

REVIEW

A review of robotic surgery in the management of recurrent ovarian carcinoma: indication and techniques

Peter C. Lim^{1,*}

¹Center of Hope, Department of Pelvic Surgery, University of Nevada School of Medicine, Reno, NV 89511, USA

***Correspondence**

plim@cohreno.com (Peter C. Lim)

Abstract

Background: Treatment of recurrent ovarian cancer may consist of salvage chemotherapy or secondary cytoreductive surgery. Retrospective studies suggest that radical secondary cytoreduction resulting in no macroscopic disease (R0) after completion of surgery benefits patients and prolongs survival. The role of robotic-assisted secondary cytoreductive surgery (RASCS) is in its infancy. The aim of this manuscript is to review the literature regarding the role, the indication, and the techniques of RASCS and to summarize the published perioperative, postoperative, and oncologic outcomes of RASCS. **Methods:** A comprehensive systemic review was conducted in the PubMed, MEDLINE, EMBASE, and Google Scholar databases from 1 January 1980 through 31 December 2021. Keywords searched were “ovarian cancer”, “recurrence”, “robotic-assisted secondary debulking/cytoreductive surgery”, “morbidity and mortality of secondary cytoreductive surgery”, “indications for secondary cytoreductive”, and combinations of these terms. Studies selected and analyzed included randomized controlled trials (RCTs) as well as prospective and retrospective analyses and case series. RASCS procedures and techniques are described. **Results:** Several retrospectives, meta-analyses and prospective randomized trials suggest that optimal secondary cytoreductive surgery is associated with extended progression-free and overall survival. Preoperative selection criteria, such as Memorial Sloan Kettering (MSK) criteria and AGO (Arbeitsgemeinschaft Gynaekologische Onkologie) scores demonstrate that clinical-pathological factors can predict optimal secondary cytoreductive surgery and correlate with improved progression-free survival and overall survival. The surgical procedures that are required in secondary cytoreductive surgery can be complex. Limited retrospective studies have demonstrated that secondary cytoreductive surgery utilizing a robotic surgical platform can achieve the same rate of optimal cytoreductive surgery as open laparotomy with decreased morbidity. The effect of RASCS on progression-free and overall survival has not been established. **Conclusions:** Early literature reports indicate that RASCS, in selected patients, can be applied for surgical treatment of recurrent ovarian cancer without compromising morbidity; long-term studies are warranted to determine the effect on progression-free and overall survival.

Keywords

Recurrent ovarian cancer; Secondary cytoreductive surgery; Robotic-assisted secondary cytoreductive surgery; RASCS

1. Introduction

Ovarian cancer is the sixth most common cancer in women. Worldwide, it is estimated that 200,000 new cases of ovarian cancer are diagnosed annually—the risk of developing ovarian cancer by age 75 ranges from 0.5% to 1.6% between countries. Optimal cytoreductive surgery is the cornerstone of advanced-stage ovarian cancer treatment, followed by platinum-based adjuvant chemotherapy [1–5]. For women in clinical remission after cytoreductive surgery followed by adjuvant chemotherapy for advanced-stage ovarian cancer, the recurrence rate has been reported to range from 40% to 60% and as high

as 70% [6, 7]. Treatment of recurrent ovarian cancer may consist of salvage chemotherapy or secondary cytoreductive surgery. Retrospective studies have strongly suggested that radical secondary cytoreduction surgery resulting in disease-free microscopic margins (R0) prolongs patient survival [8–11]. A randomized trial by the Gynecologic Oncology Group (GOG-213) questioned the benefit of secondary cytoreductive surgery based only on disease-free survival and not on overall survival [12]. More recently, another large prospective clinical trial, Descriptive Evaluation of Preoperative Criteria for Operability in Recurrent Ovarian Cancer (DESKTOP III), reported

an improved median overall survival for cohorts of patients who underwent secondary cytoreductive surgery followed by chemotherapy compared to no surgery with chemotherapy alone. This difference in survival benefit was attributed to 75% of the patients who underwent secondary cytoreductive surgery [13]. The median overall survival was 53.7 months in the surgery group and 46.0 months in the no-surgery group (HR for death: 0.75; 95% CI (Confidence interval), 0.59 to 0.96; $p = 0.02$). Patients with a complete—disease-free microscopic margins—resection had the most favorable outcome, with a median overall survival of 61.9 months.

Recurrent ovarian cancer may occur as isolated, oligo implants or diffuse peritoneal seedings along the upper abdomen, affecting anatomical structures such as the diaphragm, liver, porta hepatis, renal fossa, Gerota's fascia, spleen, and gastric and lesser omentum. Tumor implants may also occur in the abdominal cavity along the paracolic gutter, retroperitoneal paraaortic lymph nodes, and bowel. In addition, tumor recurrence can occur in the pelvic cavity along with the retroperitoneal pelvic lymph nodes, presacral space, and cul de sac region. The surgical procedure required to achieve cytoreduction is dictated by how the tumor affects the organ. If the tumor implant is on the surface of the peritoneum, it will require a simple excision such as peritonectomy without requiring removal of the organ. More radical dissection such as diaphragm resection with repair, liver wedge resection, splenectomy, bowel resection, and lymphadenectomy is needed if the tumor infiltrates the organ. Performing these complex radical dissections has traditionally required open laparotomy. The postoperative morbidity from open secondary cytoreductive surgery rate has been reported to be between 32.5% and mortality rate at 2.5% [14]. The morbidity from robotic-assisted secondary debulking is associated with less blood loss, shorter hospitalization, and lower complication rates than open secondary debulking [15, 16].

This manuscript is a review of the current literature; the role, the indication, and the techniques of RASCS, and a summary of the published perioperative, postoperative, and oncologic outcomes of robotic-assisted secondary cytoreductive surgery (RASCS).

2. Methodology of Review

PubMed, MEDLINE, EMBASE, and Google Scholar were used to identify contributing research from January 1980 to December 2021. A systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria to evaluate the effect of open secondary cytoreductive surgery and RASCS. In addition, article reference lists were reviewed for additional source references. Search keywords were “ovarian cancer”, “recurrence”, “robotic-assisted secondary debulking/cytoreductive surgery”, “morbidity and mortality of secondary cytoreductive surgery”, “indications for secondary cytoreductive”, and combinations of these terms. Selected and analyzed studies included randomized controlled trials (RCTs), prospective and retrospective studies, and case series.

The techniques and surgical considerations described are based on the author surgeon's experience performing approx-

imately 3500 robotic-assisted procedures for the treatment of gynecological cancer from March 2008 to June 2021. Approximately 50% of these robotic-assisted procedures were complex radical surgeries.

3. Results

3.1 Indication

The indication for RASCS is the same as for open laparotomy secondary debulking. The potential benefit of secondary debulking was first reported in 1983 in a retrospective study: a median survival of 20 months was reported for patients undergoing optimal cytoreductive surgery of <1.5 cm versus 5 months for those patients having suboptimal debulking of ≥ 1.5 cm [17]. Oksefjell *et al.* [18] demonstrated median overall survival (OS) correlated with the absence of macroscopic residual disease after secondary cytoreductive surgery. The authors reported a median OS of 52 months for patients with no residual tumor, 27 months for ≤ 2 cm tumors, and 8.4 months for residual tumors greater than 2 cm.

In a prospective study, complete cytoreductive surgery was the significant predictor of survival in recurrent ovarian cancer [19]. Similarly, in two other studies, improved median OS ranged from 42–69 months for R0 resections (no visible disease), 18–31 months for R1 resections (residual 0.1–1.0 cm), and 7.7–15.6 months for R2 resections (residual >1.0 cm) [20, 21]. Multiple studies, including a meta-analysis and systematic review, reported that complete cytoreduction to no visible disease (R0) was associated with increased overall survival [22–24]. Thus, the goal of secondary cytoreductive surgery must be maximal cytoreduction resulting in R0 resection. Based on these studies, the benefit of secondary cytoreductive surgery resulting in R0 resection is improved OS. However, R0 resection may not be achievable in all recurrent ovarian cancer.

It is imperative to select patients suitable for secondary cytoreductive surgery considering surgical morbidity and mortality. However, selection criteria for a candidate for RASCS have not yet been established. To identify factors that may predict who may undergo successful secondary debulking for recurrent ovarian cancer, several predictive models have been developed based on clinical and pathological data in terms of surgical outcomes, progression-free survival, and overall survival.

In a retrospective single-institution (Memorial Sloan Kettering Cancer Center) study, Chi *et al.* [25] analyzed 153 patients who underwent secondary cytoreduction surgery for recurrent epithelial ovarian cancer. The authors proposed selection criteria (MSK criteria) for successful secondary cytoreductive: patients with an isolated recurrence, oligometastatic disease without carcinomatosis, and a disease-free interval from the primary cytoreductive surgery to the secondary cytoreductive surgery of at least 12 months. Minaguchi *et al.* [26] in their single-institution retrospective analysis reported four predictive factors for successful secondary cytoreductive surgery: treatment-free interval >12 months, no distant metastasis, solitary disease, and an Eastern Cooperative Oncology Group (ECOG) score of 0. Complete resection of visible tumors was

achieved in 79% of patients with 3–4 factors, in 40% of those with 2 factors, and in 33% of those with 0–1 factors.

Angoli *et al.* [27] developed a different predictive model (SeC-Score) to assess the risk of optimal secondary cytoreductive surgery. They evaluated the following preoperative variables: age, residual tumor (RT) at primary cytoreduction (0 vs. >0 cm), preoperative CA-125 and HE-4, and ascites at recurrence. The authors determined that these variables were statistically significant in predicting the risk of suboptimal secondary cytoreductive surgery. In studied patients, the sensitivity and specificity of the SeC-Score was 82% and 83%, respectively (PPV = 0.79, NPV = 0.81). Tian *et al.* conducted a retrospective multicenter international study and found that complete secondary cytoreductive surgery correlated with the International Federation of Gynecology and Obstetrics (FIGO) staging, residual disease after primary cytoreductive surgery, progression-free interval, ECOG performance status, CA-125 level, and ascites at the time of recurrence. Based on these variables, a Tian scoring system was developed as high- or low-risk to predict the success of optimal cytoreductive surgery. They noted that complete cytoreductive surgery was favored if patients had a low-risk score compared to a high-risk score [28].

The Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) score was evaluated via the prospective Descriptive Evaluation of Preoperative Criteria for Operability in Recurrent Ovarian Cancer trial (DESKTOP I) trial [29]. The score was based on the presence or absence of the patient's health performance status based on an ECOG score of 0, stage of disease (stage I or II) and/or complete cytoreduction achieved at the primary cytoreductive surgery, and the presence or absence of ascites <500 mL. The presence of all three factors was considered a positive score. A positive AGO score predicted complete cytoreduction in 79% of patients. The AGO-DESKTOP II study subsequently showed that the AGO score predicted 76% of patients would benefit from secondary cytoreductive surgery [30].

Bogani *et al.* applied AGO and MSK model criteria and developed a nomogram in their cohort of patients to predict complete secondary cytoreductive surgery. They reported 87% of their patient population studied was able to achieve complete cytoreductive surgery, thus validating these two models [31]. Van de Laar *et al.* [32] tested the performance of AGO and the Tian Model and reported a positive predictive value for complete secondary cytoreductive surgery of 82% and 80.3%, respectively and a false negative rate of 68.5% and 55.6%, respectively. They also noted that patients who did not meet these strict criteria were also able to achieve a complete cytoreductive surgery. More important, complete cytoreductive surgery was associated with improved overall survival.

Shi *et al.* compared results from secondary cytoreductive surgery followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1) using the international model (iMODEL) score and PET-CT imaging to predict resectable disease. The iMODEL score was calculated based on six variables: FIGO stage, residual disease after primary surgery, platinum-free interval, ECOG performance status, serum level of CA-125 at recurrence, and presence of ascites. An iMODEL score of 4.7 or lower predicted a potential

for complete resection at the time of secondary debulking. This was associated with significantly longer progression-free survival of 17.4 months versus 11.9 months in the no-surgery group [33].

The clinical and pathological factors that have been evaluated and that have predicted optimal secondary cytoreduction are based on patients who underwent open secondary cytoreductive surgery. The applicability of these same predictive clinical and pathological factors in selecting patients for RASCS has not been validated. The major concern of RASCS and other MIS approaches is the inability to palpate and adequately evaluate intraabdominal disease. Preoperative imaging is essential to assess whether patients are candidates for secondary cytoreductive surgery. Currently, there are no significant data to suggest whole body magnetic resonance imaging (MRI), positron emission tomography-computerized tomography (PET-CT), or CT scan is ideal.

Selection of RASCS candidates should be based on the considerations and results from the described studies: platinum free-interval period, time of recurrence, patient's performance status, size of the lesion, location of the recurrence, presence of ascites, number of recurrences (single lesion, oligometastatic, or diffuse disease), location of the tumor, and resectability of the recurrent tumor as determined by preoperative imaging. We prefer CT scan to evaluate presence or absence of ascites and the location and resectability of the disease. Patients then undergo laparoscopic evaluation to determine whether they can undergo RASCS.

3.2 Site of Recurrent Ovarian Cancer Disease

Ovarian recurrence may manifest as an isolated tumor implant in the pelvic region or as intra-abdominal implants on the bowel, retroperitoneal lymph nodes; upper abdomen on the diaphragm, lesser omentum, stomach, liver, or spleen. Recurrence may occur as isolated oligo metastases, or multifocal peritoneal seeding. In the DESKTOP III trial (N = 407), the reported order of frequency of relapse site was pelvis (n = 237; 58.2%), intraabdominal above the pelvis (n = 213; 52.3%), retroperitoneum (n = 146; 35.9%), spleen (n = 31; 7.6%), and liver parenchyma (n = 24; 5.9%). For patients who were randomized to undergo secondary debulking in this cohort, the order of frequency of recurrence was: pelvis (n = 125; 60.7%), intraabdominal above the pelvis (n = 103; 50%), retroperitoneum (n = 73; 35.4%), spleen (n = 13; 6.3%), and liver parenchyma (n = 13; 6.3%) [34]. A similar pattern of recurrence was noted in a retrospective cohort study: 39 patients who underwent RASCS had recurrence in the pelvis (n = 20; 51%), the abdomen (n = 8; 21%), and upper abdominal disease (n = 9; 23%) [35]. In a multi-institutional retrospective study (N = 48), pelvic recurrence was the most common (n = 19; 39.6%), followed by the abdomen (n = 17; 35.4%), pelvic and abdomen (n = 11; 22.9%), and pelvic and diaphragm (n = 1; 2.1%) [16].

Given these overlapping patterns of recurrence and location, RASCS may require resection of superficial peritoneal implants or complex procedures such as robotic-assisted small and/or large bowel resection. These potential sites where

relapse may occur are difficult to access, and traditionally open laparotomy is required to access them to achieve an optimal cytoreductive surgery, particularly upper abdominal relapses such as in the diaphragm, spleen, or renal fossa along the Gerota's fascia. However, when relapse occurs in the upper abdomen, more complex upper procedures such as diaphragm peritonectomy, liver wedge resection, and splenectomy are required. The feasibility of robotic-assisted splenectomy for recurrent ovarian cancer has also been described [36–38]. Magrina *et al.* [15] reported outcomes from 10 patients who underwent robotic-assisted upper abdominal resection, 50% of whom underwent liver wedge resection or diaphragmatic resection. Tozzi *et al.* [39] reported laparoscopic diaphragmatic peritonectomy for ovarian cancer; however, nearly 50% of the patients' required open conversion due to extensive disease coalescing the liver to the diaphragm preventing safe mobilization and accidental pleural opening. Clearly, when recurrence occurs in these regions complex procedures are required to achieve cytoreduction.

The robotic surgical platform has a versatile magnified endoscope (30° degrees up and down), operative field stabilization, and 720° endowrist articulation instrumentation. The robotic technology permits complex surgical procedures in narrow, confined operative fields through a minimally invasive approach.

3.3 RASCS Techniques

When performing RASCS, factors such as positioning, the anatomical region, intended procedure, body habitus, port placement, the endoscope, and the robotic system that is employed (DaVinci Si or Xi Intuitive Surgical, Sunnyvale, CA) should be considered.

3.3.1 Positioning

Positioning is critical in robotic surgery because it must provide access to the surgical field and must accommodate the robotic camera and working arms. Positioning starts with patient placement in the dorsal lithotomy position with the legs in stirrups, similar to conventional laparoscopy. To minimize potential neuromuscular injuries, one must provide adequate padding at all pressure points and avoid extreme flexion, extension, and abduction of extremities. A standard motorized operating-room table featuring maximum tilt achieves steep Trendelenburg. A layer of eggcrate foam on top of the bed is securely taped to the surgical bed to prevent a patient in steep Trendelenburg from shifting while on the operating table. It is important that the pad rest on the shoulder and not at the pressure points. In addition, well-padded arm sleds made of rigid plastic material cradle the arm and extend under the mattress to protect and stabilize the arms, particularly in morbidly obese patients (Fig. 1).

For morbidly obese patients, we recommend the Trenguard™ foam shoulder pad brace (Model #56100 D.A. Surgical, Newbury, Ohio USA), which is anchored to the operating table (Fig. 2)

Particular consideration should be taken to protect the patient's face, particularly the eyes, which are at risk for injury during robotic-assisted surgery. The risk of facial and ocular

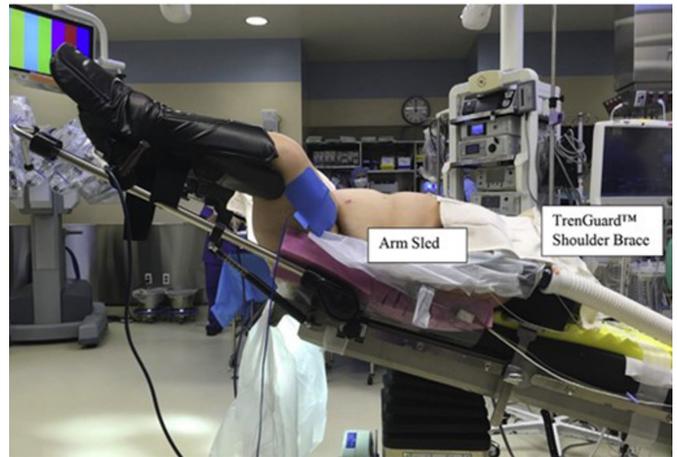


FIGURE 1. Obese patient in dorsolithotomy steep Trendelenburg position with legs in Allen Stirrups with adequate padding.



FIGURE 2. Trenguard™ shoulder brace anchored to the table to prevent sliding during steep Trendelenburg position.

trauma becomes accentuated when the robotic ports are placed superior to the umbilicus and when the robotic camera comes in contact with the face. There are no standard recommendations for the best way to protect a patient's face and eyes. We prefer the foam facemask mainly because Mayo stands often clash with the robotic arms (Fig. 3).

It is also important to keep in mind that corneal abrasion is the most common ocular complication due to failure of the eyelids to completely close, which results in corneal drying after any surgical procedure [40]. To minimize this potential complication, it is recommended that the patient's eyelids are shut after induction of general anesthesia.

The combination of dorsal lithotomy position in conjunction with steep Trendelenburg may subject a patient to certain perioperative risks and complications, such as increased laryngeal edema, facial swelling, and increased intracranial pressure. Thus, it is crucial for the surgeon, the bedside assistants, and the anesthesiologist to understand the degree of limitations of patient positioning as the positioning can lead to potential perioperative complications.



FIGURE 3. Foam face protector is placed over the face to protect the face from potential trauma from instrumentation.

After the patient is properly positioned, proper port placement is imperative to minimize potential complications and to dictate the success of the procedure.

3.3.2 Port Placement

Placement of robotic ports vary based on the anatomical region where the procedure is performed, but the general guidelines are: maximize the endoscopic view of the target anatomy (TA), maximize robotic instrument reach, optimize operative working space, and minimize external arm clashing. The camera port should align with the TA. The working ports should be 15–20 cm between the DaVinci ports and target anatomy. Ports placed close to the target anatomy impede the operative field, limit the operative working space and make the surgical procedure technically challenging. Conversely, ports placed >20 cm from the TA make it difficult to see or reach with robotic instruments. Robotic ports should be separated ideally by 8–10 cm ; however, in a thin body habitus, the spacing can be 6 cm apart for the DaVinci Xi system. We recommend utilizing all four robotic arms with the 3rd arm providing an additional assistant arm to provide static counter traction for maximal operative field exposure.

The choreography of the placement of robotic instrumentations and the assistant port is surgeon-dependent. The author proposes placement of the 3rd arm on the right side lateral to the dominant working port while the dominant hand working port is placed on the right inner port and the camera port is placed on the inner left working port; the nondominant hand port is placed lateral to the camera port on the outer left working port. The assistant port can be a 5-, 8-, or 12-mm port, and it is typically placed contralateral to the 3rd arm between the camera port and the nondominant hand working port (Fig. 4) or it can be placed on the contralateral side of the 3rd arm port in the lower quadrant at the level of the anterior superior iliac spine. The robotic ports are aligned in a straight line (Fig. 5). The robotic system is docked at the hip to allow vaginal access to complete the perineal phase.

An integrated Trumpf operating table (Trumpf Medical™ TruSystem® 7000dV, Charleston, South Carolina, USA) is

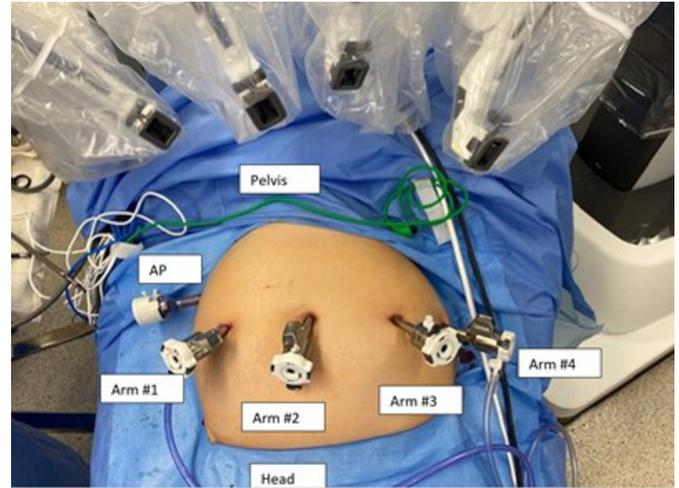


FIGURE 4. Abdominal port placement configuration for pelvic dissection. AP (assistant port) is placed left lower quadrant contralateral from 3rd arm at the level of anterior superior iliac spine. Arm #1 functions as a non-dominant hand where bipolar energy instrumentation is inserted. Arm #2 functions as a camera port. Arm #3 functions as the dominant hand where Spatula or monopolar scissors are inserted. Arm #4 serves as the robotic 3rd arm where the Prograsp grasper is placed to provide static counter traction. Instrumentation choreography through these ports is interchangeable.

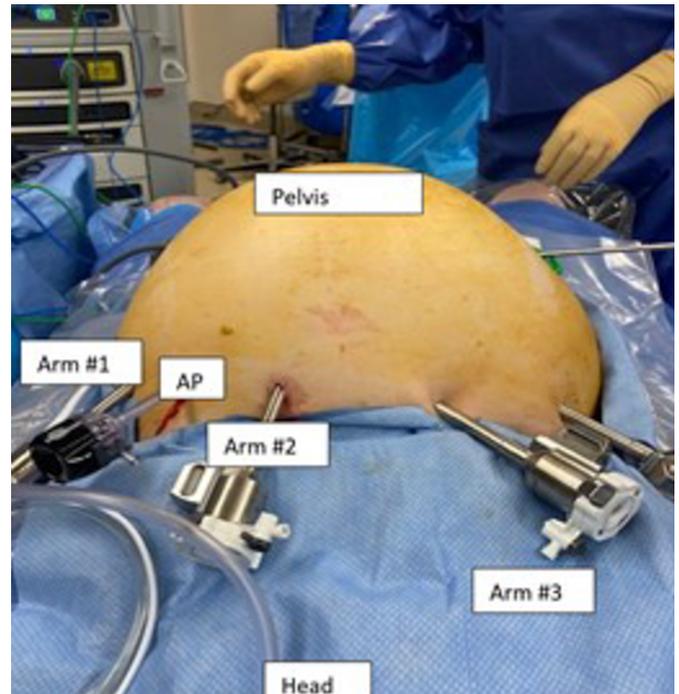


FIGURE 5. Upper abdominal port placement configuration for pelvic and abdominal dissection.

recommended to enable the DaVinci Xi Surgical System to connect to the operating table so that a patient can be dynamically positioned while the surgeon operates. The Trumpf table allows access and maximal operative field exposure and positions tissue at an ideal working angle and positions the patient throughout the case to increase autonomy for the sur-

geon and anesthesiologist. After ports are placed, they should be “burped”: rather than indenting the abdominal wall, the arms should be clutched, and the ports lifted away from the abdomen. The ports should tent the abdominal wall outward, thereby creating more intra-abdominal operative working space.

3.4 Upper Abdominal RASCS Procedures

Robotic-Assisted Diaphragm Peritonectomy

Case 1 describes recurrent ovarian cancer isolated to right diaphragm disease (Fig. 6). Robotic-assisted diaphragm peritonectomy is undertaken as the disease is adherent to the liver capsule and the right diaphragm peritoneum is coalesced with seeding to the level of the coronary ligament (Video 1).



FIGURE 6. Preoperative imaging from CT scan of upper abdomen with right diaphragm tumor seeding.

In preparation for robotic-assisted diaphragmatic resection with diaphragm muscle repair, patient positioning and port placement are crucial, requiring particular attention to ensure a smooth case. The anesthesiologist must be informed, and a double-lumen endotracheal tube should be placed if inadvertent dissection trans-diaphragmatic thoracotomy occurs.

The author recommends placing robotic ports 2 cm below the umbilicus. Port placement and choreography of the instrumentations follow for a right-handed surgeon. Working Arm #4 is positioned for the left outer lower port and will serve as the robotic 3rd arm with the Prograsp instrumentation provides static countertraction and retraction. Working Arm #3 is positioned for the left inner lower port and will serve as the dominant hand working arm and monopolar shear scissors and spatula for the main dissection. Working Arm #2 is positioned for the right inner lower port and will serve as the camera port. Working Arm #1 is positioned for the right outer lower port and will serve as the main nondominant working hand and bipolar energy grasper. For a left-handed surgeon, the monopolar shear scissors or monopolar spatula would be in Arm #1 while the bipolar energy grasper would be in Arm #3 (Fig. 7).

A 30° endoscope is recommended to maximize the view of the operative field. When the dissection commences in the anterior diaphragm peritoneum, a 30° up endoscopic view allows an optimal view of the anterior diaphragm dissection.

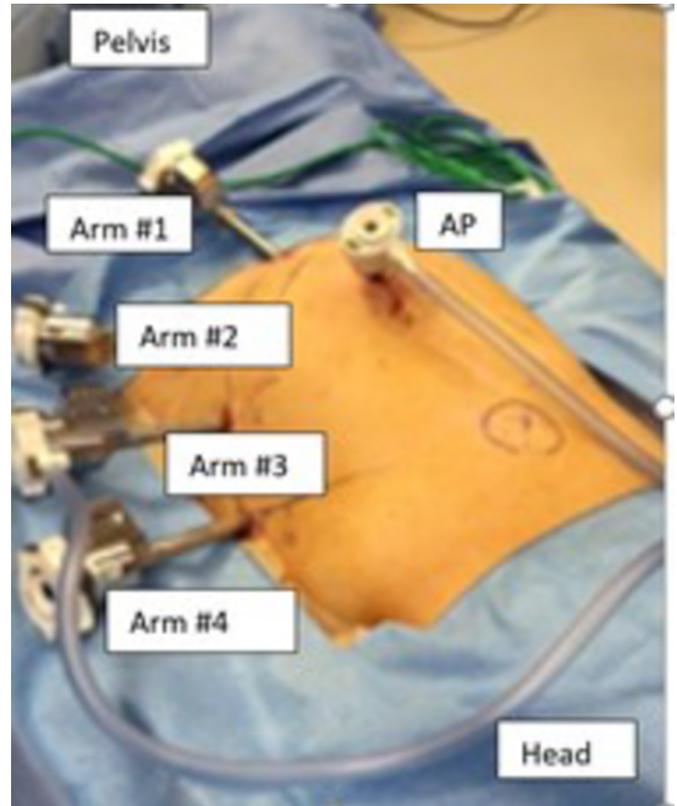


FIGURE 7. Lower pelvic port placement configuration for upper abdominal dissection.

The dissection commences in the anterior diaphragm incising the peritoneum and sharply dissecting it off the muscle. The dissection is continued along inferiorly and posteriorly. The falciform ligament should be divided to allow for the liver to be mobilized inferiorly and medially to access the inferior and posterior diaphragm region or laterally to the costophrenic region to the triangular ligament. A lap sponge or Raytech sponge is advised and placed on the surface of the liver to minimize trauma to the capsule of the liver while the Prograsp from the 3rd arm provides static gentle traction of the liver to allow for optimal exposure. We recommend utilizing a sharp dissection incising the peritoneum and dissecting the diaphragm muscle from the peritoneum when performing a peritonectomy. Once a sufficient peritoneal edge is established to provide traction, we recommend exchanging the monopolar shear scissors to Maryland Grasper and utilizing a surgical dissector peanut sponge placed in the Maryland grasper to dissect the diseased peritoneum from the diaphragm, this blunt dissection will minimize the risk of the inadvertent thoracotomy.

Case 2 presents isolated recurrent ovarian cancer invading through the diaphragm muscle (Fig. 8) necessitating a transmural diaphragmatic muscle resection to achieve complete cytoreduction (Video 2). It is imperative that a double-lumen endotracheal tube is placed by the anesthesiologist prior to the procedure. We recommend lower abdominal port placement with the robot targeting the upper abdomen. A 30° endoscope is recommended to allow a change in angle to optimize the operative view. The patient is positioned in a 5–10° reverse Trendelenburg position. Again, to achieve an optimal op-

erative field exposure on the right diaphragm, the falciform ligament should be divided, and a lap sponge or Raytech sponge must be incorporated and placed on the surface of the liver with the Prograsp from the 3rd arm providing static gentle traction of the liver. The implanted diaphragm muscle nodule is resected with monopolar shear scissors. Once the muscle is resected, the author utilizes a Prolene suture to close the diaphragm muscle. The suture begins on one end of the defect while a separate suture is run from the opposite end of the defect to the middle of the defect. A 24 French Foley catheter or Red Robinson catheter is first introduced via the assistant Port and placed into the thoracic cavity. Once the catheter is placed into the thoracic cavity, the Foley or Red Robinson catheter is then connected to suction, and the pneumothorax is evacuated via the foley or red Robinson catheter while simultaneously, tying the suture to close the defect.

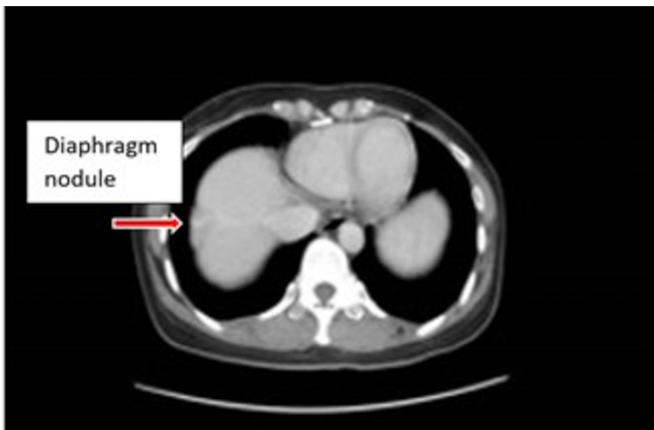


FIGURE 8. CT imaging of upper abdomen, red arrow demonstrating the diaphragm nodule.

3.5 RASCS Abdominal Procedures

Recurrent ovarian cancer that relapses in the abdomen may manifest in the small or large intestine, retroperitoneum, paraaortic lymph nodes, or renal fossa such as implant along the Gerota's fascia. Recurrences in this region may require robotic-assisted ileal cecal resection, transverse colectomy, gastric colic omentectomy, paraaortic lymph node dissection or excision of tumor implants along the renal fossa. Lower pelvic port placement should be considered for these procedures. DaVinci ports are placed 15–20 cm from the target anatomy to optimize the operative field and minimize arms clashings. Paek *et al.* [41] described lower pelvic port placement to perform a high retroperitoneal aortic node dissection.

Case 3 is recurrent ovarian cancer with oligometastatic implants on the liver capsule and Right Gerota's fascia (Fig. 9 and Fig. 10). A modified lower pelvic port placement is shown in Fig. 11: robotic-assisted excision of a tumor implant on the right renal fossa (Video 3).

3.6 RASCS Pelvic Procedures

For ovarian recurrences that occur in the pelvic region, robotic-assisted sigmoid resection, excision of recurrent pelvic mass,

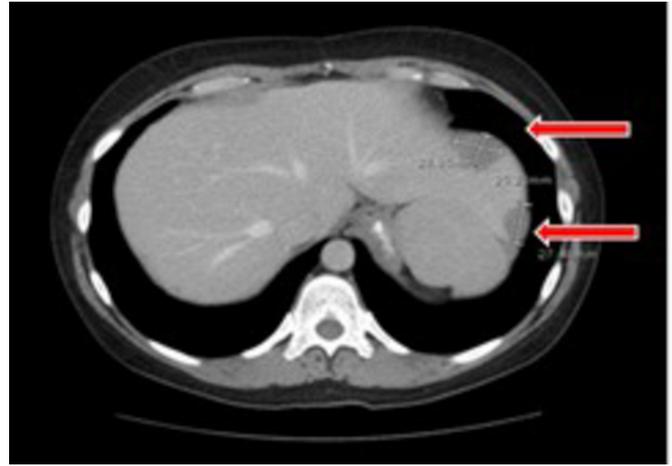


FIGURE 9. Recurrent ovarian cancer. CT scan of the upper abdomen. Red arrow demonstrating two tumor implants along Segments II and III.

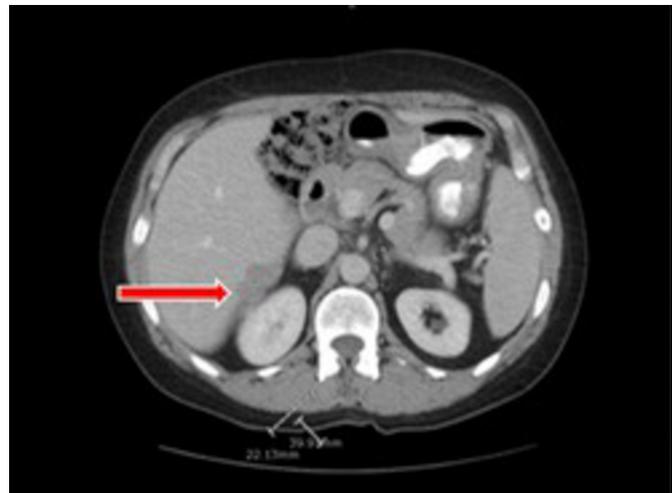


FIGURE 10. Recurrent ovarian cancer. CT scan of the upper abdomen. Red arrow demonstrating tumor implant on the anterior Gerota's fascia in the right renal fossa.

and/or urologic procedures such as ureterolysis, ureteral resection with reimplantation or partial cystectomy may be required. For these procedures, we recommend placing the DaVinci ports at the level of the umbilicus (Fig. 4). This port placement configuration facilitates pelvic procedures, such as en bloc small bowel resection with pelvic recurrent tumor, as shown in Video 4.

3.7 Robotic-Assisted Multiquadrant Procedure

Ovarian cancer may recur as oligo-metastases in a different anatomical region. This may require a multi-quadrant surgical approach. One such example is oligo-metastases, which may manifest in the upper abdominal and pelvic regions. In such a case, we recommend placing the DaVinci robot ports at the level of the umbilicus and starting the upper abdominal dissection, and performing the necessary procedure; when completed, the DaVinci robot boom is rotated to retarget the pelvic region to complete the pelvic procedure.

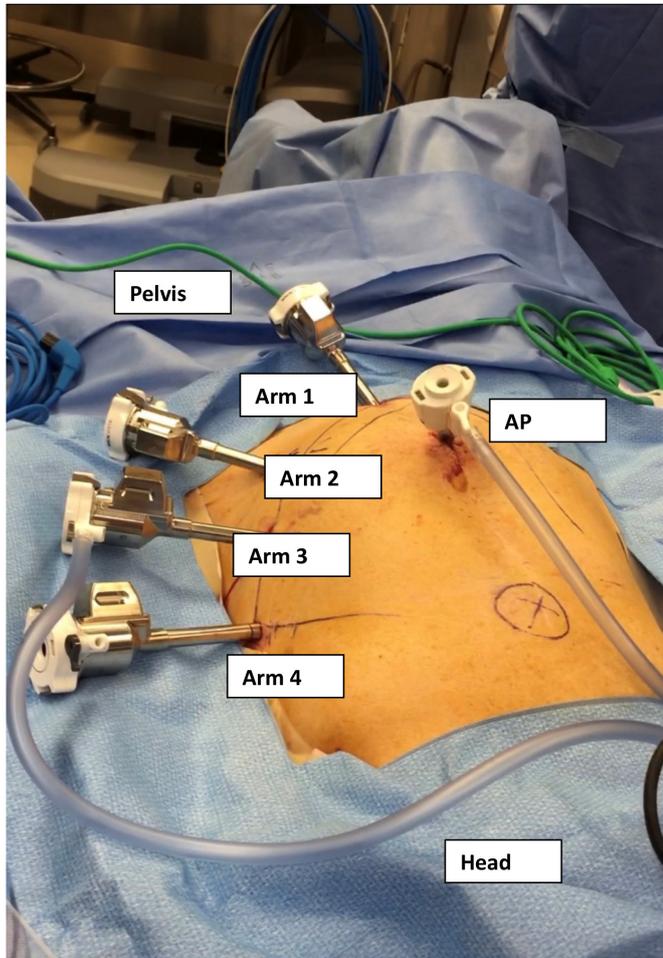
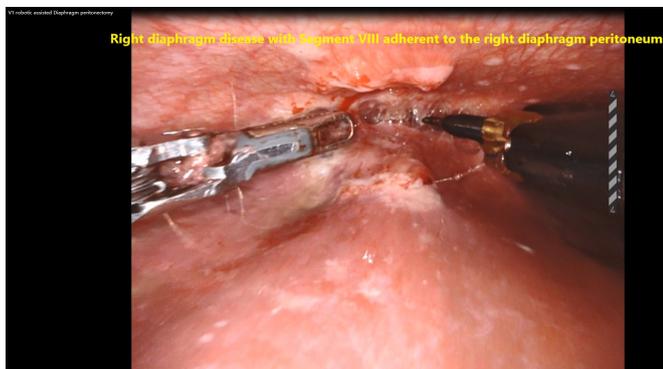


FIGURE 11. Modified lower pelvic port placement configuration for upper abdominal dissection. AP (assistant port) is placed right lower quadrant contralateral from “3 rd Arm”, at the level of the anterior superior iliac spine. Arms #1 functions as a non-dominant hand and Bipolar energy instrumentation inserted in the port. Arms #2 functions as a camera port. Arms #3 functions as the dominant hand and the Spatula or monopolar scissor is inserted in the port. Arms #4 serve as the robotic “3rd arm” and Prograsp grasper is placed to provide static counter traction. The choreography of instrumentations in these ports is interchangeable.



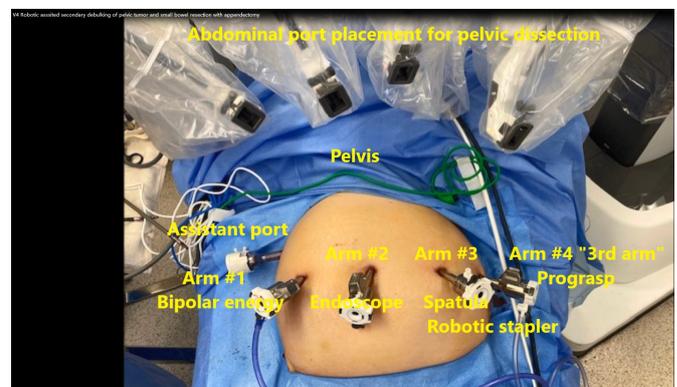
VIDEO 1. Robotic assisted Diaphragm peritonectomy. The embedded movie may also be viewed at <https://>.



VIDEO 2. RA DPRRxS & Repair. The embedded movie may also be viewed at <https://>.



VIDEO 3. Robotic assisted secondary cytoreductive surgery Excision of liver and Right Gerota's fascia implant. The embedded movie may also be viewed at <https://>.



VIDEO 4. Robotic assisted secondary debulking of pelvic tumor and small bowel resection with appendectomy. The embedded movie may also be viewed at <https://>.

3.8 Outcomes of RASCS

Limited data (N = 104) have been reported regarding RASCS. Available studies were retrospective and described the feasibility and surgical outcomes (Table 1). Collectively, optimal cytoreductive surgery was achieved in 84% of the cases, similar to that achieved via open secondary cytoreductive surgeries. All four retrospective studies reported successful RASCS including upper abdominal dissection, such as diaphragm resection, liver wedge resection, or splenectomy; small or large

TABLE 1. Baseline Characteristics.

Authors	N	Complete cytoreduction, N (%)	Median operative time, min	Median blood loss, mL	Median LOS, days	Procedures	Conversion to open, n (%)	Complications, n (%)
Magrina [15]	10	7 (70)	220	206	3.4	UAD (n = 5) BRX (n = 3) RPRX (n = 6)	NR	3 (30)
Escobar [16]	44	36 (82)	179.5	50	1	UAD (n = 3) BRX (n = 5) RPRX (n = 6)	4 (8.3)	6 (13.6)
Eriksson [39] [35]	31	37 (90)	186	50	1	BRX (n = 9) *	6 (15)	3 (8)
Lim [42]	11	9 (11)	94	86	2	UAD (n = 4) BRX (n = 2) RPRX (n = 2) RPNRX (n = 3)	0	0
Total	104	89 (85.5)	170	98	1.85		10 (9.6)	12 (11.5)

UAD, upper abdominal dissection (involves resection of the liver, splenectomy, or diaphragm peritonectomy or resection); BRX, bowel resection (small or large bowel resection); RPRX, retroperitoneal mass resection; RPNRX, retroperitoneal node dissection; NR, not reported; *, specific procedures were not reported.

bowel resection; retroperitoneal mass excision; and lymph node dissection. Each of the four studies showed acceptable operative times with a median time of 170 (94–220) minutes, median intraoperative blood loss of 94 (50–206) mL, average hospitalization 1.85 (1–3.4) days, and rate of conversion to open procedure 9.6% (n = 10). The complication rate overall for the 4 studies was 11.5% (n = 12) [14, 15, 39, 40].

Two studies reported a comparative analysis of robotic-assisted and open laparotomy secondary cytoreductive surgery [16, 27]. In the limited cohort that was analyzed, the rates of optimal cytoreductive surgery and operative time were statistically similar. The robotic-assisted approach was associated with less blood loss, shorter hospitalization, and fewer complications. The 2 and 3-year progression-free survival rates among the robotic-assisted and open cohorts were 56.1% and 43.8% respectively while the 2 and 3-year overall survival rates were 92% and 85.7%, respectively.

4. Discussion

Management of recurrent ovarian cancer continues to evolve. There are multiple treatment options including second-line chemotherapy agents, targeted therapy, and surgical options. There is a substantial level of evidence-based retrospective data, meta-analysis, and prospective trials to suggest that secondary cytoreductive surgery is an option with improved progression-free survival. Selection criteria are imperative in patients who are candidates for secondary cytoreductive surgery.

Patients should demonstrate good performance status, their recurrence should be a platinum-sensitive tumor demonstrating a progression-free interval of at least 12 months; the tumor should be isolated or oligo-metastatic disease, and there should be minimal or no ascites. Preoperative imaging is critical to evaluate the location and the size of the tumor in planning for

secondary cytoreductive procedure. The surgical procedure can be complex and difficult, depending on the location of tumor recurrence. The advent of robotic surgery with its technological advances has shifted the surgical paradigm. Employing a robotic surgical platform in the setting of secondary cytoreductive surgery allows the surgeon to perform complex procedures, such as bowel resection, diaphragm peritonectomy, liver wedge resection, splenectomy, omentectomy, and excision of tumor implants in narrow confined spaces. Historically, secondary cytoreductive surgery that requires upper abdominal dissection has been performed via open laparotomy, which may lead to increased morbidity and prolonged hospitalization and recovery, potentially delaying salvage chemotherapy.

Early retrospective studies have shown that RASCS can achieve optimal cytoreductive surgery comparable to open procedures. Surgical outcomes, such as operative time, blood loss, hospitalization, recuperation, and complications, favor the robotic surgical approach. Perhaps, the area of most potential benefit of robotic-assisted surgery is in the setting of upper abdominal dissection with diaphragm peritonectomy or resection and repair, resection of superficial liver implants, resection of implants along the Gerota's fascia, and splenectomy. With the potential drawback of RASCS being adequate evaluation of intraabdominal disease, it is imperative that patients undergo preoperative imaging studies, such as CT scan.

The current review incorporates a comprehensive literature review of the role of secondary cytoreductive surgery for the treatment of recurrent ovarian cancer. It is important to acknowledge that this review has been limited by the reality that the role and application of RASCS is in its infancy. Clearly, further studies—preferably prospective randomized trials—are required to validate the benefits and safety of secondary cytoreductive surgery with robotic surgical platforms compared to open secondary cytoreductive surgery. Important to note: surgeons must overcome the learning curve necessary

to perform these complex procedures robotically. In addition, the predictive models that have been utilized to assess the success of secondary cytoreductive surgery must be validated in the RASCS setting.

Based on the current and limited literature, RASCS seems to be safe and feasible for recurrent ovarian cancer. However, the paucity of published evidence is the principal limitation of this review. In a well-selected group of patients—based on MSK, ECOG, FIGO, and AGO findings—and due to the robot's technological attributes, RASCS may be considered for surgical treatment of recurrent ovarian cancer without compromising morbidity; long-term studies are warranted to determine the effect on overall survival.

ABBREVIATIONS

RASCS, robotic-assisted secondary cytoreductive surgery; RCT, randomized controlled trial; AGO, Arbeitsgemeinschaft Gynaekologische Onkologie; MSK, Memorial Sloan Kettering; GOG, Gynecologic Oncology Group; DESKTOP, Descriptive Evaluation of Preoperative Criteria for Operability in Recurrent Ovarian Cancer; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; OS, overall survival; R0, no visible disease; R1, residual disease 0.1–1.0 cm; R2, residual disease >1.0 cm; RT, residual tumor; PPV, positive predictive value; NPV, negative predictive value; FIGO, International Federation of Gynecology and Obstetrics; ECOG, Eastern Cooperative Oncology Group; MRI, magnetic resonance imaging; PET, positron emission tomography; CT, computerized tomography; TA, target anatomy; AP, assistant port; LOS, length of hospital stay; UAD, upper abdominal resection; BRX, bowel resection; RPRX, retroperitoneal mass resection; RPNRX, retroperitoneal node dissection; NR, not reported.

AUTHOR CONTRIBUTIONS

PCL designed the review study, performed the literature research, wrote the manuscript, contributed to editorial changes in the manuscript, and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

ACKNOWLEDGMENT

The author thanks Mimi Wainwright (Wainwright Medical Communications, Los Gatos, CA USA) for editorial support in the preparation of the revised manuscript.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

- [1] Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *Journal of Clinical Oncology*. 2002; 20: 1248–1259.
- [2] Delgado G, Oram DH, Petrilli ES. Stage III epithelial ovarian cancer: the role of maximal surgical reduction. *Gynecologic Oncology*. 1984; 18: 293–298.
- [3] Hacker NF, Berek JS, Lagasse LD, Nieberg RK, Elashoff RM. Primary cytoreductive surgery for epithelial ovarian cancer. *Obstetrics and Gynecology*. 1983; 61: 413–420.
- [4] Hoskins WJ, McGuire WP, Brady MF, Homesley HD, Creasman WT, Berman M, *et al*. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. *American Journal of Obstetrics and Gynecology*. 1994; 170: 974–979.
- [5] Piver MS, Lele SB, Marchetti DL, Baker TR, Tsukada Y, Emrich LJ. The impact of aggressive debulking surgery and cisplatin-based chemotherapy on progression-free survival in stage III and IV ovarian carcinoma. *Journal of Clinical Oncology*. 1988; 6: 983–989.
- [6] Burke TW, Morris M. Secondary cytoreductive surgery for ovarian cancer. *Obstetrics and Gynecology Clinics of North America*. 1994; 21: 167–178.
- [7] Ushijima K. Treatment for recurrent ovarian cancer-at first relapse. *Journal of Oncology*. 2010; 2010: 497429.
- [8] Colombo N, Sessa C, Bois AD, Ledermann J, McCluggage W, McNeish I, *et al*. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *International Journal of Gynecologic Cancer*. 2019; 30: 672–705.
- [9] Lee CK, Lord S, Grunewald T, GebSKI V, Hardy-Bessard A, Sehouli J, *et al*. Impact of secondary cytoreductive surgery on survival in patients with platinum sensitive recurrent ovarian cancer: analysis of the CALYPSO trial. *Gynecologic Oncology*. 2015; 136: 18–24.
- [10] Fotopoulou C, Zang R, Gultekin M, Cibula D, Ayhan A, Liu D, *et al*. Value of tertiary cytoreductive surgery in epithelial ovarian cancer: an international multicenter evaluation. *Annals of Surgical Oncology*. 2013; 20: 1348–1354.
- [11] Cianci S, Ronsini C, Vizzielli G, Tropea A, Biondi A, Scambia G, *et al*. Cytoreductive surgery followed by HIPEC repetition for secondary ovarian cancer recurrence. *Updates in Surgery*. 2019; 71: 389–394.
- [12] Coleman RL, Brady MF, Herzog TJ, Sabbatini P, Armstrong DK, Walker JL, *et al*. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. *The Lancet. Oncology*. 2017; 18: 779–791.
- [13] Du Bois A, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, *et al*. Randomized phase III study to evaluate the impact of secondary cytoreductive surgery in recurrent ovarian cancer: Final analysis of AGO DESKTOP III/ENGOT-ov20. *Journal of Clinical Oncology*. 2020; 38: 6000–6000.
- [14] Bacalbasa N, Balescu I, Dimitriu M, Iliescu L, Diaconu C, Dima S, *et al*. The Influence of the Preoperative Status on the Risk of Postoperative Complications after Cytoreductive Surgery for Advanced-stage Ovarian Cancer. *In Vivo*. 2020; 34: 839–844.
- [15] Magrina JF, Cetta RL, Chang Y, Guevara G, Magtibay PM. Analysis of secondary cytoreduction for recurrent ovarian cancer by robotics, laparoscopy and laparotomy. *Gynecologic Oncology*. 2013; 129: 336–340.
- [16] Escobar PF, Levinson KL, Magrina J, Martino MA, Barakat RR, Fader AN, *et al*. Feasibility and perioperative outcomes of robotic-assisted surgery in the management of recurrent ovarian cancer: a multi-institutional study. *Gynecologic Oncology*. 2014; 134: 253–256.
- [17] Berek JS, Hacker NF, Lagasse LD, Nieberg RK, Elashoff RM. Survival

- of patients following secondary cytoreductive surgery in ovarian cancer. *Obstetrics and Gynecology*. 1983; 61: 189–193.
- [18] Oksefjell H, Sandstad B, Tropé C. The role of secondary cytoreduction in the management of the first relapse in epithelial ovarian cancer. *Annals of Oncology*. 2009; 20: 286–293.
- [19] Scarabelli C, Gallo A, Carbone A. Secondary cytoreductive surgery for patients with recurrent epithelial ovarian carcinoma. *Gynecologic Oncology*. 2001; 83: 504–512.
- [20] Tian W, Jiang R, Cheng X, Tang J, Xing Y, Zang R. Surgery in recurrent epithelial ovarian cancer: benefits on Survival for patients with residual disease of 0.1-1 cm after secondary cytoreduction. *Journal of Surgical Oncology*. 2010; 101: 244–250.
- [21] Sehouli J, Richter R, Braicu EI, Bühling KJ, Bahra M, Neuhaus P, *et al.* Role of secondary cytoreductive surgery in ovarian cancer relapse: who will benefit? A systematic analysis of 240 consecutive patients. *Journal of Surgical Oncology*. 2010; 102: 656–662.
- [22] AlRawahi T, Lopes AD, Bristow RE, Bryant A, Elattar A, Chattopadhyay S, *et al.* Surgical cytoreduction for recurrent epithelial ovarian cancer. *The Cochrane Database of Systematic Reviews*. 2013; 2013: CD008765.
- [23] Bristow RE, Puri I, Chi DS. Cytoreductive surgery for recurrent ovarian cancer: a meta-analysis. *Gynecologic Oncology*. 2009; 112: 265–274.
- [24] Margul D, Coleman RL, Herzog TJ. The current status of secondary cytoreduction in ovarian cancer: a systematic review. *Clinical Advances in Hematology & Oncology*. 2020; 18: 332–343.
- [25] Chi DS, McCaughy K, Diaz JP, Huh J, Schwabenbauer S, Hummer AJ, *et al.* Guidelines and selection criteria for secondary cytoreductive surgery in patients with recurrent, platinum-sensitive epithelial ovarian carcinoma. *Cancer*. 2006; 106: 1933–1939.
- [26] Minaguchi T, Satoh T, Matsumoto K, Sakurai M, Ochi H, Onuki M, *et al.* Proposal for selection criteria of secondary cytoreductive surgery in recurrent epithelial ovarian, tubal, and peritoneal cancers. *International Journal of Clinical Oncology*. 2016; 21: 573–579.
- [27] Angioli R, Capriglione S, Aloisi A, Ricciardi R, Scaletta G, Lopez S, *et al.* A Predictive Score for Secondary Cytoreductive Surgery in Recurrent Ovarian Cancer (SeC-Score): a Single-Centre, Controlled Study for Preoperative Patient Selection. *Annals of Surgical Oncology*. 2015; 22: 4217–4223.
- [28] Tian W, Chi DS, Sehouli J, Tropé CG, Jiang R, Ayhan A, *et al.* A risk model for secondary cytoreductive surgery in recurrent ovarian cancer: an evidence-based proposal for patient selection. *Annals of Surgical Oncology*. 2012; 19: 597–604.
- [29] Harter P, du Bois A, Hahmann M, Hasenburger A, Burges A, Loibl S, *et al.* Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. *Annals of Surgical Oncology*. 2006; 13: 1702–1710.
- [30] Harter P, Sehouli J, Reuss A, Hasenburger A, Scambia G, Cibula D, *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 OVAR, AGO Study Group, NOGGO, AGO-Austria, and MITO. *International Journal of Gynecological Cancer*. 2011; 21: 289–295.
- [31] Bogani G, Tagliabue E, Signorelli M, Ditto A, Martinelli F, Chiappa V, *et al.* A score system for complete cytoreduction in selected recurrent ovarian cancer patients undergoing secondary cytoreductive surgery: predictors- and nomogram-based analyses. *Journal of Gynecologic Oncology*. 2018; 29: e40.
- [32] van de Laar R, Massuger LFAG, Van Gorp T, IntHout J, Zusterzeel PLM, Kruitwagen RFP. External validation of two prediction models of complete secondary cytoreductive surgery in patients with recurrent epithelial ovarian cancer. *Gynecologic Oncology*. 2015; 137: 210–215.
- [33] Shi T, Zhu J, Feng Y, Tu D, Zhang Y, Zhang P, *et al.* Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial. *The Lancet Oncology*. 2021; 22: 439–449.
- [34] Harter P, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, *et al.* Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer. *New England Journal of Medicine*. 2021; 385: 2123–2131.
- [35] Eriksson AGZ, Graul A, Yu MC, Halko A, Chi DS, Zivanovic O, *et al.* Minimal access surgery compared to laparotomy for secondary surgical cytoreduction in patients with recurrent ovarian carcinoma: Perioperative and oncologic outcomes. *Gynecologic Oncology* 2017; 146: 263–267.
- [36] Holloway RW, Brudie LA, Rakowski JA, Ahmad S. Robotic-assisted resection of liver and diaphragm recurrent ovarian carcinoma: description of technique. *Gynecologic Oncology*. 2011; 120: 419–422.
- [37] Paterniti TA, Ahmad S, Holloway RW. Robotic-Assisted Laparoscopic Splenectomy for Recurrent Ovarian Cancer. *International Journal of Gynecological Cancer* 2020; 30: 1189–1194.
- [38] Katebi Kashi P, Rojas C, Casablanca Y, Garg R. A seven-step surgical strategy for robotic splenectomy. *International Journal of Gynecological Cancer*. 2020; 30: 1079–1080.
- [39] Tozzi R, Soleymani Majd H, Campanile RG, Ferrari F. Feasibility of laparoscopic diaphragmatic peritonectomy during Visceral-Peritoneal Debulking (VPD) in patients with stage IIIC-IV ovarian cancer. *Journal of Gynecologic Oncology*. 2020; 31: e71.
- [40] Gkegkes ID, Karydis A, Tyrizis SI, Iavazzo C. Ocular complications in robotic surgery. *The International Journal of Medical Robotics + Computer Assisted Surgery: MRCAS*. 2015; 11: 269–274.
- [41] Paek J, Kang E, Lim PC. Robotic lower pelvic port placement for optimal upper paraaortic lymph node dissection. *Journal of Gynecologic Oncology*. 2019; 29: e87.
- [42] Lim PC, Kang EY. Feasibility and Survival Outcomes of Robotic Secondary Debulking for Recurrent Ovarian Cancer. *Journal of Minimally Invasive Gynecology*. 2018; 25: S62–S63.

How to cite this article: Peter C. Lim. A review of robotic surgery in the management of recurrent ovarian carcinoma: indication and techniques. *European Journal of Gynaecological Oncology*. 2022; 43(4): 1-11. doi: 10.22514/ejgo.2022.030.