



Laparotomy vs. minimally invasive surgery for ovarian cancer recurrence: a systematic review

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Abstract: The objective of the present review is to thoroughly investigate the role of minimally invasive surgery (MIS) in the setting of secondary cytoreduction for ovarian cancer recurrence, comparing this approach to traditional open surgery. PubMed, ClinicalTrials.gov, Scopus and Web of Science databases (between 1st January 1989 and 1st January 2020), have been systematically queried to identify all articles reporting either laparoscopic or robotic-assisted secondary surgical cytoreduction for recurrent ovarian cancer. We also manually searched the reference lists of the identified studies. Only English language papers were considered. Two independent reviewers screened and identified the reports. A sub-analysis was performed including studies comparing MIS *vs.* open abdominal secondary cytoreduction. A total of 617 articles were considered. Among them, we included 12 retrospective studies on minimally invasive secondary cytoreduction, enrolling 372 patients (260 of whom were submitted to whether robotics or laparoscopy). Three studies compared 69 patients who underwent MIS *vs.* 112 cases of open abdominal secondary cytoreduction. Other 9 articles described a total of 191 patients who had minimally invasive secondary cytoreduction for recurrent ovarian cancer without a comparative arm. The quality of the evidence was low. The decision regarding the use of MIS was left to surgeon's discretion; in general, the candidates to MIS were selected patients with single-site disease or few localizations of relapse. Compared to open surgery, MIS was associated with significantly lower blood loss, shorter hospital stay and less postoperative complications; the rate of complete cytoreduction to residual tumor =0 was 95.5% in MIS cases *vs.* 87.5% in laparotomy cases. The risk of complications was generally low. Disease-free and overall survival were comparable between groups. There is no consensus on the criteria to select patients for laparoscopic or robotic secondary cytoreduction. Intra-operative ultrasound has been proposed as a possible tool to better identify the site of recurrence and for confirmation of complete resection of disease. In conclusion, MIS is an option in selected patients with recurrent ovarian cancer, provided there is no widespread disease. Selection of patients appears of utmost importance to obtain satisfactory survival outcomes.

Keywords: Ovarian cancer; relapse; minimally invasive surgery (MIS); laparoscopy; robotics; open surgery

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Introduction

Ovarian cancer represents the most lethal malignancy of the female genital tract (1). Even in cases of optimal initial treatment, the majority of the affected patients will experience a relapse (2), and the probability of recurrence is almost certain in case of advanced-stage disease at initial diagnosis.

Retrospective reports have strongly suggested that, in case of recurrence of ovarian cancer, radical secondary cytoreduction is beneficial to the patients and prolongs survival if no macroscopic disease is left at the end of surgery (3-7). These assumptions have been recently questioned by a large randomized trial promoted by the Gynecologic Oncology Group (GOG-213), in which the benefit of secondary surgery was only on disease-free survival and not on overall survival (8). The results of the GOG-213 have been strongly criticized, mainly because of the low rate of complete cytoreduction (63%) in patients assigned to secondary surgical effort. In 2018, the preliminary results of another randomized trial (the DESKTOP-3) have been presented at the ASCO meeting (9): with a higher rate of complete surgical eradication (74%) the trial showed a survival advantage of a secondary surgical effort in patients with ovarian cancer relapse. However, data from this trial are still immature and final reports are awaited.

A relevant and partially different issue is the occurrence of lymphatic relapses: the complete eradication of them has been shown to be associated with a substantial improvement in patients' prognosis and represents a widely accepted indication to perform surgery (10-12).

Regardless of all the debates on these topics, surgical secondary cytoreduction (SSC) is considered an important option in case of ovarian cancer recurrence (3). As for upfront surgery, the possibility to perform SSC by laparoscopy or robotics has been taken into consideration because of the well-known beneficial effects of minimally-invasive surgery on intra-operative blood-loss, risk of transfusions, rate of peri-operative complications and post-operative recover, including a shorter time to initiation of adjuvant chemotherapy (13-29). Few reports have investigated the role of minimally invasive SSC, and even less have compared endoscopic techniques to traditional open surgery (10,30,31). The aim of this review has been to investigate in depth the role of minimally invasive surgery (MIS) in the setting of secondary cytoreduction in case of ovarian cancer recurrence, and to summarize the available

evidence and possible indications for MIS in this setting. We present the following article in accordance with the PRISMA reporting checklist (available at <http://dx.doi.org/10.21037/gs-20-353>).

Methods

This review was performed according to the PRISMA statement and was registered in the PROSPERO register (CRD42020173156).

A reference librarian with expertise in electronic search strategies for systematic reviews conducted the literature search in conjunction with a senior gynecologist (SU). PubMed, ClinicalTrials.gov, Scopus and Web of Science databases were systematically searched for records from January 1st 1989, to January 1st 2020.

No institutional review board approval was required, because the present study deals with already existing data. All authors participated in the search strategy design and in the definition of the inclusion and exclusion criteria.

The final literature search was performed in February 2020, using the following strings: "ovarian neoplasm" or "ovarian cancer" or "ovarian malignancy" AND "secondary cytoreduction" or "recurrence" or "relapse" or "failure" and "laparoscopy" or "robotics" or "minimally-invasive surgery".

Eligibility assessment was performed independently by two reviewers (SU, PCZ). All pertinent articles were carefully evaluated. Full manuscripts were obtained for all selected articles, and the decision for final inclusion was made after a detailed examination of the paper. To avoid missing any relevant publication, a manual search of the reference lists of the retrieved studies and review articles was performed. We included only studies written in English and describing the use of laparoscopy or robotics for secondary surgical cytoreduction for recurrent ovarian cancer. Abstract at conferences not followed by full-text articles were not considered. Published cases incorporated in subsequent series were excluded. Only cases of secondary cytoreduction were included (therefore cases of tertiary or quaternary cytoreduction were excluded). In case of any disagreement between the two reviewers regarding the inclusion of studies, a third author (MPF) was asked to take the final decision.

The same authors independently extracted data from the articles. The quality of the included studies was graded according to the Grading of Recommendations, Assessment Development, and Evaluation system (32). The Grading

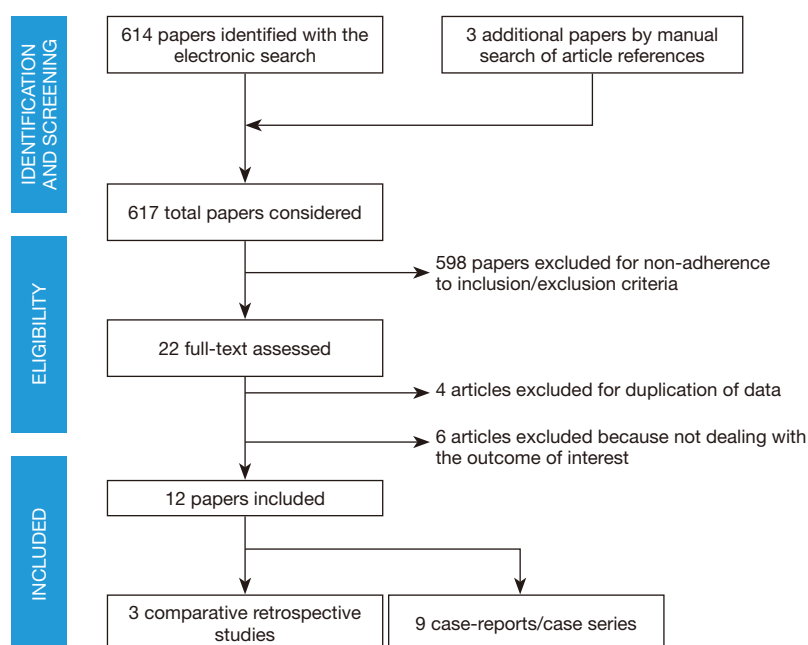


Figure 1 PRISMA diagram-transparent reporting of systematic reviews and meta-analysis flow diagram outlining the search strategy results from initial search to included studies.

of Recommendations, Assessment, Development, and Evaluation Working Group classifies the quality of studies as follows: high quality (further research is very unlikely to change our confidence in the estimate of effect), moderate quality (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low quality (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), and very low quality (we are very uncertain about the estimate).

Only studies including patients with epithelial ovarian malignancies were considered. The literature search (Figure 1), based on our predefined key search items, identified 617 publications after adjusting for duplicates.

Main review outcomes

- (I) To summarize the available reports regarding the outcomes of MIS (whether laparoscopic or robotic) compared to traditional open surgery;
- (II) to summarize the articles describing the use of MIS in the setting of SSC for recurrent ovarian cancer;
- (III) to provide possible strategies to select patients for minimally invasive secondary cytoreduction and to improve outcomes.

Statistical analysis

Categorical data are presented as absolute number (percentage). Continuous data are presented as mean \pm standard deviation or median (range). The chi square test was used to calculate P values of the comparison of MIS *vs.* open surgery in case of categorical variables.

Results

A total of 12 articles including 372 patients were identified. Three studies compared 69 patients who underwent MIS SSC *vs.* 112 cases of open abdominal SSC. Other 9 articles described a total of 191 patients who had minimally invasive secondary cytoreduction for recurrent ovarian cancer without comparison with traditional open treatment. Overall, the number of patients reported in the literature who received MIS debulking for relapse of ovarian cancer is 260.

The quality of the evidence is definitely low, being based on 3 retrospective comparative studies, 6 retrospective case series and 3 case reports. In all cases, only selected patients underwent MIS for SSC. No clear criteria to identify cases suitable for laparoscopic or robotic debulking were adopted and the decision was left to surgeon's discretion; in general,

Table 1 Characteristics of the study included

Study	Study design	Quality of evidence	Selection of patients for MIS	Choice of MIS approach	Nr. of patients	Follow-up (months)	Notes
Magrina <i>et al.</i> [2013] (35)	Retrospective	Low	Yes	Surgeon's discretion	LPS: 9; LPT: 33; Robot: 10	>3 years	
Fagotti <i>et al.</i> (2015) (33)	Retrospective	Low	Yes	Surgeon's discretion	MIS: 11; LPT: 11	Not available	Use of HIPEC at the end of the procedure
Eriksson <i>et al.</i> [2019] (36)	Retrospective	Low	Yes	Surgeon's discretion	MIS: 39; LPT: 68	>2 years	LPS: 8 cases; Robot: 31 cases
Total	All retrospective	Low	All	Surgeon's discretion	MIS: 69; LPT: 112	Variable	/

LPS, laparoscopy; LPT, laparotomy; MIS, minimally invasive surgery.

Table 2 Operative procedures

Study	Liver resection	Bowel resection	Diaphragmatic resection	Peritoneal abdominal carcinosis resection	Ureter/Bladder resection	Lymphadenectomy
Magrina <i>et al.</i> [2013] (35)	LPS 1 (11.1%); LPT 5 (15.2%); Robot 5 (50%)	LPS 1 (11.1%); LPT 21 (63.6%); Robot 3 (30%)	LPS 3 (33.3%); LPT 6 (18.2%); Robot 5 (50%)	LPS 6 (66.6%); LPT 31 (93.7%); Robot 9 (90%)	LPS 0; LPT 2 (6.1%); Robot 1 (10%)	LPS 2 (22.2%); LPT 13 (39.4%); Robot 6 (60%)
Fagotti <i>et al.</i> [2015] (33)	MIS 0; LPT 0	MIS 3 (27.3%); LPT 1 (9.1%)	MIS 0; LPT 3 (27.3%)	MIS 8 (72.7%); LPT 7 (63.6%)	MIS 0; LPT 0	MIS 0; LPT 0
Eriksson <i>et al.</i> [2019] (36)	MIS 0; LPT 0	MIS 9 (23%); LPT 22 (32%)	Not available	Not available	Not available	Not available

we noticed that the candidates to MIS had single-site disease or few localizations of relapse. Only 3 studies (31,33,34) provided details regarding the performance status of patients included; when mentioned, only patients in good performance status (0 to 2) were included.

Studies comparing SSC by MIS vs. laparotomy (Tables 1-4)

The three available studies comparing MIS to open surgery included both cases of laparoscopic and robotic SSC (33,35,36). Two of the three studies provided oncological outcomes (35,36). The study by Eriksson *et al.* (36) did not describe in detail the type of surgical procedures performed.

MIS is associated with significantly lower blood loss, shorter hospital stay and less postoperative complications. Of note, the surgical effort appears less extended in the MIS group. Complete cytoreduction to residual tumor =0 was overall achieved in 95.5% of MIS cases *vs.* 87.5% of laparotomy cases in the three studies. Disease-free and overall survival were comparable between groups: in the study by Magrina *et al.* the 3-year disease-free survival was

22.9% for laparoscopic surgery, 33.1% for laparotomy and 43.8% for robotics ($P=0.95$), while the 3-year overall survival was 66.7%, 48.4% and 85.7%, respectively; in the study by Eriksson *et al.* the 2-year disease-free survival was 56.1% for MIS *vs.* 63.5% for laparotomy and the 2-year overall survival was 92.2% and 81.4% for MIS and laparotomy, respectively.

Case series and case reports describing robotic or laparoscopic SSC (Table 5)

Nine reports for a total of 120 laparoscopic and 71 robotic cases of SSC have been described in non-comparative literature (10,31,34,37-42). Several types of surgical procedures have been reported, including liver resection, bowel resection, diaphragmatic resection, splenectomy, and extended peritoneal stripping. The rate of complete cytoreduction to no residual tumor is high (91.6%) and the risk of complications is low 11.5%.

Survival outcomes, although limited by the study design and possible reporting bias, are extremely encouraging, with

Table 3 Perioperative outcomes

Study	Operative time (min)	Blood loss (mL)	Hospital stay (days)	Intraoperative complications	Postoperative complications
Magrina <i>et al.</i> [2013] (35)	LPS 167 [61–320]; LPT 219 [75–492]; Robot 247 [75–465]; (P=0.33)	LPS 100 [0–500]; LPT 675 [20–3,000]; Robot 100 [50–800]; (P<0.0001)	LPS 2 [1–19]; LPT 7 [3–35]; Robot 2.5 [1–7]; (P=0.0002)	LPS 2 (22.2%); LPT 7 (21.2%); Robot 1 (10%); (P=0.77)	LPS 3 (33.3%); LPT 14 (42.4%); Robot 2 (20%); (P=0.46)
Fagotti <i>et al.</i> [2015] (33)	MIS 125 [95–150]; LPT 295 [180–420]; (P=0.001)	MIS 50 [50–100]; LPT 500 [50–1,300]; (P=0.025)	MIS 4 [3–17]; LPT 8 [4–30]; (P=0.002)	MIS 0; LPT 1 (9.1%); (P=0.92)	MIS 2 (18.2%); LPT 3 (27.3%); (P=0.33)
Eriksson <i>et al.</i> [2019] (36)	MIS 186 [56–482]; LPT 216 [64–539]; (P=0.2)	MIS 50 [5–500]; LPT 150 [0–1,500]; (P=0.001)	MIS 1 [1–23]; LPT 5 [1–21]; (P=0.001)	MIS 0; LPT 0	MIS 3 (8%); LPT 15 (22%); (P=0.06)
Total	MIS range: 56–482; LPT range: 64–539	MIS range: 0–500; LPT range: 0–3,000	MIS range: 1–23; LPT range: 1–35	MIS 3 (4.3%); LPT 8 (7.1%); (P=0.58)	MIS 10 (14.5%); LPT 32 (28.6%); (P=0.03)

Table 4 Survival outcomes

Study	Complete cytoreduction (residual tumor =0)	Progression-free survival	Overall survival
Magrina <i>et al.</i> [2013] (35)	LPS 8 (88.9%); LPT 24 (72.7%); Robot 7 (70%); (P=0.66)	3-year: LPS 22.9%; LPT 33.1%; Robot 43.8%; (P=0.95)	3-year: LPS 66.7%; LPT 48.4%; Robot 85.7%; (P=0.18)
Fagotti <i>et al.</i> [2015] (33)	MIS 11 (100%); LPT 11 (100%); (P=1.00)	Not available	Not available
Eriksson <i>et al.</i> [2019] (36)	MIS 37 (95%); LPT 63 (93%); (P=1.0)	2-year: MIS 56.1%; LPT 63.5%; (P=1.0)	2-year: MIS 92.2%; LPT 81.4%; (P=0.7)
Total	MIS 63 (95.5%); LPT 98 (87.5%); (P=0.81)	–	–

disease-free survival ranging between 13 and 71.9 months.

Possible strategies to select patients and improve outcomes

As mentioned, there is no consensus on the criteria to select patients for laparoscopic or robotic secondary cytoreduction. However, all the available series point out that only localized disease is suitable for MIS approach. Ideally, a diagnostic laparoscopy, combined with preoperative imaging may provide adequate evaluation of the peritoneal cavity to confirm or discourage MIS (43).

Intra-operative ultrasound has been proposed as a possible tool for better identification of localizations and recurrence of ovarian cancer and for improved tailoring of SSC (44,45). Mascilini *et al.* in 2018 have described a series of 51 MIS debulking procedures for recurrent ovarian

cancer; among them, intraoperative ultrasound allowed proper identification of recurrence and confirmation of complete resection in 25% of cases, thus extending the applicability of minimally invasive technique and reducing the need for open surgery (44).

The summary of the evidence, with the main results of this review and the implications for research are summarized in *Table 6*.

Discussion

The present review shows that MIS in selected cases is an option for secondary cytoreduction in recurrent ovarian cancer. In cases of localized relapses, laparoscopic and robotic approaches provide improved peri-operative outcomes and, apparently, satisfactory survival outcomes.

Table 5 Non-comparative studies (laparoscopic and robotic surgery)

Study	Type of study/ approach	Nr of patients	Procedures	Complete cytoreduction	Complications	Follow-up
Trinh <i>et al.</i> 2004 (37)	Retrospective/ LPS	34	Peritonectomy with LEEP + Argon Beam: 34	32/34 (96%)	2/34 (5.9%)	Disease-free survival: 13 months
Holloway <i>et al.</i> 2011 (38)	Case report/ ROBOT	1	Liver Resection + Diaphragm resection: 1	1/1 (100%)	1/1 (100%)	Not available
Nezhat <i>et al.</i> 2012 (34)	Retrospective/ LPS	19	Resection of vaginal cuff, pelvis, abdominal wall, diaphragm, liver, spleen, omentum, mesentery, and small and large bowel.	15/19 (78.9%)	1/19 (7.1%)	Disease-free survival: 71.9 months
Nezhat <i>et al.</i> 2014 (39)	Retrospective/ ROBOT	4	Not available	4/4 (100%)	Not available	Not available
Escobar <i>et al.</i> 2015 (40)	Retrospective/ ROBOT	44	Peritonectomy: 35; Bowel resection: 5; Diaphragm resection: 2; Liver resection: 1; Splenectomy: 5	36/44 (82%)	6/44 (13.6%)	Disease-free survival: 24.5 months; overall survival: 50.1 months
Gallotta <i>et al.</i> 2018 (31)	Retrospective/ LPS	58	Lymphadenectomy: 24; Peritonectomy: 28; Rectosigmoid resection: 1; Colpectomy: 1; Radical omentectomies: 3; Splenectomy: 5; Liver resection: 1	58/58 (100%)	10/58 (17.2%)	Disease-free survival: 28 months
Uccella <i>et al.</i> 2019 (10)	Case report/ LPS	1	Retroaortic lymphadenectomy: 1	1/1 (100%)	0	NED after 14 months
Mutlu <i>et al.</i> 2019 (41)	Case report/ ROBOT	1	Pelvic lymphadenectomy: 1	1/1 (100%)	0	Not available
Magrina <i>et al.</i> 2019 (42)	Retrospective/8 LPS+21 ROBOT	29	Diaphragmatic stripping: 23; Diaphragmatic resection: 6	29/29 (100%)	2/29 (6.9%)	16 (55.2%) Recurrences time- to-recurrence: 2 yrs
Total	Retrospective	191	Various	175/191 (91.6%)	22/191 (11.5%)	DFS: 13–71.9 months

LEEP, loop electrosurgical excisional procedure; NED, no evidence of disease at last follow-up; DFS, disease-free survival.

MIS has been proposed for more than one decade in the treatment of both early and advanced ovarian cancer at the time of primary diagnosis (13–24). Interestingly, the role of laparoscopy appears crucial in the development of new strategies such as sentinel node biopsy for disease macroscopically limited to the ovary at upfront surgery (13,15,17–19). Although much less investigated, laparoscopic and robotic surgery have been used also in complex procedures for primary interval debulking surgery (14).

The use of MIS in secondary cytoreduction has been very scarcely explored and the available evidence is of low quality. The reasons for this paucity of data is due to: (I) uncertainties regarding the role of secondary surgical cytoreduction in ovarian cancer; (II) the technical difficulties of MIS in this setting; (III) unclear criteria to select patients.

Surgery for advanced ovarian cancer is associated with a high risk of complications due to the widespread disease and the poor preoperative nutritional status of the patient

Table 6 Main results of the review and implications for research

Main results: the present review shows that

- (I) Minimally invasive Surgery is an option in selected cases with localized or not widespread recurrent ovarian cancer
- (II) Selection of patients is of utmost importance to obtain complete cytoreduction and adequate survival outcomes

Limitations: the literature on this issue is very scant and based on case reports and case series or retrospective comparisons with traditional open surgery

Implications for future research: the efforts of researchers should be focused on:

- (I) Providing more reliable evidence on the real impact of minimally invasive surgery on survival outcomes, with prospective, comparative possibly randomized trials
- (II) Another important aspect is the identification of reliable tools to select patients for minimally invasive secondary surgical cytoreduction. The development of a score, possibly including a diagnostic laparoscopy may be useful
- (III) The implementation of intraoperative ultrasound should be further tested in order to understand its possible benefits in terms of correct identification of the site of recurrence and confirmation of complete disease resection

(46-50). In case of recurrent ovarian cancer with localized relapses, MIS may at least theoretically be of great benefit to the patients, because it reduces the surgical trauma and enhances recovery after surgery. A particular subset of patients who may benefit more from MIS approach is represented by subjects with lymphatic failure. Outcomes in this particular subset of patients appear extremely favorable both in terms of peri-operative results and long-term survival (10,43,51).

The use of pre-operative laparoscopic exploration and intra-operative ultrasound may enhance the ability to select patients and, at the same time, may improve the ability to radically resect the disease without opening the abdomen with a wide surgical incision (43).

Inevitably, MIS requires a high level of expertise and skills when applied to the field of recurrent ovarian cancer and it should be performed only in oncological centers with adequate background in complex surgical procedures.

The present review has two main limitations:

- (I) The inherent bias deriving from the type of the studies included. No randomized trials are available and the cases undergoing MIS are inevitably more favorable than those submitted to laparotomy. This imbalance negatively affects the conclusions of the published series. The reduced amount of evidence as well as its low quality should encourage researchers to adopt this approach in the context of well-designed, possibly prospective clinical trials, in order to provide more reliable knowledge on this issue.
- (II) The exclusion of articles dealing with tertiary or quaternary MIS cytoreduction. However, the

number of cases in which MIS was adopted for second or third relapse of ovarian cancer was so low that it may be regarded as anecdotal.

In conclusion, ovarian cancer still represents a difficult diagnostic and therapeutical challenge (52). MIS should be considered as a possible alternative to laparotomy for SSC of recurrent ovarian cancer in highly selected cases, at dedicated oncological centers and possibly in the context of well-conducted scientific research.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020;70:7-30.
2. du Bois A, Reuss A, Pujade-Lauraine E, et al. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). *Cancer* 2009;115:1234-44.
3. Colombo N, Sessa C, du Bois A, et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease†. *Ann Oncol* 2019;30:672-705.
4. Harter P, Sehouli J, Reuss A, et al. Prospective validation study of a predictive score for operability of recurrent ovarian cancer: the Multicenter Intergroup study DESKTOP II. A project of the AGO Kommission Annals of Oncology Special article doi:10.1093/annonc/mdz062 | 703 OVAR, AGO Study Group, NOGGO, AGO-Austria, and MITO. *Int J Gynecol Cancer* 2011;21:289-95.
5. Lee CK, Lord S, Grunewald T, et al. Impact of secondary cytoreductive surgery on survival in patients with platinum sensitive recurrent ovarian cancer: analysis of the CALYPSO trial. *Gynecol Oncol* 2015;136:18-24.
6. Fotopoulou C, Zang R, Gultekin M, et al. Value of tertiary cytoreductive surgery in epithelial ovarian cancer: an international multicenter evaluation. *Ann Surg Oncol* 2013;20:1348-54.
7. Cianci S, Ronsini C, Vizzielli G, et al. Cytoreductive surgery followed by HIPEC repetition for secondary ovarian cancer recurrence. *Updates Surg* 2019;71:389-94.
8. Coleman RL, Spirtos NM, Enserro D, et al. Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer. *N Engl J Med* 2019;381:1929-39.
9. Du Bois A, Vergote I, Ferron G, et al. Randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer: AGO DESKTOP III/ENGOT ov20. *J Clin Oncol* 2017;15S:5501.
10. Uccella S, Zorzato PC, Forliti E, et al. Laparoscopic Excision of a 5-cm Retroaortic Relapse of Ovarian Cancer. *J Minim Invasive Gynecol* 2020;27:1017-8.
11. Legge F, Petrillo M, Adamo V, et al. Epithelial ovarian cancer relapsing as isolated lymph node disease: natural history and clinical outcome. *BMC Cancer* 2008;8:367.
12. Gadducci A, Cosio S, Zola P, et al. The clinical outcome of epithelial ovarian cancer patients with apparently isolated lymph node recurrence: a multicenter retrospective Italian study. *Gynecol Oncol* 2010;116:358-63.
13. Tinelli R, Stomati M, Trojano G, et al. Laparoscopic treatment of ovarian granulosa cells tumor developed in the pelvic anterior preperitoneal space 20 years after laparotomic salpingo-oophorectomy: case report and review of literature. *Gynecol Endocrinol* 2020. [Epub ahead of print].
14. Scambia G, Nero C, Uccella S, et al. Sentinel-node biopsy in early stage ovarian cancer: a prospective multicentre study (SELLY). *Int J Gynecol Cancer* 2019;29:1437-9.
15. Gueli Alletti S, Vizzielli G, Lafuenti L, et al. Single-Institution Propensity-Matched Study to Evaluate the Psychological Effect of Minimally Invasive Interval Debulking Surgery Versus Standard Laparotomic Treatment: From Body to Mind and Back. *J Minim Invasive Gynecol* 2018;25:816-22.
16. Uccella S, Zorzato PC, Lanzo G, et al. The role of sentinel node in early ovarian cancer: a systematic review. *Minerva Med* 2019;110:358-66.
17. Gueli Alletti S, Capozzi VA, Rosati A, et al. Laparoscopy vs. laparotomy for advanced ovarian cancer: a systematic review of the literature. *Minerva Med* 2019;110:341-57.
18. Uccella S, Nero C, Vizza E, et al. Sentinel-node biopsy in early-stage ovarian cancer: preliminary results of a prospective multicentre study (SELLY). *Am J Obstet*

- Gynecol 2019;221:324.e1-10.
19. Uccella S, Fagotti A, Zannoni GF, et al. Presumed early ovarian cancer with isolated tumor cells in para-aortic sentinel nodes. *Int J Gynecol Cancer* 2019;29:216-20.
 20. Uccella S, Gisone B, Stevenazzi G, et al. Laparoscopic sentinel node detection with ICG for early ovarian cancer: Description of a technique and literature review. *Eur J Obstet Gynecol Reprod Biol* 2018;221:193-4.
 21. Ceccaroni M, Roviglione G, Bruni F, et al. Laparoscopy for primary cytoreduction with multivisceral resections in advanced ovarian cancer: prospective validation. "The times they are a-changin'". *Surg Endosc* 2018;32:2026-37.
 22. Ghezzi F, Cromi A, Fanfani F, et al. Laparoscopic fertility-sparing surgery for early ovarian epithelial cancer: A multi-institutional experience. *Gynecol Oncol* 2016;141:461-5.
 23. Gallotta V, Ghezzi F, Vizza E, et al. Laparoscopic Management of Ovarian Cancer Patients With Localized Carcinomatosis and Lymph Node Metastases: Results of a Retrospective Multi-institutional Series. *J Minim Invasive Gynecol* 2016;23:590-6.
 24. Gallotta V, Ghezzi F, Vizza E, et al. Laparoscopic staging of apparent early stage ovarian cancer: results of a large, retrospective, multi-institutional series. *Gynecol Oncol* 2014;135:428-34.
 25. Cromi A, Bogani G, Uccella S, et al. Laparoscopic fertility-sparing surgery for early stage ovarian cancer: a single-centre case series and systematic literature review. *J Ovarian Res* 2014;7:59.
 26. Ghezzi F, Malzoni M, Vizza E, et al. Laparoscopic staging of early ovarian cancer: results of a multi-institutional cohort study. *Ann Surg Oncol* 2012;19:1589-94.
 27. Ghezzi F, Cromi A, Uccella S, et al. Incorporating laparoscopy in the practice of a gynecologic oncology service: actual impact beyond clinical trials data. *Ann Surg Oncol* 2009;16:2305-14.
 28. Ghezzi F, Cromi A, Bergamini V, et al. Should adnexal mass size influence surgical approach? A series of 186 laparoscopically managed large adnexal masses. *BJOG* 2008;115:1020-7.
 29. Uccella S, Cromi A, Seveso A, et al. Comprehensive laparoscopic surgical staging of ovarian dysgerminoma in a 13-year-old girl: a case report. *J Minim Invasive Gynecol* 2008;15:110-2.
 30. Ghezzi F, Cromi A, Uccella S, et al. Laparoscopy versus laparotomy for the surgical management of apparent early stage ovarian cancer. *Gynecol Oncol* 2007;105:409-13.
 31. Gallotta V, Conte C, Giudice MT, et al. Secondary Laparoscopic Cytoreduction in Recurrent Ovarian Cancer: A Large, Single-Institution Experience. *J Minim Invasive Gynecol* 2018;25:644-50.
 32. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-6.
 33. Fagotti A, Costantini B, Gallotta V, et al. Minimally invasive secondary cytoreduction plus HIPEC versus open surgery plus HIPEC in isolated relapse from ovarian cancer: a retrospective cohort study on perioperative outcomes. *J Minim Invasive Gynecol* 2015;22:428-32.
 34. Nezhat FR, Denoble SM, Cho JE, et al. Safety and efficacy of video laparoscopic surgical debulking of recurrent ovarian, fallopian tube, and primary peritoneal cancers. *JLS* 2012;16:511-8.
 35. Magrina JF, Cetta RL, Chang YH, et al. Analysis of secondary cytoreduction for recurrent ovarian cancer by robotics, laparoscopy and laparotomy. *Gynecol Oncol* 2013;129:336-40.
 36. Eriksson AGZ, Graul A, Yu MC, et al. Minimal access surgery compared to laparotomy for secondary surgical cytoreduction in patients with recurrent ovarian carcinoma: Perioperative and oncologic outcomes. *Gynecol Oncol* 2017;146:263-7.
 37. Trinh H, Ott C, Fanning J. Feasibility of laparoscopic debulking with electrosurgical loop excision procedure and argon beam coagulator at recurrence in patients with previous laparotomy debulking. *Am J Obstet Gynecol* 2004;190:1394-7.
 38. Holloway RW, Brudie LA, Rakowski JA, et al. Robotic-assisted resection of liver and diaphragm recurrent ovarian carcinoma: description of technique. *Gynecol Oncol* 2011;120:419-22.
 39. Nezhat FR, Finger TN, Vetere P, et al. Comparison of perioperative outcomes and complication rates between conventional versus robotic-assisted laparoscopy in the evaluation and management of early, advanced, and recurrent stage ovarian, fallopian tube, and primary peritoneal cancer. *Int J Gynecol Cancer* 2014;24:600-7.
 40. Mutlu L, Khadraoui W, Khader T, et al. Robotic Tumor Debulking off External Iliac Vessels for the Management of Recurrent Ovarian Cancer. *J Minim Invasive Gynecol* 2020;27:1021-2.
 41. Magrina JF, Guardiola TC, Magtibay PM 3rd, et al. Minimally Invasive Surgery for Resection of Diaphragm Metastases in Ovarian Cancer. *J Minim Invasive Gynecol* 2019;26:1268-72.
 42. Yang W, Cheng Z, Dai H, et al. Laparoscopic-based score assessment combined with a multiple disciplinary team

- in management of recurrent ovarian cancer: A single-center prospective study for personalized surgical therapy. *Medicine (Baltimore)* 2017;96:e7440.
43. Mascilini F, Quagliozzi L, Moro F, et al. Role of Intraoperative Ultrasound to Extend the Application of Minimally Invasive Surgery for Treatment of Recurrent Gynecologic Cancer. *J Minim Invasive Gynecol* 2018;25:848-54.
 44. Moro F, Uccella S, Testa AC, et al. Intraoperative Ultrasound-Guided Excision of Cardiophrenic Lymph Nodes in an Advanced Ovarian Cancer Patient. *Int J Gynecol Cancer* 2018;28:1672-5.
 45. Uccella S, Mele MC, Quagliozzi L, et al. Assessment of preoperative nutritional status using BIA-derived phase angle (PhA) in patients with advanced ovarian cancer: Correlation with the extent of cytoreduction and complications. *Gynecol Oncol* 2018;149:263-9.
 46. Cianci S, Rumolo V, Rosati A, et al. Sarcopenia in Ovarian Cancer Patients, Oncologic Outcomes Revealing the Importance of Clinical Nutrition: Review of Literature. *Curr Pharm Des* 2019;25:2480-90.
 47. Cianci S, Tarascio M, Rosati A, et al. Sexual function and quality of life of patients affected by ovarian cancer. *Minerva Med* 2019;110:320-9.
 48. Cianci S, Abatini C, Fagotti A, et al. Hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal malignancies using new hybrid CO2 system: preliminary experience in referral center. *Updates Surg* 2019;71:555-60.
 49. Petrillo M, De Iaco P, Cianci S, et al. Long-Term Survival for Platinum-Sensitive Recurrent Ovarian Cancer Patients Treated with Secondary Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy (HIPEC). *Ann Surg Oncol* 2016;23:1660-5.
 50. Gallotta V, Giudice MT, Conte C, et al. Minimally invasive salvage lymphadenectomy in gynecological cancer patients: A single institution series. *Eur J Surg Oncol* 2018;44:1568-72.
 51. Gallotta V, Bruno M, Conte C, et al. Salvage lymphadenectomy in recurrent ovarian cancer patients: Analysis of clinical outcome and BRCA1/2 gene mutational status. *Eur J Surg Oncol* 2020;46:1327-33.
 52. Giampaolino P, Della Corte L, Foreste V, et al. Unraveling a difficult diagnosis: the tricks for early recognition of ovarian cancer. *Minerva Med* 2019;110:279-91.

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