomy. Bilateral pelvic lymphadenectomy was performed and in all patients, external iliac, internal iliac, and obturator lymph nodes were removed. The peritoneum was opened over the common iliac arteries and the incision was extended cephalad over the underlying inferior vena cava and abdominal aorta, exposing the ureters, gonadal vessels, and inferior mesenteric artery. Under direct vision of the above mentioned structures, common iliac, precaval, and para-aortic nodal dissection were performed. In some cases an additional three-mm ancillary trocar was placed in the left hypochondrium in order to introduce a grasper to retract the visceral peritoneum, allowing an easier access to the retroperitoneal space. The upper limit of the nodal harvest was the insertion of the right ovarian vein in the vena cava on the right side and the left renal vein on the left side. In order to prevent the contamination of the abdominal wall with malignant cells, a specimen bag was used to retrieve the lymph nodes, separately from each sidewall. Total infracolic omentectomy was then performed using scissors and bipolar coagulation. Appendectomy was performed by coagulation of the mesoappendix, ligature of the appendix by endoloops, and resection. The surgical specimens were extracted from the abdomen by individual endobags. In case of unilateral tumor, fertility-sparing surgery was offered to young patients who desired preservation of reproduction potential, after a biopsy of the contralateral ovary ruled-out the presence of malignant cells. In case of adhesions between the ovarian tumor and the pelvic peritoneum we performed pelvic peritonectomy. In all cases, the peritoneal cavity was reinspected laparoscopically after closing the vaginal cuff to ensure adequate haemostasis and abundant washing of the peritoneal cavity was then performed.

Results

A total of 19 patients underwent laparoscopic staging for presumed Stage I ovarian or fallopian tube cancer. Mean age of patients was 51 ± 14 years (range 20-74), mean body mass index was 22 ± 3 kg/m². Eleven patients had previous laparotomic surgery (eight appendectomies, one myomectomy, one hysterectomy, and three cesarean sections), and four patients had a history of previous laparoscopic surgery (one hysterectomy, one myomectomy, and three diagnostic laparoscopies). Thirteen (68%) patients presented with an adnexal mass and had their malignancies diagnosed on frozen-section analysis at the time of laparoscopic surgery at the present institution. One of them had received neoadjuvant chemotherapy before the end-staging operation. Six (32%) patients referred to the present Center for restaging after undergoing cystectomy or salpingo-oophorectomy after diagnosis on final pathology of an occult cancer. Histologic types and tumor grading are outlined in Table 1.

Three patients had fertility sparing treatment: one patient was 31-years-old with an endometrioid ovarian cancer developed in an endometriotic ovarian cyst. One

Table 1. — *Histological characteristics and grading of tumor.*

Histologic type	N. patients (%)
Serous	3 (16%)
Endometrioid	3 (16%)
Clear cell	3 (16%)
Mucinous	1 (5,2%)
Mixed	3 (16%)
Adenoca NOS	3 (16%)
Granulosa Cell	2 (10,5%)
Dysgerminoma	1 (5,2%)
Grade:	
G1	4 (21%)
G2	2 (10.5 %)
G3	11 (58%)
Not specified	2 (10.5 %)

Table 2. — *Laparoscopic procedures performed.*

Procedures	N = 19
Pelvic lymphadenectomy	19 (100%)
Lumboaortic lymphadenectomy	19 (100%)
– transperitoneal	18 (95%)
– retroperitoneal	1 (5%)
Peritoneal biopsies	19 (100%)
Omentectomy	19 (100%)
Peritoneal cytology	19 (100%)
Pelvic peritonectomy	9 (47%)
Appendectomy	6 (31%)
Endobag used	15 (79%)
Intraperitoneal tumor rupture	3 (16%)

Table 3. — *Surgical outcomes.*

Variables*	N = 19
Surgical time (min)	212 \pm 69 (110-360)
Estimated blood loss (g/dl)	2 \pm 2 (0.7-5)
Hospital stay (d)	6 \pm 2 (2-13)
Volume of the ovarian/tubal tumor (cm ³)	119 \pm 148 (1.5-500)
Number of pelvic nodes	17 \pm 7 (7-27)
Number of lumboaortic nodes	14 \pm 5 (8-21)
Omental specimen (mm)	90 \pm 30 (75-250)
Rate of upstaging	10/19 (52%)
Major intraoperative complications (%)	1/19 (5 %)

* Data are presented as mean \pm SD (range), where appropriate.

patient was 31-years-old and had granulose cells ovarian tumor grade 2. One patient was 20-years-old and had dysgerminoma tumor. The number and type of procedures performed in primary surgery and completion of staging are described in Table 2. The surgical outcomes are shown in Table 3.

A transaction of the right ureter during lumboaortic lymphadenectomy was the only intraoperative complication. The urologist attempted without success to perform ureteral reanastomosis through laparoscopy. The patient finally underwent laparotomic ureteral reanastomosis.

Regarding postoperative complications (within 30 days from surgery), there were three minor complications: one paralytic ileus, one vulvar edema, and one umbilical hematoma which were managed conservatively and resolved spontaneously. There was one major postopera-

tive complication: a patient who had ureteral fistula diagnosed 24 days from surgery. The woman presented urine loss from the vagina. She underwent blind stenting with complete spontaneous resolution.

After a mean follow up of 30 ± 16 months (range ten-74), three recurrences occurred: two of them were patients previously treated in other Centers who underwent restaging surgery at the present Institution. One had pelvic recurrence at 30 months follow up and the other had a presacral lymph node recurrence at ten months follow up. One patient had pelvic and abdominal recurrences at 18 months follow up.

Discussion

From the results, some important questions emerged:

Is the laparoscopic staging of EOC feasible?

An important factor when a new approach is evaluated is the feasibility, defined as the state of being easily or conveniently performed. In the authors' opinion, parameters which must be considered to assess the feasibility of laparoscopic technique are: operative time, rate of conversion to laparotomy, frequency of intraoperative mass rupture, and the possibilities to perform other surgical procedures. These parameters are strictly related with laparoscopic experience and its high learning curve [6]. In the present Minimally Invasive Surgery Center, the same surgeon and surgical team which have a consistent background in laparoscopic approach performed all the procedures. This may explain the relatively low operative time (around 212 minutes) compared to other studies [7-9]. The authors had one case of laparotomic conversion at the last step of the staging procedure due to intraoperative right ureteral resection. Mass rupture occurred in three patients: one patient was treated in another center and subsequently restaged in the present Center, two occurred in women with an apparent endometriotic ovarian cyst which was discovered to be malignant at the intraoperative frozen section examination. Tumor spillage into the peritoneal cavity is one of the major concerns of minimally invasive approach. However, the risk of tumor spillage is not specific to laparoscopy. Several studies were published on patients with EOC whose tumor was ruptured at the time of laparotomy [10-12]. Other surgical procedures performed by laparoscopic approach in the present series were appendectomy (31%) and pelvic peritonectomy (47%). Fertility sparing surgery which was performed in three patients without recurrence during a mean follow up of 30 months, has demonstrated to be a reasonable alternative treatment for young women with Stage I epithelial ovarian cancer desiring fertility preservation [13, 14].

Is the laparoscopic staging of EOC safe?

The frequency of intraoperative complications in the present study was 1/19 (5%): a case of ureteral injury during lumboaortic lymphadenectomy. The present

results seem comparable with the ones of Colomer *et al.*: in the 20 patients identified in this retrospective review, one case of vascular injury was reported [15]. The study of Spirtos *et al.* evidenced a higher rate of intraoperative complications even if borderline ovarian tumors were considered, however it was a multicenter study, with different surgeons involved [16]. No intraoperative complications were noticed in other retrospective studies [9, 17].

The present results confirmed the well-known advantages of laparoscopy with a short hospital stay and reduced intraoperative blood loss.

Is the laparoscopic staging of EOC adequate?

The etymology of the word "adequacy" is "to make equal". Laparoscopy has to make equal results of laparotomy, which is the gold standard surgical approach to ovarian cancer [18], to be considered as an alternative approach to EOC. From the present results, the rate of upstaging, which may be considered as an index of adequacy of staging [17], was 10/19 (52%), higher compared to previous study [9, 15-17, 19] and to other studies using a laparotomic approach [5]. Five of them were upstaged to Stage IC due to positive peritoneal cytology, five were upstaged due to positive nodes or peritoneal biopsy. This data may be related with the high rate (58%) of undifferentiated tumor, G3 which affected the present patients.

In line with other studies [9, 15-17, 19] the mean number of nodes obtained in the present series of patients was 17 for pelvic nodes and 14 for para-aortic nodes. Three previous retrospective reviews evidenced no statistical difference in the number of pelvic and para-aortic lymph nodes retrieved with the two approaches [7, 8, 20]. Moreover, several studies with a larger number of patients have demonstrated the adequacy of laparoscopy for lymph node dissection [17].

The rate of recurrence in the present study was higher compared to other studies [4, 21], however it has to be underlined that their mean follow up evaluation was shorter and that the recurrences occurring in the present study involved patients who underwent a restaging procedure in this Center and not the primary treatment. This result may stress the importance of performing the tumor staging in tertiary care Center with a gynecologist oncologist expert.

This study is not without limitations. First limit is its retrospective design. Second, the fact that six patients were previously treated in another Center and restaged in the present Institution may bias the results. Third, the mid-term follow up evaluation: long-term survival results are important to compare minimally invasive surgical staging to the laparotomic approach.

In conclusion, when performed by appropriately skilled surgeons, laparoscopic comprehensive staging of EOC seems feasible and adequate with undoubted benefits for the women who may improve their functional status, lessen their suffering, and maintain their life's dignity.

References

- [1] Le Roux C., Sentilhes L., Catala L., Lefebvre-Lacoeuille C., Poilblanc M., Descamps P.: "Laparoscopy for surgical treatment for uterine and ovarian cancer in France: a national practice survey". *J. Gynecol. Obstet. Biol. Reprod. (Paris)*, 2011, 40, 231.
- [2] Iglesias D.A., Ramirez P.T.: "Role of minimally invasive surgery in staging of ovarian cancer". *Curr. Treat. Options Oncol.*, 2011, 12, 217. doi: 10.1007/s11864-011-0155-3.
- [3] Seracchioli R., Mabrouk M., De Iaco P., Facchini C., Vincenzi C., Di Donato N. *et al.*: "Laparoscopic surgery for endometrial cancer in overweight women". *Minerva Gynecol.*, 2011, 63, 315.
- [4] Ghezzi F., Cromi A., Siesto G., Serati M., Bogani G., Sturla D., Bolis P.: "Use of laparoscopy in older women undergoing gynecologic procedures: is it time to overcome initial concerns?". *Menopause*, 2010, 17, 96.
- [5] Young R.C., Decker D.G., Wharton J.T., Piver M.S., Sindelar W.F., Edwards B.K., Smith J.P.: "Staging laparotomy in early ovarian cancer". *JAMA*, 1983, 250, 3072.
- [6] Brummer T.H., Seppälä T.T., Härkki P.S.: "National learning curve for laparoscopic hysterectomy and trends in hysterectomy in Finland 2000-2005". *Hum Reprod.*, 2008, 23, 840.
- [7] Ghezzi F., Cromi A., Uccella S., Bergamini V., Tomera S., Franchi M., Bolis P.: "Laparoscopy versus laparotomy for the surgical management of apparent early stage ovarian cancer". *Gynecol. Oncol.*, 2007, 105, 409.
- [8] Chi D.S., Abu-Rustum N.R., Sonoda Y., Ivy J., Rhee E., Moore K., Levine D.A., Barakat R.R.: "The safety and efficacy of laparoscopic surgical staging of apparent Stage I ovarian and fallopian tube cancers". *Am. J. Obstet. Gynecol.*, 2005, 192, 1614.
- [9] Jung U.S., Lee J.H., Kyung M.S., Choi J.S.: "Feasibility and efficacy of laparoscopic management of ovarian cancer". *J. Obstet. Gynaecol. Res.*, 2009, 35, 113.
- [10] Pomel C., Provencher D., Dauplat J., Gauthier P., Le Bouedec G., Drouin P. *et al.*: "Laparoscopic staging of early ovarian cancer". *Gynecol. Oncol.*, 1995, 58, 301.
- [11] Dembo A.J., Davy M., Stenwig A.E., Berle E.J., Bush R.S., Kjorstad K.: "Prognostic factors in patients with Stage I epithelial ovarian cancer". *Obstet. Gynecol.*, 1990, 75, 263.
- [12] Sainz de la Cuesta R., Goff B.A., Fuller A.F. Jr, Nikrui N., Eichhorn J.H., Rice L.W.: "Prognostic importance of intraoperative rupture of malignant ovarian epithelial neoplasms". *Obstet. Gynecol.*, 1994, 84, 1.
- [13] Satoh T., Hatae M., Watanabe Y., Yaegashi N., Ishiko O., Kodama S. *et al.*: "Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient selection". *J. Clin. Oncol.*, 2010, 28, 1727.
- [14] Schlaerth A.C., Chi D.S., Poynor E.A., Barakat R.R., Brown C.L.: "Long-term survival after fertility-sparing surgery for epithelial ovarian cancer". *Int. J. Gynecol. Cancer*, 2009, 19, 1199.
- [15] Colomer A.T., Jiménez A.M., Bover Barceló M.I.: "Laparoscopic treatment and staging of early ovarian cancer". *J. Minim. Invasive Gynecol.*, 2008, 15, 414.
- [16] Spirtos N.M., Eisekop S.M., Boike G., Schlaerth J.B., Cappellari J.O.: "Laparoscopic staging in patients with incompletely staged cancers of the uterus, ovary, fallopian tube, and primary peritoneum: a Gynecologic Oncology Group (GOG) study". *Am. J. Obstet. Gynecol.*, 2005, 193, 1645.
- [17] Nezhat F.R., Ezzati M., Chuang L., Shamshirsaz A.A., Rahaman J., Gretz H.: "Laparoscopic management of early ovarian and fallopian tube cancers: surgical and survival outcome". *Am. J. Obstet. Gynecol.*, 2009, 200, 83.e1.
- [18] National Comprehensive Cancer Network (NCCN Guidelines™) Clinical Practice Guidelines in Oncology Ovarian Cancer including fallopian tube cancer and primary peritoneal cancer. Version 2.2011
- [19] Tozzi R., Köhler C., Ferrara A., Schneider A.: "Laparoscopic treatment of early ovarian cancer: surgical and survival outcomes". *Gynecol. Oncol.*, 2004, 93, 199.
- [20] Park J.Y., Kim D.Y., Suh D.S., Kim J.H., Kim Y.M., Kim Y.T., Nam J.H.: "Comparison of laparoscopy and laparotomy in surgical staging of early-stage ovarian and fallopian tubal cancer". *Ann. Surg. Oncol.*, 2008, 15, 2012.

Address reprint requests to:

R. SERACCHIOLI, M.D.

Minimally Invasive Gynaecological Surgery Unit

S. Orsola Hospital, University of Bologna

Via Massarenti, 13, 40138 Bologna (Italy)

e-mail:renato.seracchioli@aosp.bo.it