Chapter

The Role of Ultra-Radical Surgery in the Management of Advanced Ovarian Cancer: State of the Art

Felicia Elena Buruiana, Lamiese Ismail, Federico Ferrari and Hooman Soleymani Majd

Abstract

The ovarian cancer, also known as "silent killer", has remained the most lethal gynaecological malignancy. The single independent risk factor linked with improved survival is maximum cytoreductive effort resulting in no macroscopic residual disease. This could be gained through ultra-radical surgery which demands tackling significant tumour burden in pelvis, lower and upper abdomen which usually constitutes bowel resection, liver mobilisation, ancillary cholecystectomy, extensive peritonectomy, diaphragmatic resection, splenectomy, resection of enlarged pelvic, paraaortic, and rarely cardio-phrenic lymph nodes in order to achieve optimal debulking. The above can be achieved through a holistic approach to patient's care, meticulous patient selection, and full engagement of the family. The decision needs to be carefully balanced after obtaining an informed consent, and an appreciation of the impact of such surgery on the quality of life against the survival benefit. This chapter will describe the complexity and surgical challenges in the management of advanced ovarian cancer.

Keywords: ovarian cancer, stage III and IV, cytoreductive surgery, ultraradical surgery, residual disease, holistic approach, quality of life

1. Introduction

The most common gynaecological cancer treated in women is uterine cancer, however the number of women who die from ovarian cancer is much higher [1]. Ovarian cancer has remained the most lethal cancer treated by gynaecological oncological surgeons and is often referred to as the "silent killer".

Ovarian cancer is the 7th most common cancer, and 8th most common cause of death from cancer in women in the world [2]. World Ovarian Cancer Coalition 2018 estimated that by 2035, the incidence of ovarian cancer will increase to 371, 000 per year. It is currently around 239, 000 cases annually [2]. The crude incidence is 23 to 30 in 100 000 women and most women present with advanced disease and little prospect of cure; the five-year survival rate for all stages of ovarian cancer is just over 40% and has remained quite low [3].

The treatment for patients with ovarian cancer is debulking surgery and platinum-based chemotherapy. The amount of residual disease after surgery is the most important prognostic factor for survival [4–11] and a recent phase III clinical trial [9]

confirmed this finding. Debulking surgery is a multi-visceral operation involving the pelvis, lower and upper abdomen, aiming at a complete resection (CR) of all visible disease to a microscopic cellular level [8–11]. This is also called cytoreductive surgery.

We present the latest surgical developments in ultra-radical surgery for the management of advanced ovarian cancer.

2. Evolution of gynaecological oncology surgery

Gynaecological oncological surgery has a rather interesting evolution. This is evident in the management of uterine and vulval cancers, where there has been transition to less aggressive surgery. In vulval cancer the utilisation of sentinel node biopsy plays a major role to reduce the morbidity associated with lymphadenectomy, whilst the application of minimal access surgery in the management of uterine cancer, has ensured faster surgical recovery and significantly shortened length of hospital stay. In contrast, the surgical approach to ovarian cancer has gone through an inverse transition in the last twenty years and despite all efforts to optimise

Carcinoma of the Ovary
Stage I: Tumour confined to ovaries
IA. Tumour limited to 1 ovary, capsule intact, no tumour on surface, negative washings
IB. Tumour involves both ovaries otherwise like IA
IC. Tumour limited to 1 or both ovaries
IC1. Surgical spill
IC2. Capsule rupture before surgery or tumour on ovarian surface
IC3. Malignant cells in the ascites or peritoneal washings
Stage II: Tumour involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer
IIA. Extension and/or implant on uterus and/or fallopian tubes
IIB. Extension to other pelvic intraperitoneal tissues
Stage III: Tumour involves 1 or both ovaries, confirmed spread to extra-pelvic peritoneum and/or metastasis to the retroperitoneal lymph nodes
IIIA. Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis
IIIA1. Positive retroperitoneal lymph nodes only
IIIA1(i). Metastasis ≤10 mm
IIIA1(ii). Metastasis >10 mm
IIIA2. Microscopic, extra-pelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes
IIIB. Macroscopic, extra-pelvic, peritoneal metastasis ≤2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.
IIIC. Macroscopic, extra-pelvic, peritoneal metastasis >2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.
Stage IV: Distant metastasis excluding peritoneal metastasis
IVA. Pleural effusion with positive cytology
IVB. Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Table 1.
Ovarian cancer staging (Society of Gynaecologic Oncology).

medical management throughout the introduction of targeted therapies, surgery has remained the mainstay of treatment and has progressively more radical [12].

In ovarian cancer, a midline laparotomy is usually performed to fully access anatomical structures in the pelvis and intra-abdominal cavity. With a midline laparotomy the patient will have a longer hospital stay, as opposed to laparoscopy, or robotic surgery.

Minimally invasive surgery can be performed when the disease is confined to the primary site (stage I ovarian cancer). In widespread disease, total hysterectomy with bilateral salpingo-oophorectomy, infracolic omentectomy and systematic pelvic/para-aortic lymphadenectomy are required in order to determine the need for adjuvant treatment and complete full surgical staging. However, the latter does not regularly apply to ovarian cancer since 80% of patients with ovarian cancer present with advanced disease (stages III and IV) Advanced disease implies a short time for management and treatment; as usually the cancer has spread to the upper abdomen, mandating multi-visceral resection.

Before effective treatment can be offered for ovarian cancer, the disease needs to be correctly staged. This can be achieved by means of radiological modalities or exploratory laparoscopy, or a combination of both. Ovarian cancer staging is presented in **Table 1** [13].

3. Ovarian cancer treatment

3.1 Background

Historically the treatment of ovarian cancer was primary debulking surgery followed by chemotherapy, whenever it was deemed to be feasible.

When to perform the debulking surgery in advanced ovarian cancer (AOC) has been the cause of debate and controversy for almost a decade [14]. The supporters of primary debulking surgery (PDS) advocate significantly better overall survival (OS) and progression-free survival (PFS) rates, whilst the opponents argue higher surgical morbidity and often fatal disease [14–17]. It is well recognised that for each 10% increase in maximal cytoreduction, there is an associated 5.5% increase in median survival [14, 18, 19]. However, in the vast majority of cases, complete debulking is associated with multivisceral resection which requires extensive surgical expertise, training and infrastructural support.

Neoadjuvant chemotherapy (NACT) and interval debulking surgery (IDS) have been considered as means to reduce surgical morbidity.

In 2010, Vergote et al. conducted a phase III randomised control trial (EORTC) [9] where neoadjuvant chemotherapy followed by interval debulking surgery (IDS) was compared with upfront primary debulking surgery (PDS) followed by adjuvant chemotherapy. This trial demonstrated that survival in both arms was similar (29 and 30 months, respectively), however there was less morbidity in patients who had chemotherapy first, mainly in those cases deemed difficult to operate [9]. The same findings were corroborated by the CHORUS phase III randomised controlled trial [20] that was used as a benchmark to justify the role of neoadjuvant chemotherapy in patients who were not candidates for upfront surgery. The survival remained 22 and 24 months, respectively. There have been many debates since the publication of these two RCTs, with regards to survival outcome and the need for a more radical surgical approach, in order to achieve complete cytoreduction.

The Trial on Radical Upfront Surgery in Advanced Ovarian Cancer (TRUST) will hopefully enlighten the adequate management of patients with AOC and will also establish predictive and prognostic biomarkers of operability and survival,

as well as identify valid fragility scores for vulnerable patients, with the aim of obtaining a more individualised surgical approach [14, 21].

Radical procedures to resect advanced ovarian cancer have been reported since 1965 [22]. In the late 70′s the "peritoneal compartment" concept was developed, with the introduction of en-bloc resection of pelvic organs and the surrounding peritoneum [23]. The logic of en-bloc resection is based on the notion of ovarian cancer as a peritoneal disease, where the peritoneum acts as a dissemination conduit but also limiting the spread. In fact, it is less frequent to see dissemination to the retroperitoneal organs. The en-bloc resection aims at seeking dissection planes within healthy tissue, minimising tumour manipulation and avoiding cutting through cancer tissue. Rapid tumour growth is usually supported by significant angiogenesis, primarily at the tumour periphery. As a result, there is a distortion of normal anatomy and findings of aberrant vascularisation. Therefore, a surgical technique that finds cleavage planes beyond the tumour growth is likely to reduce blood loss.

Visceral-Peritoneal Debulking (VPD) is offered to patients with stage III–IV ovarian cancer [24]. VPD applies the concept of en-bloc resection to all abdominal quadrants.

Maximal cytoreductive surgery aims at total macroscopic tumour clearance combined with platinum-based chemotherapy, these being the cornerstone of modern primary epithelial ovarian cancer (EOC) management [25]. Numerous prospective and retrospective series have demonstrated a strong positive association between total macroscopic tumour clearance rates and survival [25, 26]. A study comparing a surgical population, with a population who received chemotherapy alone (in 2 different cancer centres) showed that 43.8% of patients who had surgery died versus 86% of patients in the chemotherapy group [25].

Cytoreductive surgery is a standard part of national and international guidelines [25, 27, 28], hence surgical management with maximal therapeutic effort is the aim of treatment, even for patients with a higher tumour load, as survival of the patients has been clearly demonstrated [25].

3.2 Patient selection

The mainstay of treatment is a holistic approach to the patient's care. The patient needs to fully understand the benefits, risks and alternatives to surgery. Consent for this procedure needs to be carefully considered and fully informed.

3.3 Clinical assessment

The patient needs to be assessed with regards to their ability to walk and carry out ordinary activities independently, which includes climbing a flight of stairs. The advice of the anaesthetist is valuable, and cardiopulmonary exercise testing (CPET) may also be required to determine the anaerobic threshold of the patient prior to major surgery [24].

Demographic characteristics which have to be considered when selecting patients are age, previous abdominal surgery, ASA score, presence of ascites, preoperative Ca125, preoperative level of haemoglobin, albumin, FIGO stage, histological cancer type [29].

The triage process of patients for debulking includes:

a. a suitable WHO Performance Status (PS) at the preoperative assessment.

b. absence of lung or multiple parenchymal liver metastases on the CT scan.

c. exploratory laparoscopy did not demonstrate small bowel serosal disease or porta hepatis encasement [30].

Liu et al. [31, 32] reported that more than a quarter of women with advanced ovarian cancer treated with neoadjuvant chemotherapy (NACT) do not ever undergo cytoreductive surgery. Significant risk factors contributing to the inability to undergo surgery were advanced age, low albumin levels, frailty scores and extensive disease of predominantly high-grade serous histology. The main reasons identified were extent of disease not amenable to surgery or lack of response to NACT, patient co-morbidities preventing surgery and extent of disease. The patients who did not have debulking surgery, had an over 3-fold increase in mortality of any cause, compared to those who had surgery at some point [31, 32].

In patients with advanced disease, there is a strong rationale to personalise the surgical treatment and implement predictive and prognostic scores [31]. The aim is to allocate the right treatment to the right patient, in order to avoid unnecessary iatrogenic damage [31].

Appreciation of potential impact on the quality of life (QoL) has to be thoroughly assessed and balanced against survival benefit.

3.4 Investigations

A pre-operative CT scan for the thorax, abdomen and pelvis with contrast is essential. The patients with disease progression with lung metastasis or three or more liver segments involvement should be triaged for neo-adjuvant chemotherapy strategy [24]. Tozzi et al. has shown that exploratory laparoscopy added to the CT scan could potentially identify porta hepatis peritoneal disease [33] as well as small bowel serosal involvement. Several advantages of the exploratory laparoscopy have been reported, amongst which a correct diagnosis based on the histology of the tissue biopsy, accurate evaluation of the spread of the disease, including the spread of small military disease, a better selection of the patients for ultra-radical surgery and a better planning of resources in view of the surgery [34]. The authors concluded that this combination of investigations is of a high reliability, and encouraged surgical outcomes [33, 34].

3.5 Diagnostic laparoscopy

Following confirmation of suitability for surgery based on the CT scan, it is recommended to consider an exploratory laparoscopy to rule out diffuse small bowel serosa deposits and porta hepatis encasement [24]. There are controversies around this approach, however it has been demonstrated [24] that the use of Palmer's point and Hasson's technique to enter the abdomen is an easy and safe technique. This is a short procedure, very informative, allowing a thorough assessment of the intraabdominal cavity, and helps in avoiding a laparotomy if the chances of no residual disease are unlikely.

3.6 Systematic abdominal exploration

A systematic approach is required, and this is performed by assessing in systematic manner.

a. In the *upper abdomen* the diaphragm, liver, with its Glisson's capsule, falciform ligament, ligamentum teres, Morison's pouch, the stomach, lesser omentum also known as gastro-hepatic ligament, spleen, tail of pancreas, porta hepatis also known as hepato-dudenal ligament, foramen of Winslow, and the coeliac

trunk needs to be assessed. The latter two can be examined by palpation at laparotomy only, and this represents a limiting factor.

b. In the *mid abdomen* the omentum is fully assessed, the ileocaecal junction is identified and small bowel is run u to the point of DJ junction (duodeno-jeoujenal junction), as well as the root of the small bowel mesentery and the small bowel serosa. If the small bowel serosa is extensively affected requiring removal of a large part of the small bowel in order to achieve R0 (leaving a small bowel of less than 150 cm), a debulking procedure should be abandoned.

c. The *lower abdomen (pelvis)* - a thorough assessment looks at the extent of the disease in the pelvis starting with spread to the uterine body, fallopian tubes, round ligaments and sigmoid, with further assessment of the pouch of Douglas and the bladder peritoneum.

After all these assessments the conclusion can be withdrawn as whether the surgery will be beneficial and results in no residual disease. This often requires an intra-operative multi-disciplinary consultation between two senior gynaecological oncologist.

4. Surgical procedure

4.1 Preoperatively

A close collaboration and clear communication with the anaesthetist and the other members of the team are hugely important, as the preparation of the patient is paramount. The patient is positioned in Lloyd Davis with attention to avoiding common peroneal nerve injury/femoral nerve neuropraxia or lower limb compartment syndrome. The use of the correct retractor (i.e. Greys, Bookwalter) will also help in gaining an optimal access to the pelvis, but also to the right and left upper quadrants.

4.2 Intraoperatively

A midline laparotomy is always required in order to allow a good access to all the pelvic and intraabdominal areas mentioned above. An understanding about the radicality of the procedure is further required, and this is highlighted in **Table 2** [35].

The majority of ovarian cancers present in advanced stages and are treated by debulking surgery and platinum-based chemotherapy. The disease starts in the pelvis, involving the ovaries, tubes, the uterus, and the bowel and then spreads to the upper abdomen. Once established that an R0 is feasible the procedure starts in the pelvis.

In the case all pelvic organs are matted, a technique is needed to remove the tumour with cancer free margins. To achieve the least residual disease, multivisceral pelvic and upper abdominal surgery is often necessary [36–39].

Ten steps of the en-bloc resection of the pelvis (**Figure 2**) are described below [24]:

1. Access to the retroperitoneal space: isolation of the ureter, ligation of the infundibulo-pelvic ligament.

2. Resection of sigmoid.

Classification	Groups	Criteria
NICE	Standard	Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy (**Figure 1**), pelvic and/or para-aortic lymphadenectomy, bowel surgery outside the definition of 'ultra-radical' (localised colonic resection, non-multiple bowel resection)
	Ultraradical	Diaphragmatic stripping, extensive peritoneal stripping, multiple resections of the bowel (excluding localised colonic resection), liver resection, partial gastrectomy, cholecystectomy, splenectomy
Pomel	Standard	Hysterectomy, bilateral salpingo-oophorectomy, pelvic peritonectomy, total omentectomy, appendicectomy, pelvic and/or para-aortic lymphadenectomy
	Radical	Recto-sigmoid resection
	Supra-radical	Diaphragmatic stripping, liver resection, cholecystectomy, splenectomy, any digestive resection excluding recto-sigmoid resection

Table 2.
Description of surgical radicality.

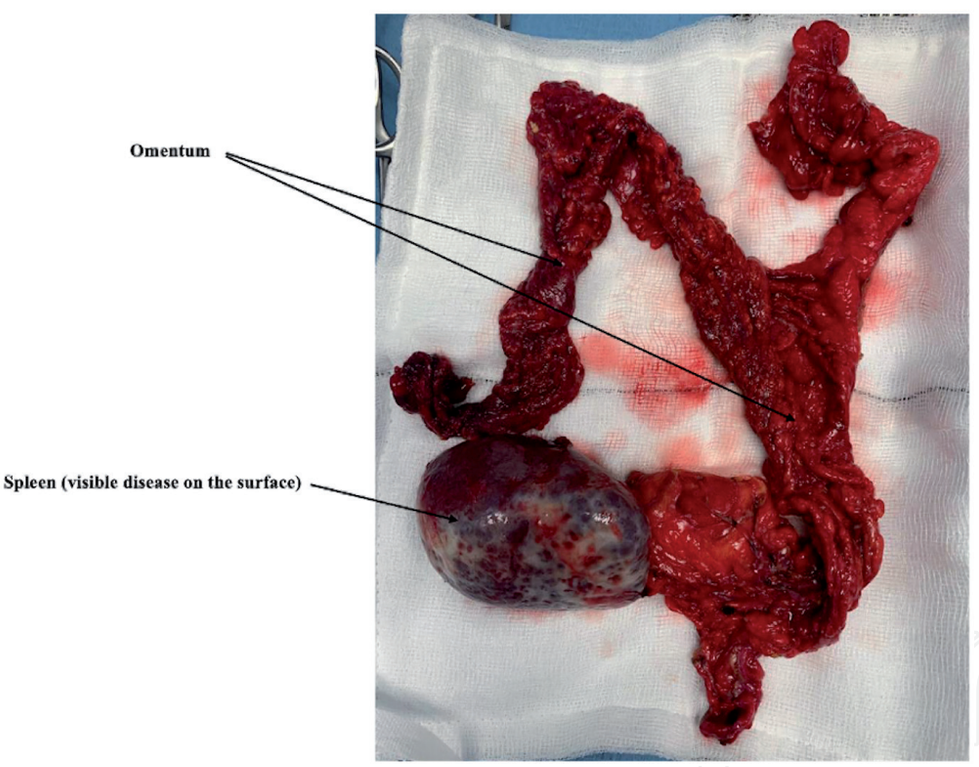

Figure 1.
Total omentectomy.

3. Mobilisation of the sigmoid from the sacrum by coagulation and resection of the meso-sigmoid

4. Access to the pre-sacral space.

5. Mobilisation of the bladder peritoneum with access to the vesico-vaginal space.

6. Colpotomy of the anterior vaginal wall.

7. Retrograde resection of the parametria.

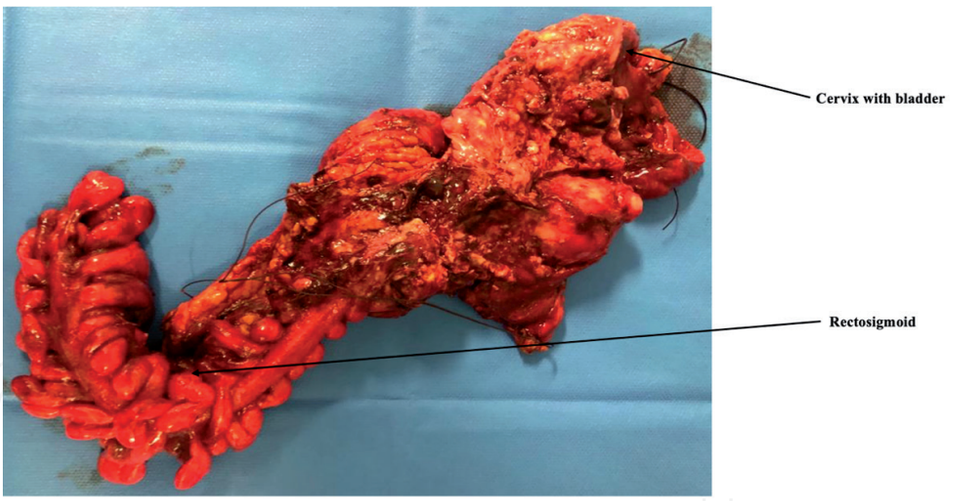

Figure 2.
En-bloc modified posterior pelvic exenteration-including bladder, pelvic, peri-ureteric peritoneum, uterus, cervix, tubes, ovaries and rectosigmoid.

8. Colpotomy of the posterior vaginal wall, access to the recto-vaginal septum.

9. Dissection, coagulation and division of the meso-rectum.

10. Resection of rectum ± anastomosis.

A particular attention needs to be given to bowel resection. Recto-sigmoid resection (RSR) is the most commonly non-gynaecologic procedure performed. It can be associated with early postoperative complications, most severe being the breakdown of the anastomosis or anastomotic leak [36, 40, 41].

The literature reports 0.8% - 6.8% risk of anastomotic leak in patients who underwent bowel resection during debulking surgery for ovarian cancer [36]. Therefore, sigmoid rectum resection is sometimes accompanied by a diverting loop ileostomy (DLI) with the aim to reduce the anastomotic leak. This is not without complications, and although it is typically intended to be reversible, the non-reversal rate of ileostomy is 9.5–35% in the colorectal literature [36, 42–46].

RSR is the resection of any large bowel segment from the pelvic brim to the anal canal. The decision to undertake RSR is made at the time of surgery and was usually part of an en-bloc resection of the pelvis [36, 47].

DLI is a loop of small bowel, 10–15 cm proximal to the ileocaecal junction, used to divert the faecal stream and protect the colorectal anastomosis. The indications for DLI are [29, 33]:

- multiple bowel resections.
- RSR < 6 cm from anal verge.
- non-tension free anastomosis.
- poor tissue quality.
- air spillage through the anastomosis at trans-anal air test.

DLI reversal was planned at the end of the chemotherapy and if the patient has three months disease-free interval verified on CT scan. The morbidity of DLI is

very challenging, and more for patients who are metabolically deranged, older age, low albumin level, fluid imbalance. DLI morbidity can delay chemotherapy due to dehydration. The optimal timing for reversal remains unclear, usually 6–8 weeks postoperatively [36]. End-colostomy is easier to manage than an end-ileostomy [36, 48], hence for the patients presenting with risk factors for non-reversal, a careful consideration should be given to the type of bowel diversion performed during debulking surgery [36, 47].

According to a study performed by Tozzi et al. [47] patients in IDS had a slightly higher rate of bowel diversion compared to patients in PDS group (46% vs. 26.5%). Also, patients in IDS were more likely to receive bowel diversion due to impaired tissue quality (44.8% vs. none) while patients in PDS were more likely to receive a bowel diversion when receiving multiple bowel resections (92.3% vs. 34.5%) [47].

Bowel resection has to be limited to what is required, as multiple bowel resections will increase the morbidity [29], as already mentioned above. The tumour must be excised whilst the blood supply is avoided. In order to safely do this, a technique is to dim the theatre light, assess the blood supply and identify the right colic, middle colic, left colic. Once the bowel resection is performed, further assessment for potential ischaemic changes is required.

It is possible to perform small bowel mesenteric peritonectomy or excision of the mesocolon without the need to perform full bowel resection.

After the disease in the pelvis has been tackled the procedure continues in the upper abdomen. To achieve complete resection, extensive upper abdominal procedures are warranted. Strong evidence suggests that upper abdominal procedures improve the survival rates regardless of the time of the debulking [33, 49–55].

The upper abdomen is divided in right and left quadrant and a systematic approach is required. The assessment starts with the mobilisation of the liver (**Figures 3**–**5**), dividing the falciform ligament, the coronary ligaments in order to assess the posterior aspect of the liver.

Diaphragmatic peritonectomy (**Figures 6** and **7**) with or without pleurectomy, partial liver resection, cholecystectomy, splenectomy with or without distal pancreatectomy and resection of the tumour at the porta hepatis (PH) may be required in order to achieve complete resection [33].

Diaphragmatic assessment for cancer invasion is paramount. One of the key dilemmas is to decide which patient would benefit from full diaphragmatic resection, as opposed to peritonectomy only [56, 57]. Tozzi et al. performed a study on

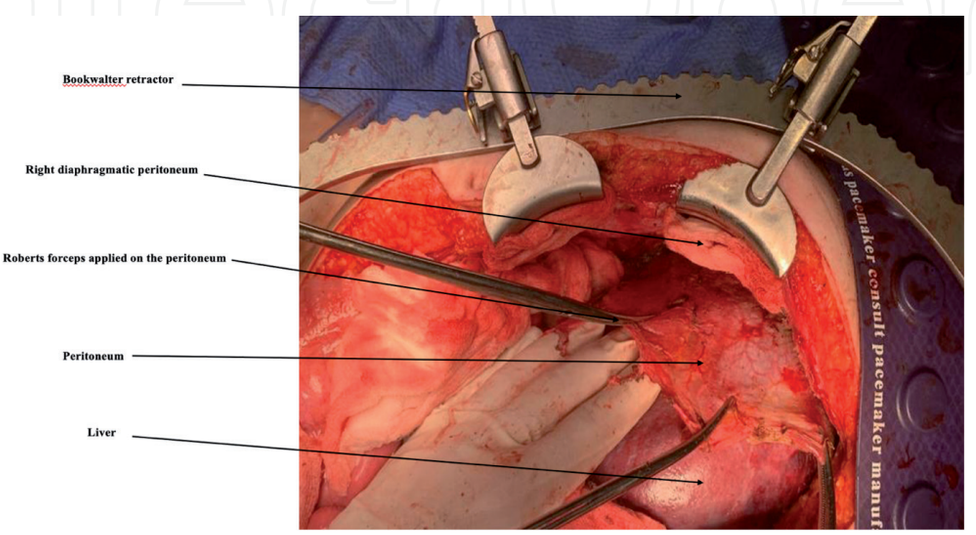

Figure 3.
Mobilisation of the liver. Large xiphopubic incision required.

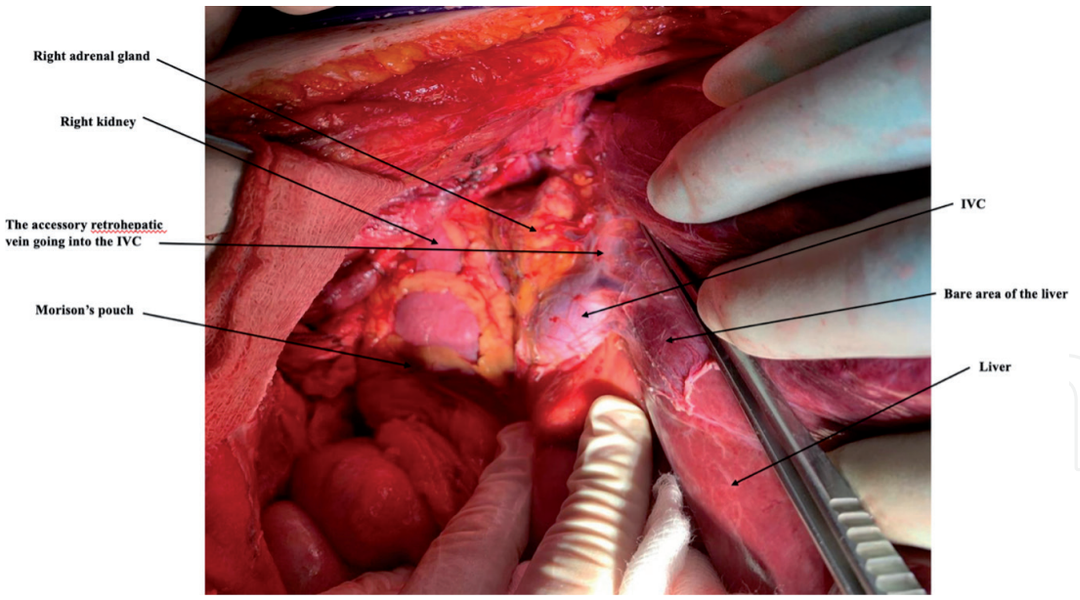

Figure 4.
Type III liver mobilisation exposing retrohepatic space.

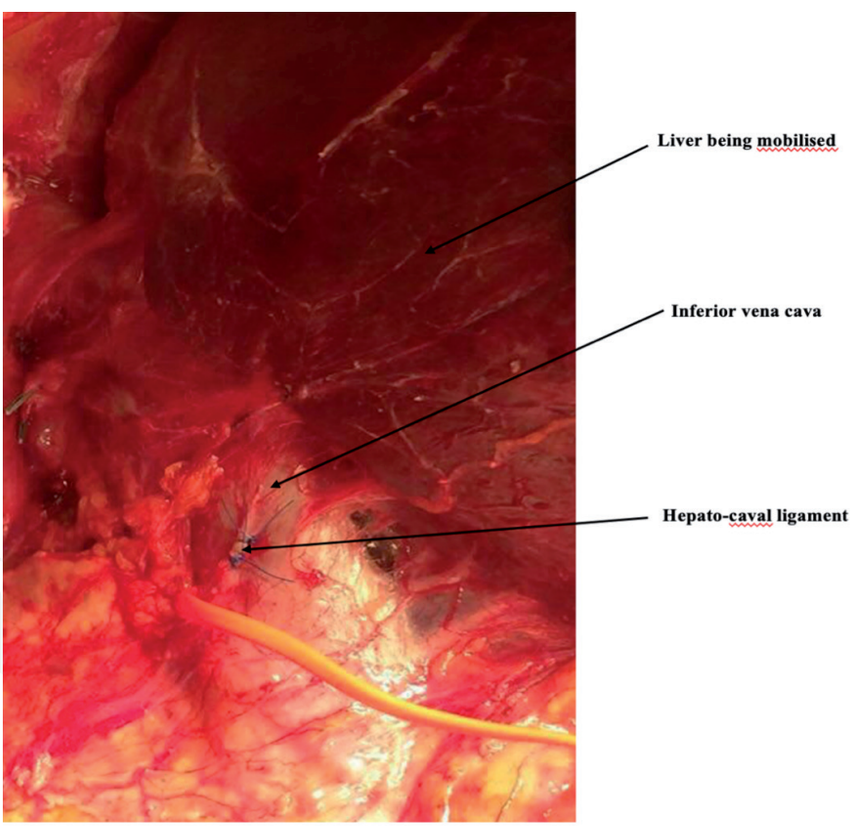

Figure 5.
Liver mobilisation.

170 patients who underwent diaphragmatic surgery and described a meticulous classification to reduce the morbidity but also achieve maximum cytoreductive effort in the upper abdomen. Soleymani majd et al. reported that in patients with diaphragmatic metastasis, 28% had disease spread to the muscle, and 20% of patients had full thickness disease involving the pleura [57–59]. Hence diaphragmatic peritonectomy alone would have left disease in the muscle and the pleura, and complete cytoreduction would not have been possible. The decision about full

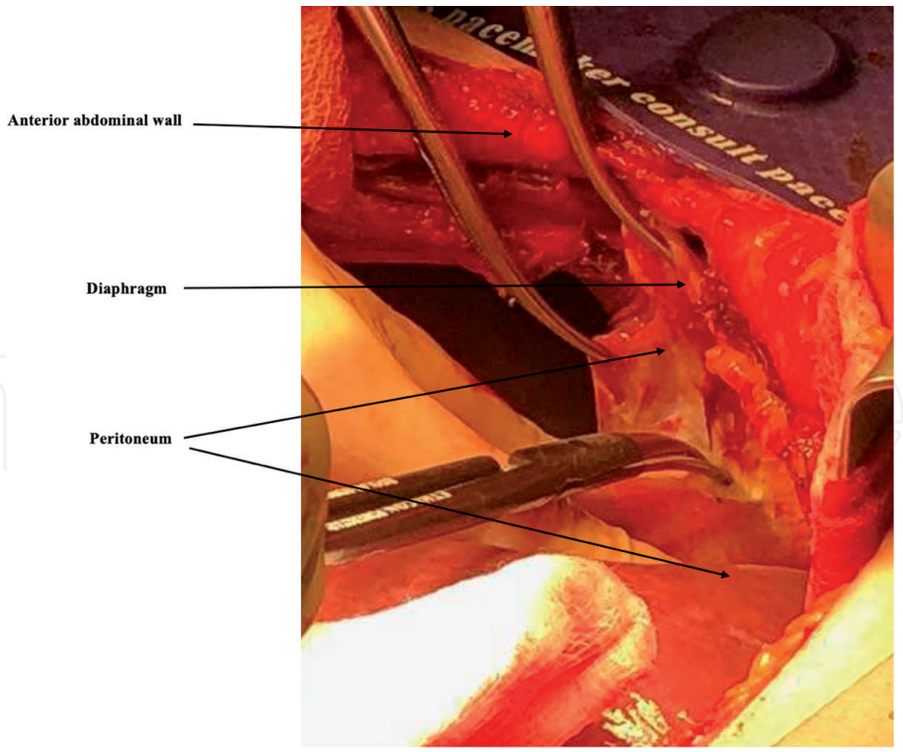

Figure 6.
Diaphragmatic peritonectomy.

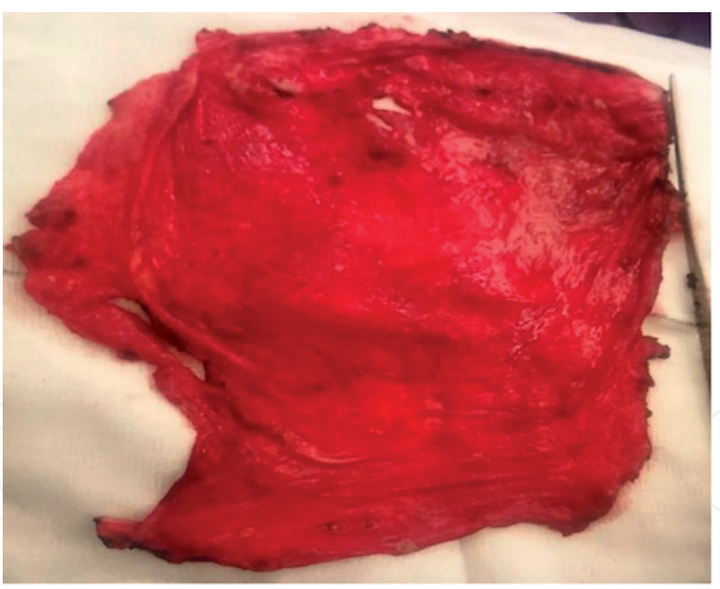

Figure 7.
Peritoneum after diaphragmatic peritonectomy (removal in one piece).

thickness diaphragmatic resection versus diaphragmatic peritonectomy requires prospective studies balancing morbidity against survival benefits [56].

The porta hepatis (PH) shall always be assessed prior to laparotomy, as encasement of the vessels is an absolute contraindication to proceed with radical debulking surgery. Inspection and palpation of the portal vein, hepatic artery, and bile duct are required, along with assessment of the hepato-coeliac lymph nodes. The pringle manoeuvre should be performed prior to liver mobilisation to maximise surgical safety.

Resection of ovarian disease at the PH was feasible in 90.3% of patients in the Tozzi et al. study [33]. No intra- or postoperative complications were associated with

tumour resection at the PH, moreover the resection of PH disease was effective, significantly contributing to a 90% rate of achieving R0. Raspagliese et al. [33, 60], along with this study [33] highlight the importance of routinely exploring the PH area, if aiming for complete cytoreduction.

The excision of lymph nodes beyond abdomen and pelvis is controversial, however leaving an enlarged/bulky lymph node despite all other maximal cytoreductive efforts, may mean that no residual disease status was not achieved. Removal of the cardio-phrenic lymph nodes has to be assessed on individual circumstances and localization of the lymph nodes. In the circumstance, that an enlarged pericardiac lymph node is noted, and the gynaecological oncologist is not trained or confident in removing it, then cardiothoracic expertise would be required in order to achieve complete cytoreduction. The Lion study intraoperatively randomly assigned 647 patients with newly diagnosed advanced ovarian cancer (Stage IIB to IV) who had undergone macroscopically complete resection and had normal lymph nodes (both before and during surgery) to either undergo or not undergo lymphadenectomy. In total, 323 had lymphadenectomy whilst 324 did not. The median overall survival was 69.2 months in the non-lymphadenectomy group and 65.5 months in the lymphadenectomy group. The median progression-free survival was 25.5 months in both groups. Postoperative complications were more prevalent in the lymphadenectomy group. Therefore, the Lion study concluded that systematic pelvic and para-aortic lymphadenectomy in patients with advanced ovarian cancer, was not associated with longer overall or progression-free survival but was associated with a higher incidence of postoperative complications, when compared with those who had no lymphadenectomy [61].

Figure 8 illustrates the opening of the right pelvic side wall.

Surgical debulking in ovarian cancer (especially for advanced disease) has traditionally been performed via an open abdominal route. Laparoscopy in advanced ovarian cancer has mostly been used to explore the feasibility of a complete surgical resection [30]. However, there are a few recent studies in the literature, which report complete response to chemotherapy and no gross residual disease after a laparoscopic approach. In the past, concern about the use of laparoscopy included inadequate radicality, the risk of vaginal and/or port site metastasis secondary to

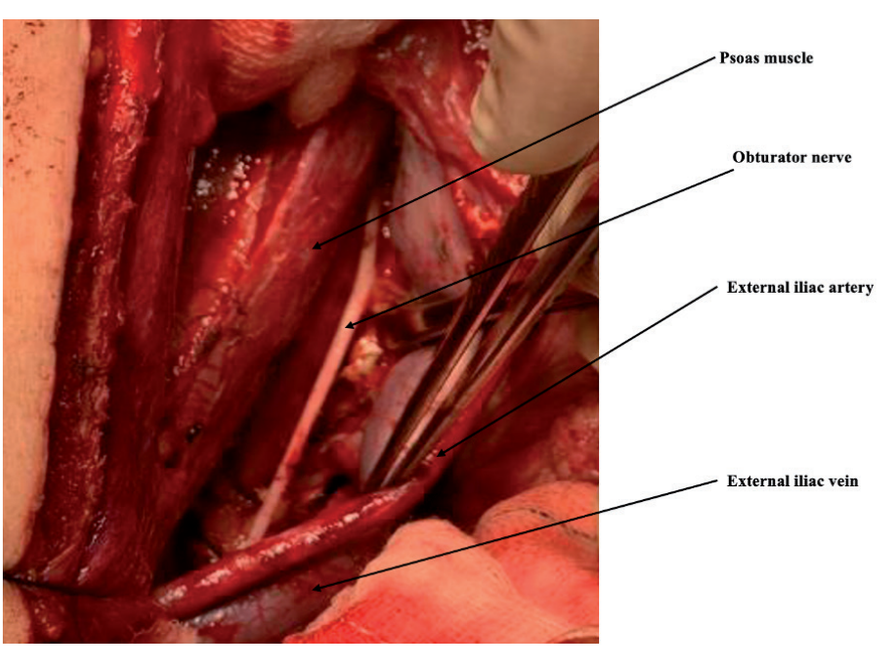

Figure 8.
Right pelvic side wall- exposure of lumbosacral and obturator fossae.

tumour contamination and the use of CO2. In the recent reports, complete resection was achieved at laparoscopy, making it a potentially feasible alternative, warranting consideration [30]. Safe laparoscopy in advanced ovarian cancer consists of thorough preoperative preparation and study of the CT scan images, matching it with the laparoscopic findings, and exploring all peritoneal surfaces. Particular care needs to be taken in avoiding tumour contamination, seeking for cleavage planes in healthy tissue and minimising tumour manipulation. Endobags should be used to extract all specimens, which should be removed intact. Tumour extraction through the vagina is ill advised, if compliance is not adequate [30].

There are a number of well-known benefits of a laparoscopic approach, including: reduced blood loss, decreased pain, earlier discontinuation of analgesia, shorter hospital stay, lower rate of complication and infection. Some researchers report that a short postoperative period is very important in the prognosis of cancer patients and affects survival [30, 62–66]. Surgery has been associated with an increased risk of metastasis and tumour recurrence. The main responsible mechanisms are tumour cell dissemination, shedding, enhanced adhesion, increased tumour growth secondary to reduced apoptosis, increased release of growth factors and angiogenesis, transient but profound suppression of cell-mediated immunity (CMI). The latter controls the minimal residual disease which is present at a cytological level in patients with ovarian cancer. The degree of surgical trauma is noted to correlate with immune depression and with tumour growth [30, 62–66]. Laparoscopy, however, causes reduced trauma and as a consequence a lower inflammatory response, an increased TH1 cytokine production, faster return to normal lymphocyte count and an absence of tumour growth factors in the serum [30, 65]. These effects contribute to a reduced recurrence rate [30, 66], as well as a faster recovery of the immune system in patients with ovarian cancer during their chemotherapy, as they are more prone to anaemia and infections [30, 66].

The data reported so far is for the use of laparoscopy in interval debulking surgery, there is no data on its use in primary debulking surgery [30].

5. Quality of Life

The Quality of Life (QoL) needs to be assessed after such a major and long surgery, which sometimes lasts up to ten hours. QoL questionnaires were sent out to the patients in the Lion study [61]. At the time of discharge, most patients had a poor quality of life, but this improved at follow up (at the end of chemotherapy).

An ultra-radical surgery with the aim of leaving no residual disease (R0) is not successful if the approach to the patient is not holistic; an assessment of whether the patient's quality of life could be improved has to be performed. This surgery should be offered to suitable patients only. Du Bois et al. demonstrated in their study that the benefit was exclusively seen in patients with complete resection (R0) indicating the importance of both the optimal selection of the patients, and of centres with expertise and a high chance of achieving R0 [26, 67, 68].

In ovarian cancer surgery, a multidisciplinary approach is required for successful cytoreductive surgery, keeping the patient at the centre of care.

Conflict of interest

The authors declare no conflict of interest.

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