
Radical Hysterectomy Techniques – Indications and Complications

Ambrogio P Londero, Serena Bertozzi,
Luca Martella, Giulio Bertola, Giorgio Giorda,
Angelo Calcagno, Arrigo Fruscalzo and Ralph J Lellé

Additional information is available at the end of the chapter

Abstract

Radical hysterectomy is an important surgical procedure in gynecologic oncology. New technologies are changing hysterectomy techniques, and integrated treatments could expand the surgical indications in gynecologic oncology. Minimally invasive (laparoscopic or robotic surgery) radical hysterectomy adoption is slowed by different factors despite the apparent improvement of morbidity outcomes. Moreover, data about oncologic long-term outcomes of minimally invasive radical hysterectomy are relatively sparse, and more research is needed.

Keywords: Radical hysterectomy, Gynecologic oncology, Hyperthermic intraperitoneal chemotherapy (HIPEC), Open surgery, Laparoscopic surgery, Robotic surgery

1. Introduction

Hysterectomy is the surgical removal of the uterus, and it may be total (removal of the body, fundus, and cervix of the uterus) or partial (removal of the uterine body while leaving the cervix intact; also called supracervical). It is the most commonly performed gynecological surgical procedure, and in the majority of cases, it is performed for benign conditions. This procedure in particular could be:

- Subtotal hysterectomy (supracervical): removal of the uterus, leaving the cervix in situ.
 - Total hysterectomy: complete removal of the uterus and cervix.
-

- **Radical hysterectomy:** complete removal of the uterus, cervix, upper vagina, and parametrium. Indicated for cancer. Lymph nodes, ovaries, and fallopian tubes are also usually removed in this situation.

This chapter would relate about radical hysterectomy performed by abdominal way, taking into consideration also robotic techniques. This technique is performed in cases of malignant diseases affecting the uterus.

2. Indications

Radical hysterectomy is still the treatment of choice for women with early stage cervical cancer [1, 2]. However, modified radical hysterectomy or total hysterectomy is indicated in uterine and ovarian cancers as well. Also in these cases, lymph nodes, ovaries, and fallopian tubes are usually removed as well as the omentum and peritoneum in some circumstances.

3. Historical notes

Radical hysterectomy with pelvic lymphadenectomy is a key intervention in gynecologic oncology, proposed by Wertheim (without lymphadenectomy) for the first time in 1898, and has gradually been enriched by numerous contributions until the excision of pelvic lymph nodes proposed by Meigs (1951) [3].

There is also a vaginal radical hysterectomy, not particularly diffused. That is performed only in a few centers even though the mortality from the beginning was much lower than the laparotomy. Schuchardt had the idea to offer this type of surgery against cervix carcinoma; Schauta codified and made him known to scientific societies; Amreich took care of the details.

4. Preoperative preparation of the patient

The staging of cervical cancer, and thus the decision for surgery versus radiation, is based on the subjective impression of a clinical investigation. Cystoscopy and sigmoidoscopy are only useful for advanced tumors. In such tumors, however, the primary combined radiotherapy with chemotherapy is usually the treatment of choice.

An intravenous pyelogram is necessary to show or exclude urinary tract duplication or other anomalies. Furthermore, the International Federation of Gynecology and Obstetrics (FIGO) staging system can only be specified if the result of the intravenous pyelogram is known. In fact, a renal accumulation corresponds to a clinical stage IIIB.

Computed tomography scan and magnetic resonance imaging are not necessary and do not provide any additional information. However, a computed tomography scan showing the renal apparatus by contrast medium represents a valid alternative to intravenous pyelogram.

A bowel preparation with polyethylene glycol (PEG) is not necessary and represents only an additional burden on the patient. Before the operation, antibiotic prophylaxis is performed, for example, 2 g cefoxitin intra venous at induction of anesthesia and again two hours after surgery begins, since cephalosporins have only a short half-life of approximately 45 min. Antibiotic prophylaxis should be continued for up to 24 h.

The patient is always examined again under anesthesia, by vaginal (index finger) and rectal (middle finger) exploration.

In case of endometrial cancer, the histologic information obtained from endometrial biopsy (fractionated dilatation and curettage or hysteroscopy and biopsies) usually is sufficient to plan definitive treatment. Other useful tests such as computed tomography, magnetic resonance imaging, and positron emission tomography are used to evaluate extrauterine disease.

5. Abdominal hysterectomy

5.1. Operators and operative theater

Not least, radical hysterectomies have become less frequent, even on larger hospitals; each of these operations should be used for training. With proper instruction, this is not associated with an increased risk for the patient, possibly with a prolongation of the duration of surgery.

After anesthesia induction, the patient is placed in a supine position. Three doctors are involved in the operation. The forming and ultimately for the operation responsible physician is the right of the patient and demonstrates each operation step on one side, including the specific steps below abdominal opening described. In the beginning, it is recommended that the preparation of the uterus is performed on the ipsilateral side and the pelvic lymphadenectomy on the contralateral side. Over time, however, all phases of operation should be practiced from all angles. The third doctor observes the operation and is relieved by the use of the self-holding frame, which is shown to increase its concentration. Depending on the level of training, he may be involved in some operation steps, e.g., abdominal opening and closure.

5.2. Abdominal opening

5.2.1. Morley laparotomy modified by Lellé

Before skin disinfection (as precaution until the level of the nipples) and sterile covering, the incision site is drawn. The Morley interiliac transverse incision [4] is a slightly curved bisiliac cross section. Suitable for marking is the concave side of the Toussaint ruler [5].

Using a scalpel (number 10 or 21), the abdominal skin is incised superficially. The incision can be carried so superficially that there is no bleeding and the subcutaneous fatty tissue is not yet visible. The wound margins are tight and it is possible to continue the incision with the needle electrode of the argon plasma coagulation. Minor bleeding can be directly stopped with the coagulator. If major bleeding occurs, it is coagulated using a modified bipolar forceps with a DeBakey grip panel. The skin edge should not be violated. In the area of the wound, the inferior superficial epigastric veins are coagulated before cutting.

After incision, the fascia is raised with a Péan and further cut across by argon plasma coagulation.

Now, the superficial connective tissue of the right lateral rectus muscle is opened. The Army-Navy hook lifts the edge of the rectus muscle slightly. The deep inferior epigastric artery and vein are identified and disposed by two Overholt clamps. The ligature is like all these ligatures with the strength Polysorb™ (Lactomer glycolide/Lactide copolymer coated

with caprolactone and calcium stearoyl lactylate) 4-0, although this is a relatively small thread. However, the tensile strength of the material is much higher than polyglactin 910 (Vicryl™). Crucial here is that the node is right and not “falling out.” All ligatures are attached by a Pean to a terminal (this is valid in all steps in this description).

Rarely, it may happen that the epigastric vessels are not identified on a side. If the vessels are not even clearly identified, one can instead perform the following procedure: the rectus muscle pitched up by the fingers and cut coming from the lateral until the epigastric vessels are visible. These are then ligated as described above.

The rectus muscle is divided from the peritoneum by the fingers. The Army-Navy retractor is inserted under the muscle and raised. Here, it must be ensured that the peritoneum was not opened accidentally because the intestine can be injured. The rectus muscle is slowly cut by argon plasma coagulation. Bleeding muscle fibers are taken by a Russian forceps and coagulated. Then hemostasis is carefully performed.

The peritoneum is opened best starting from the left, especially if one has gone through appendectomy before, and adhesions may exist on the right side. The peritoneum is lifted with two surgical forceps and opened with a scalpel until the index and middle fingers can be inserted without problems. Above these fingers, with the help of argon plasma coagulation, the peritoneum is fully opened.

5.2.2. Median laparotomy

After skin disinfection by povidone-iodine or clorexidine and sterile covering, the skin is cut along a line which connects the umbilicus to the middle point of the pubis. In fact, this incision is usually called subumbilicus-pubic incision. After the skin, the different abdominal layers are ordinally cut as follows: subcutaneous tissue, linea alba connecting the two rectum muscles of the abdomen, and finally peritoneum, paying attention not to injure the intra-abdominal organs.

This kind of incision could be performed even on a previous median laparotomic scar, obviously more carefully due to the probable presence of adhesions. Moreover, during surgical intervention, it may be elongated from the umbilicus until the xiphoid process if required.

5.3. Exploration of abdominal cavity

First, with the aid of a 50 ml syringe filled with 30 ml of saline, a Douglas lavage is performed and the collected sample is sent for cytological examination. Then the entire abdominal cavity is carefully and systematically examined by visual inspection and/or palpation. In this occasion, the abdominal wall can be lifted with a large Langenbeck hook. In particular, the following structures should be evaluated: the right and the left diaphragm, liver, gallbladder, spleen, stomach (check correct nasogastric tube placement), pancreas, kidney, omentum (also visual inspection), and colon frame down to the rectum. Particularly important is the assessment of the para-aortal region. This can be best assessed from the left side if the mesenteric root is pushed to the side.

The cecum and optionally the appendix are inspected. Then the small bowel is inspected from the ileocecal valve (beginning of the small bowel) down to the mesenteric root. In fact,

the small bowel is drawn between the forefinger and thumb and until the Treitz ligament is reached.

Now the surgical retractor is used (Omni-Tract or Bookwalter surgical retractor), leaving the bowel in the abdominal cavity. Then, a Kocher clamp is placed in the middle of each utero-ovarian ligament. This must be taken to ensure that uterine veins and arteries will not be accidentally injured. Finally, the two Kocher clamps are pulled with one hand, and with the other hand, the cervical length, the parametrium, the paracolpos, and the pelvic lymph nodes are assessed. Also, the peritoneal surfaces and the adnexa are here carefully inspected.

5.4. Preparation of operative field

The Omni-Tract™ surgical retractor is mounted on the top left of Maquet™ table. Although it is a cross section of “Wishbone,” it is placed along frames. Four Mayo hooks are used. The two caudal hooks must be taken with caution especially in thin patients that no pressure is exerted on the femoral nerve. During the procedure, the position is reviewed regularly, taking care that the hooks are not pressed posteriorly.

A damp cloth belly, which was folded and rolled into thirds, is placed in each of the right and left para coli rule gutter. The intestine is wrapped with an open cloth and pushed cranially, with one end of cloth in the para-coli. If required, a long reel is inserted transversely. The cranial Mayo hook Omni-Tracts™ can be set slightly posteriorly to fix the towels. The big or small flexible window hook should preferably not be used to save space.

5.5. Preparative assessment of operability

The following preparation is exclusively sharply with small steps using the Stevens scissors and Münster forceps, the latter for bipolar coagulation. The Münster forceps is a modified DeBakey forceps with the typical grip profile and bipolar coagulation capability. Forceps is used both for preparation and for coagulation. The coagulation is controlled via a footswitch.

First, the peritoneum is opened in the lateral pelvic area to the right, and the round ligament is exposed. The incision is carried away from the bladder reflection fold. An Overholt clamp is passed under the round ligament and is placed far laterally; then by means of two clamps, the round ligament is held, cut, and tied by a 4-0 Polysorb™ ligature. All of the following ligatures are immediately cut off by the assistant doctor. Then, using the closed scissors and the closed forceps, the pararectal space is opened (“chopstick technique”).

Usually, here the ureter is already visible, which is fixed at the medial peritoneal leaf. If the ureter is not clearly visible, you can always palpate it well by scanning the medial peritoneal leaf between the thumb and forefinger.

Index and middle fingers are following introduced pararectal to continue to open the space of the sacrum cave. With the help of a DeBakey forceps, the bladder peritoneum is raised caudally to the right. One sees here a discrete indentation of the bound tissue. Here you go once again with the “chopstick technique” in order to open the paravesical space. With the fingers, the space is stretched again.

Often you can see here already that lateral umbilical ligament, that represents the terminal ramifications of the internal iliac artery. Sometimes one has the impression that it could be

the ureter. The ureter is, however, more dorsally and medially visible and is so far caudally never visible because it runs in the bladder pillars. If during this phase of preparation bleeding occurs - usually venous bleeding in pararectal space - it is compressed with a cloth strip and hemostasis is not attempted.

With the index and middle fingers, the parametrium can be palpated and a possible infiltration detected.

The same steps will be executed on the left side.

Then the urinary bladder is sharply dissected from the uterus' anterior wall. The hemostasis is carried out with the Münster bipolar forceps. If strong adhesions exist and the bladder anatomy is unclear, a targeted opening of extraperitoneal bladder is considered to prevent thinning of the detrusor muscle in the trigone and the emergence of a bladder-vaginal fistula [6]. If the bladder is not infiltrated, the operation is continued.

5.6. Pelvic lymphadenectomy

Typically, the operator standing on the right begins with the pelvic lymphadenectomy on the left, so the opposite side of him.

The peritoneum is further cleaved along the para-coli channel cephalad, just caudal to the external iliac artery. Either a Mayo hook Omni-Tract™ is readjusted caudally and slid under the peritoneum or a Roux hook is used by the assistant and pulled caudally.

Cranial iris hooks of Omni-Tract™ are used (corresponding to the heart-shaped Harrington hook), pulling it medially and superiorly.

The ureter crosses the common iliac artery just before its bifurcation and is deported medially from the surgical field.

The resection limits are described in Table 1.

Lateral	Genitofemoralis nerve/iliopsoas muscle
Medial	Internal iliac artery or caudal lateral umbilical ligament
Cranial	Bifurcation of the common iliac artery into the external and internal iliac artery
Caudal	V. circumflex ileum profunda

Table 1. Resection limits of pelvic lymphadenectomy

In detail, the procedure is as follows:

It is only in sharp dissection that the Stevens scissors and Münster forceps are used. Blunt dissection, spreading the tissue with scissors should be avoided since significant leverage forces occur and the tissue is torn violently. In fact, blunt dissection only appears safer than a sharp dissection but it is not.

Hemostasis is always bipolar or done by setting titanium clips. In fact, monopolar coagulation cannot precisely control the coagulation site, and this could lead to damage of important structures.

The fat and the connective tissue are just longitudinal and medial to the genitofemoral nerve split. Here and in the following preparations, it will always work full length of the resection territory described above. Now a blunt instrument is entered between the iliopsoas and external iliac artery or vein with the finger and the vessels are bluntly detached from the muscle. The mobilization is due to the full-length resection described above. Occasionally, a perforator vessel must be coagulated. On the rear wall of the external iliac artery, tissue is dissected using Stevens scissors and Münster forceps laterally to medially.

The external iliac artery is undermined and a Lidhaken (vein retractor after Cushing) is used. The tissue is further dissected until the entire artery is exposed. Subsequently, the preparation of the external iliac vein analog proceeds.

For the part of the lymph node dissection, the internal iliac artery serves as the lead structure, which expires lateral to the umbilical ligament. Usually, in this step, the origin of the uterine artery is already visible.

The whole preparation of lymph node and adipose tissue is done in a single block. This procedure should be learned as a systematic preparation.

For small bleeding, the artery or vein can be attempted in a bipolar coagulation with the Münster forceps when vascular stumps are still present. When bleeding comes from the vein, a small titanium clip can be set alternatively. In the presence of greater bleeding, a vessel could be sutured with a 5-0 polypropylene suture (Prolene™) by using a C-1 needle. If necessary, the artery can be briefly turned off by delicate vascular clamps. In the vein, a small Satinsky clamp could be placed tangentially to the vascular injury.

With the help of the Lidhakens, the external iliac vein is slightly raised to mobilize the tissue directly below the vein. The obturator nerve is also shown by sharp dissection and deported with a small dissection of the ventral fat tissue from the nerves. If no macroscopically tangible lymph node metastases are present, the lymph nodes and fatty tissue are removed anterior to the nerve. Caution should be taken in the area of bifurcation of the common iliac vein in the external and internal iliac vein. The latter consists only of a venous plexus, which is easily vulnerable, leading to problematic bleeding.

For the final preparation of the lymph node and adipose tissue, the lead structures are the internal iliac artery and the lateral umbilical ligament. Usually, the origin of the uterine artery can be already identified.

The lymph nodes in the area of the common vessels are separated for histological examination. Should be noted that no or very little tissue is available on the left side, while on right side the lymph nodes and the fatty tissue are located lateral to the common iliac artery.

The common iliac vein lies just posterior to the tissue to be removed. To avoid injury to the vein - a "classic" complication, if the specific anatomy is not sufficiently known to the surgeon - the vein wall should be identified early and prepared within the vascular sheath. Laterally, attention is paid to the protection of the genitofemoral nerve. Using a Breisky hook, the peritoneum is pushed cranially. The tissue is so far mobilized and it may be discontinued cranially with a large titanium clip.

5.7. Para-aortic lymphadenectomy

The role of para-aortic lymphadenectomy as part of a radical hysterectomy is controversial in the treatment of cervix cancer, while in case of stage II corpus carcinoma, the para-aortic lymphadenectomy is indicated.

Follow the right common iliac artery superiorly to the aorta and cut through the peritoneum as far as necessary. Here, the right ureter must be “skipped” during the preparation. This can then be deported easily laterally. For a more extensive lymphadenectomy, the flexible window hook is used, so that all surgeons and assistants have their hands on the preparation and the control of the possible complications. The hook here pushes the duodenal “C” cranially. Again, the sharp dissection is directly on the vessels which is the safest way. A few finger-widths above the aortic bifurcation is the origin of the inferior mesenteric artery. The artery is preferably protected so as not to influence negatively the colonic blood supply.

Even more than in the pelvic lymphadenectomy, the procedure of dissecting should be gradually carried on with a careful preparation, bipolar hemostasis, and generous setting of titanium clips. Small venous and arterial bleeding in this region is more severe than in the pelvic lymph node dissection.

5.8. Preparation of the ureter and parametrium

With the help of a caudal Breisky hook, the lateral umbilical ligament is put under train.

The uterine arteries are exposed directly to their end from the internal iliac artery. The end of the uterine artery is remarkably conservative in this case. In fact, after an anatomical study by Roberts and Krisingner [7], the artery was in 42 of 44 cases starting from the internal iliac artery or the lateral umbilical ligament.

The artery is clamped by two Meigs forceps or two Overholt forceps. The ligature is performed with a 4-0 Polysorb™. The remaining uterine stump is secured with a small titanium clip that is located upward of the uterus thread that is cut and fixed with a Péan to set something in train for the subsequent preparation. Now, the uterine vein is identified and clamped through small titanium clips. This avoids accidental tear.

When the anatomy is clear enough and the ureter can be clearly identified, the uterine vessels are prepared up to the point where they cross the ureter. The uterine artery over-crosses the ureter, while the vein rarely in some instances could under-cross the ureter as well.

Now the ureter cephalad from the medial peritoneal sheet is sharply dissected and it is mobilized caudally. Here, the ureter is closed to numerous vessels related to the final part of this area, and it is useful to use bipolar coagulation for coagulation before cutting (do not use in this passage unipolar instruments).

Whenever the anatomical relationships are less clear, the ureter is also dissected as previously, used as referral point and mobilized caudally. During the procedure, the ureter with a lid retractor is pulled cranially, to put it under tension; then the ureter has to be followed caudally with an Overholt clamp. The laterally located tissue is cut between two Overholt clamps and ligated with 4-0 Polysorb™.

During the initial bladder mobilization, it was prepared as well for a non-radical hysterectomy in the midline; the bladder will now be further mobilized laterally, so as to

isolate the bladder pillar. After a recent blunt mobilization step with the Overholt clamp, the bladder pillar is withdrawn and ligated. In this step, particular attention must be paid to the fact that the ureter is not to be violated. The closed Overholt is used to perforate the tissue, and the movement is medial and forward. Even in the presence, sometimes, of considerable venous hemorrhage, the preparation must be carried out slowly and subtly.

When the ureter is finally exposed to its confluence point into the bladder, the vaginal mucosa could be exposed by rolling further up the bladder.

5.9. Ovariectomy

If a salpingo-oophorectomy is planned, the peritoneum below the infundibulopelvic ligament is windowed using an Overholt clamp. By previous preparation steps, the ureter is here always very visible and usually cannot be violated. Thanks to two Overholt clamps, the ligament is transected and ligated with 4-0 Polysorb™. The proximal clamp is doubly ligated. When you create the first ligature, the clamp is only slightly opened and closed again. The thread is the same cut off to avoid slipping of the ligature by train on the thread. The thread at the distal stump of the uterus situated downward the infundibulopelvic ligament is first left. The peritoneum is sharp cut toward the uterus, and then the thread is tied around the respective Kocher clamp on the uterus.

If the adnexa are left, first the peritoneum between the ligamentum teres uteri and adnexa toward uterus is cut. Then the peritoneum is windowed below the ovarian ligament and the tube. The two structures are then held through an Overholt clamp. Here, it should be ensured that the clamp is not carried too far on the ovary, to avoid injury and bleeding. As a counter clamp is then used a Kocher clamp. The Overholt clamp is replaced by two ligatures - as described above.

5.10. Rectal dissection

The peritoneum is divided transversely in the Douglas area. It is lateral to the two respective ureters, which, however, now should be completely detached from peritoneal leaf. The uterus is then at a maximum to the front pulled to the symphysis under the hand. With the index and middle finger of the other hand, the rectovaginal spatium is dissected and the rectum is displaced from the vagina. Here, a blunt dissection with moderate pressure is only allowed, since the rectum during this step can be quite injured. However, if necessary, the dissection must be sharp under direct vision and directly closed to the vagina. The vagina is dissected here only so far as for the planned discontinuation of the vaginal cuff is necessary. In fact, too-deep pushing leads to unnecessary bleeding.

5.11. Hysterectomy

With the help of slightly curved Zeppelin clamps, the sacrouterine ligaments on both sides should be cut. Here, the clamps are set as close as possible to the sacrum.

However, one must pay attention especially on the left side so that the rectum is not opened. To suture, use Vicryl size 0 on a CT-2 needle. Caution is advised when CR needles are used ("controlled release," "peel needle") so that the needle does not get lost in the operation area.

Finally, when the vagina is opened, all the threads are gathered using a forceps. Moreover, using long clamps, the tissue is cut and ligated until the uterus is completely settled with the vaginal cuff. The still open vagina is completely closed with a Z-suture.

5.12. Radical hysterectomy classification

Radicality of oncological interventions needs always to be balanced with preservation of functional tissues and organs which can be spared by surgical demolition. That is why not only one type of hysterectomy exists, but a variety of possible interventions based on their surgical extension. As a consequence, a consensus about hysterectomy classification has become of crucial importance in order to standardize the nomenclature and consent of a proper comparison of surgical and oncological outcomes.

In 2008, Querleu and Morrow proposed a new classification of radical hysterectomy based on the lateral extent of resection, which takes also into consideration the eventual nerve preservation and separately divides lymphadenectomy into four levels. In particular, hysterectomy has been then classified as follows [8]:

- Type A: Minimum resection of paracervix.
The cervix is entirely removed through an extrafascial resection, after transection of the paracervix medially to the ureter and laterally to the cervix itself. A minimal (less than 1 cm in length) resection of the vaginal wall is also performed. Indications of this type of hysterectomy are the radical excision of early invasive cancers, as well as the palliative debulking of advanced cancers in a multidisciplinary setting.
- Type B: Transection of the paracervix at the ureter.
The paracervix is transected at the level of the ureteral tunnel, sparing the caudal neural component of the paracervix caudal to the deep uterine vein, after partial resection of the uterosacral and vesicouterine ligaments. The vagina is resected at least 1 cm from the cervix or from the tumor. These type of hysterectomy results are also indicated for early stage cancers. This procedure may include (B2) or not (B1) paracervical and iliac lymphadenectomy.
- Type C: Transection of paracervix at junction with internal iliac vascular system.
Hysterectomy is performed through transection of the uterosacral ligament at the rectum, transection of the vesicouterine ligament at the bladder, complete mobilization of both ureters, and vagina resection for about 15-20 mm from the cervix or tumor. This kind of procedure may be performed with (C1) or without (C2) nerve preservation. This intervention is indicated for advanced stage tumors which may be treated with radical intention.
- Type D: Laterally extended resection.
This kind of hysterectomy consists of the resection of the entire paracervix at the pelvic sidewall (C1), along with the exposure of the sciatic nerve and the resection of hypogastric vessels and vessels which arise from the internal iliac system and reach the lateral part of the paracervix (inferior gluteal vessels, internal pudendal vessels, and obturator vessels). This procedure may additionally be accompanied by resection of the adjacent fascial or muscular structures (C2). In any case, this intervention is rarely performed and is usually part of an ultraradical operation known as pelvic exenteration.

Moreover, lymphadenectomy has been classified based on four levels as follows:

- Level 1: External and internal iliac lymph nodes;
- Level 2: Common iliac lymph nodes (including presacral);
- Level 3: Aortic infra-mesenteric lymph nodes;
- Level 4: Aortic infrarenal lymph nodes.

5.13. Hemostasis and drainage

Hemostasis occurs only after the pelvis is washed extensively. Hereby, the major bleeding will be immediately apparent. After washing, the entire pelvis is compressed with a dry belly cloth. First, the deposition stump of the adnexa or the infundibulopelvic ligament needs to be checked and then the vaginal surgical margins. If necessary, hemostasis is done again with CT-2 or CT-1 Vicryl 0.

The rest of the bleeding is stopped by bipolar coagulation. In case of diffused venous bleeding, stitches are preferably done with 4-0 Vicryl on SH needle.

Special care is often necessary for the hemostasis in the area of the bladder pillar or distal ureter. The smallest is the probability of injury of the ureter, if it is explicitly stitched. In fact, the ureter can be detected by palpation up into the bladder.

Since the peritoneum is completely left open, a drainage of the pelvis is not mandatory [9] and only makes sense if no complete hemostasis was achieved; otherwise, a complete hemostasis should always be sought.

If it is decided for a drainage, a Robinson drainage or better a 10-mm-wide Jackson-Pratt drainage should be taken into consideration. For this, the skin is incised laterally with a scalpel number 11. With an Overholt clamp, the abdominal wall is perforated from the outside inward and the drainage is pulled through from the inside to the outside. For the attachment, a polypropylene suture is used (e.g., Seralene™). Braided threads as Vicryl or Ethibond are less suitable because of their wick effect.

5.14. Suprapubic bladder catheter

By means of the transurethral catheter, the bladder is retrograde filled with saline. Then the sleeve 10 Ch (Charrieres, also known as French Grade (FG): 1 Ch = 1/3 mm diameter) is introduced. Silicone catheter is then inserted in the suprapubic, while with the other hand, the bulging bladder is covered, perforating the bladder. The balloon is filled with 3 ml of saline (at a 12 Ch catheter balloon 5 ml). With pressure on the bladder, it is checked whether the liquid is discharged from the catheter. At the same time, the balloon can be checked and thus the correct location is also reviewed. The transurethral catheter is opened again. At the end of the operation, the transurethral catheter is removed.

5.15. Transposition of the ovaries (in case of pelvic radiotherapy)

Considering the ureter course, the peritoneum is medial to the infundibulopelvic ligament (suspensory ligament). Further severed and isolated the adnexa, in the area of vascular

stump two large titanium clips are left. Thereby, the adnexa are shifted upward in women that could necessitate pelvic radiotherapy. By using 4-0 Vicryl on an SH needle on a long needle holder, the adnexa are mounted as high as possible on the lateral peritoneum of the para-coli rule gutters.

The aim is that the ovaries are placed above the promontory; that is the usual radiation limit. With the help of another 4-0 suture, the lateral peritoneal gap is closed. If by mistake a vessel of the infundibulopelvic ligament is injured and cannot be secured by hemostasis, the adnexa must be removed for safety's sake, to prevent re-bleeding.

Figure 1 shows the situs at the end of the operation.

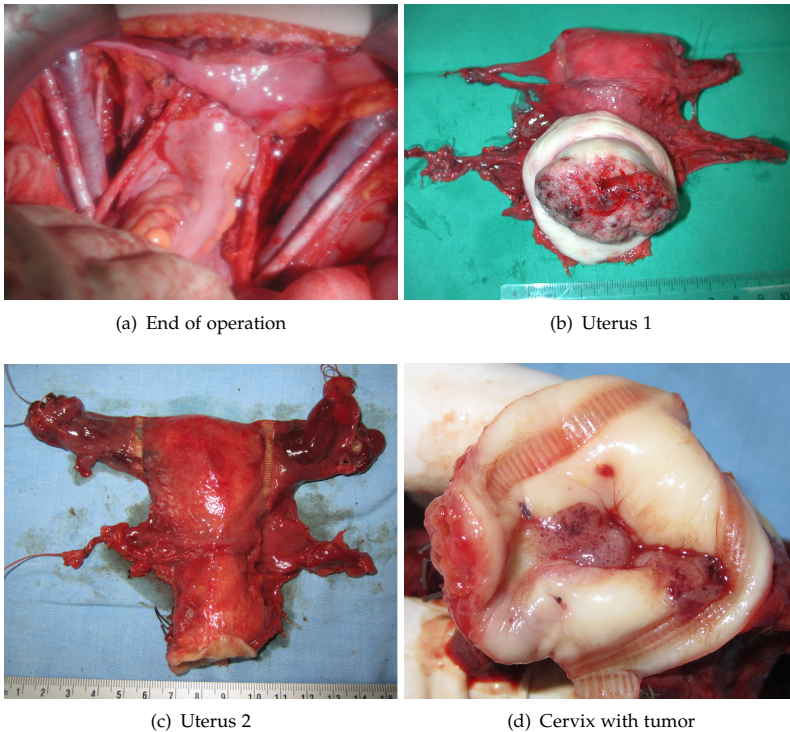


Figure 1. Figures showing the end of operation

5.16. Abdominal cavity closure

Although the completeness of abdominal swabs and instruments is checked by the nurse, before closure, the abdominal wall of the abdomen is scanned as a precaution.

The table is tilted so that the legs are slightly lifted. An abdomen cloth is laid over the intestine; if necessary, in addition, a flexible blade is used. The fascial corner is pulled using a Roux hook. One last time, it is ensured that the severed muscle bellies and the deposition sites of the epigastric vessels are free from bleeding. The abdominal wall is closed

by continuous suture with Biosyn™ (thickness of 1 to a 150-cm-long thread that is embedded as a loop in the needle). The needle is guided either by hand, since the needle tip is blunt (pp = “protect point”), or with the Russian forceps. It is important that plenty of tissue is taken, especially in the area of the fascial corner. Otherwise, the rectus muscle or the peritoneum is not combined well. In the center line, one of the two threads is immediately cut at the needle; then the needle is punched for the last time and a knot is done.

The needle is now tied and the thread ends completely removed. At this point, at least six or, better, eight knots must be placed. Biosyn™ threads are unlike PDS™ threads that lessen the chances of thread “breaks.” A second suture is placed starting from the contralateral fascial corner.

Finally, a thread end of the two seams is knotted together in each case. The subcutaneous tissue is checked for blood dryness. The skin is closed by intradermic suture with 5-0 Biosyn™ C-13 needle. Instead of a patch association, wide Steri-Strips are stuck in the wound direction.

5.17. Postoperative patient monitoring

The antibiotic (cefoxitin) is added over 24 h and then discontinued. A stomach probe is not required. Once the patient is fully awake, she is allowed to drink and immediately take light food. A gradual approach is not required.

Early mobilization is very important, however, the patient receives a thrombosis prophylaxis with low-molecular-weight heparin in a sufficiently high dose.

The currently inserted Jackson-Pratt drainage is removed after 24 or 48 hours when the postoperative coagulation conditions have stabilized. On the sixth postoperative day, the sovra-pubic catheter is disconnected and the bladder training is started.

The patient can be discharged on the seventh postoperative day, provided that a good home care and short-term medical monitoring are guaranteed. If there is still residual urine at this time, the patient either learns self-catheterization or will be dismissed with a horizontal sovra-pubic catheter.

5.18. Intraoperative and postoperative complications

The main intraoperative complications are ureteral laceration, rectal injury, main arteries or vein injury, and eventual bladder laceration (if not opened intentionally).

The main postoperative complications could be hemorrhage, wound infection, urine retention, ureter stricture, and lymphedema.

In addition, the nerve-sparing radical hysterectomy was introduced with the intent to spare autonomic nerves and in particular bladder function but not compromising surgical radicality [2].

In general, open surgery compared to laparoscopic approach seems to be more prone to have operative complications and stump recurrence [10]. Furthermore, the laparoscopic approach seems to have significant reduction of blood loss and hospital stay [11].

6. The role of laparoscopy in gynecologic oncology and laparoscopic radical hysterectomy

In general, laparoscopic hysterectomy represents very advantageous in comparison with the laparotomic approach, reducing the surgical trauma on pelvic structures with a consequent reduction also in adherence formation, improving postoperative course with a quicker functional recovery (deambulation, canalization, etc.), less pain perception and less drug administration, reduction of the hospitalization length with a quicker recovery of both work activities and social life, and reduction of the postoperative complications.

Common indications for the laparoscopic hysterectomy are uterine myomas and abnormal uterine bleeding but also uterine and cervix carcinoma. However, the laparoscopic approach is not always feasible. Another field of application in gynecologic oncology is ovarian cancer. In fact, laparoscopic staging could be of paramount importance before open surgery. Furthermore, it is considered also the possibility to treat intraperitoneal cancer spread by laparoscopy eventually before intraperitoneal local chemotherapy.

Basically, the laparoscopic technique for hysterectomy differs from previous laparotomic description for the following issues.

6.1. Patient preparation and positioning

After anesthesia induction, women are placed in a dorsal lithotomy position with the arms tucked at the sides. The legs are bent, mildly elevated, and closed in boots in order to allow Trendelenburg during intervention phases.

The insertion of a uterine manipulator for hysterectomy (e.g., uterine HOHL manipulator or uterine Clermont-Ferrand manipulator) through a speculum results very helpful to improve pelvic visibility during the whole intervention. It is of crucial importance to choose the correct size in order to prevent the risk of ureteral injury with larger manipulators and to avoid a bad vaginal fornix delineation in case of smaller ones. The manipulator insertion could be eventually omitted in cases of women who have never had any intercourse or those long-standing treated with testosterone.

6.2. Abdominal entry and trocar placement

Usually the laparoscopic approach is made through four trocars placed as follows:

- 12-mm umbilical trocar, which may be inserted under direct vision or after pneumoperitoneum induction through the Verres needle;
- 5-mm trocar in the right fossa iliaca, lateral to the rectus abdominis muscle 2-cm above and 2-cm medial to the anterior superior iliac spine;
- 12-mm trocar in the left fossa iliaca, lateral to the rectus abdominis muscle 2-cm above and 2-cm medial to the anterior superior iliac spine;
- 5-mm trocar on the left side, 8-cm above and parallel to the lower left trocar site.

During surgery, the uterine manipulator is being pushed upward and to the contralateral side to provide an optimal visualization of the surgical field.

6.3. Uterus removal

After separation of the uterus and cervix from the vaginal apex, the uterus is pulled into the vagina in order to maintain pneumoperitoneum while suturing by laparoscopy. However, it is possible to remove the uterus by vaginal way, closing the vagina with a pneumatic cuff to maintain the pneumoperitoneum. Afterward, it is still possible to close the vagina by laparoscopic approach, but also vaginal approach to close the vaginal apex is feasible.

The vaginal cuff is then sutured, beginning from its distal angle and making sure to include both the vaginal mucosa and the rectovaginal fascia.

Hemostasis is controlled at least three times before port closure.

7. Notes on robotic surgery applied on radical hysterectomy

Robotic surgery represents the new frontier of mini-invasive gynecologic surgery. Along with the same quality and efficacy of traditional surgery, robotic surgery offers all the benefits of mini-invasive surgery, including the absence of big abdominal scars, reduced operative time, reduced blood loss, and reduced postoperative pain. In particular, robots add to the surgical procedure a precision which is not comparable to the other techniques. Moreover, through the great versatility of their instruments, robots may reach very narrow and deep anatomical spaces, being very comfortable especially in the pelvic surgery.

Mini-invasive laparoscopic surgery has experienced a great spread in the gynecologic field at the beginning of the 1990s. Then, robotic surgery represented an evolution of laparoscopic surgery and succeeded in overcoming the limits of laparoscopic surgery itself in reaching anatomically difficult regions.

Surgical robots are constituted by a surgical console and a surgical cart. Sit by the surgical console, the surgeon controls the surgical instruments through some handpieces which are able to complete 360° movements and looks at the operative field through a tridimensional telecamera. The surgical cart is the true robot, obviously localized by the operative table, and usually includes four operative arms.

Surgical instruments are introduced in the abdomen by 8 mm trocars and fixed to the arms of the surgical cart. They are in a continuous technological evolution in order to satisfy surgeons' needs in any surgical discipline. And, most important, they are very versatile and may completely articulate their movements, in order to reach any region of the abdomen, being very advantageous in pelvic surgery or among obese patients, where the intestinal encumbrance reduces the action field.

Actually, all laparoscopic interventions may be converted to robotic ones. Moreover, robotic surgery reduces operative time and consequently anesthesiologic risks and physical stress for the patient. Furthermore, even complex patients may undergo robotic surgery as the CO₂ pressure within the abdomen is lower than those of laparoscopic surgery.

Finally, tridimensional vision helps the surgeon in the identification of nerves, vessels, or ligamentous structures.

7.1. Robotic surgery of the tubes

The first robotic intervention was performed on the tubes. Tubaric surgery, in fact, results particularly difficult especially when they require to be reopened after binding with voluntary sterilization intent. The indication for robotic surgery in this case lays in the evident quality of robotic sutures, which result more simple and safe if performed by robotic instruments.

In particular, tubaric anastomosis requires a suture with very thin reabsorbable threads (6-0 to 8-0), which are used to reconstruct both the muscular and serous layers of the tubes. Moreover, tridimensional vision gives the operator more precision to perform such complex sutures.

7.2. Robotic surgery of uterine myomas

The maximal spread of laparoscopic surgery for the excision of uterine myomas developed during the 1990s, even if the laparotomic approach results were still very frequently used. In fact, laparotomic myomectomy allows a good suture quality and is surely easier to learn while completing the learning curve of a gynecologic surgeon. However, nowadays it has been widely demonstrated that the quality of laparoscopic sutures is comparable to that of laparotomic ones. Moreover, the suture with the robot results in easy and faster execution and thus reduces even the operative and anesthesiologic time.

Thanks to robotic needle holders and to the versatility of their movements, the surgeon can make sutures on the uterus after the myoma excision, even in more layers, in less time and with less blood loss.

7.3. Robotic surgery of endometriosis

Surgery for rectum-vaginal endometriosis is nowadays performed by laparoscopy, and in this case, robotic techniques improve the approach to narrow spaces. The excision of vesical and/or rectal endometriosis is then another fundamental indication for robotic surgery in the gynecologic field, as well as the rectum resection for endometriosis.

Robotic surgery aims to reduce the incidence of stoma formation and to reduce hospitalization time, which results about 5 days, although women result completely autonomous within the second postoperative day.

7.4. Robotic surgery of uterine cancer

In the gynecologic oncologic field, the robotic surgical approach finds nowadays its principal role in the treatment of uterine cancer. In fact, if once this neoplastic disease was treated only by laparotomic incision, now it is possible to operate patients through 3-4 8 mm-sized incisions on their abdominal wall with a consequent increased benefit on their psychophysical wellness.

In this perspective, during the last decade, many authors published their casistic in order to assess feasibility and safety of this procedure in comparison with the traditional approach. And actually, they assessed its feasibility and safety in case of both cervical cancer and endometrial cancer, as well as sarcomas.

Tanks to the tridimensional vision of robot, it is possible to better identify the nerves and to spare them when possible while removing the uterus and consequently to reduce postoperative complications such as urinary retention or urinary incontinence.

In addition, mean operative time results surely inferior than that required for laparotomic hysterectomy and pelvic lymphadenectomy, as well as blood loss and hospitalization time, which for the robotic procedure is about 3 days.

Finally, more rare is the use of robotic approach in case of pelvic recurrences after hysterectomy, but it is not contraindicated.

8. HIPEC in gynecologic oncology

8.1. Definition and epidemiology of peritoneal carcinomatosis in gynecologic malignancies

Peritoneal carcinomatosis is defined as the spread of neoplastic cells in the peritoneal cavity, which usually forms a multitude of nodules on the parietal peritoneum as well as on the visceral peritoneum. It is considered a terminal stage of many solid intra-abdominal tumors, including those of the digestive tract or of the female reproductive system, usually leading to death due to a chronic, progressively worsening, occlusive status [12]. It has a very unfavorable prognosis, and in the literature, the median survival of patients diagnosed with peritoneal carcinomatosis traditionally was not longer than 6 months [13, 14].

Among gynecologic malignancies, epithelial ovarian cancer is recognized to have the most marked propensity for peritoneal involvement. In fact, about 50 to 75% of women with ovarian cancer will develop persistent or recurrent disease [15]. Invasion of the ovarian capsule and dissemination in the peritoneal cavity is the main route by which ovarian carcinoma spreads [15], accounted for about 82% of the cases, whereas in 12% it involves the retroperitoneal lymph nodes [12].

For what concerns uterine cancer, the current literature reported some cases of peritoneal carcinomatosis of endometrial origin, justifying then interest in the loco-regional treatment for such poor prognosis lesions [16, 17].

8.2. Preoperative assessment of peritoneal carcinomatosis

Although the majority of patients affected by gynecologic malignancies undergo computer tomography (CT) scan or magnetic resonance imaging (MRI) or positron emission tomography (FDG/PET-CT) during their pre-recovery period, the diagnosis of peritoneal carcinomatosis remains a great challenge for the radiologist.

In fact, CT scan has a very low sensitivity for nodules smaller than 5 mm, and the 80% of sensitivity is reached in case of CT scan only among patients with diffuse peritoneal carcinomatosis [18, 19].

For what regard FDG/PET-CT, its accuracy results strongly compromised by previous systemic therapies that may lead to an underestimation of disease due to dormant neoplastic foci, as well as to an overestimation of disease because of increased contrast medium uptake in scars or fibrotic areas [20].

In order to standardize peritoneal carcinomatosis assessment, Sugarbaker introduced the Peritoneal Cancer Index (PCI) in 1995 [21], which consists of a score ranging from 0 to 39, depending on both the localization and the size of neoplastic nodules within the peritoneal cavity. In particular, the abdomen is divided into 12 areas (Figure 2), and to any area is given a score considering nodules size as follows:

- 0 no macroscopic disease
- 1 nodules less than 2.5 mm
- 2 nodules between 2.5 mm and 2.5 cm
- 3 nodules greater than 2.5 cm

A second classification exists, introduced by Gilly [22], which is actually more in use only by the French school.

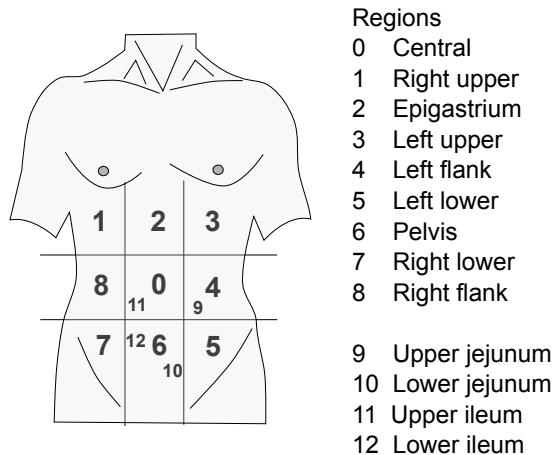


Figure 2. Sugarbaker regions

8.3. Intraoperative assessment of peritoneal carcinomatosis

Intraoperative assessment of peritoneal carcinomatosis is performed before and after CRS. First, peritoneal involvement is evaluated by PCI score as previously described. This is a very important step, because it may predict the radicality of CRS and consequently the possibility to perform the HIPEC. It is possible to perform this step also by laparoscopic approach.

After surgical demolition, residual peritoneal disease is usually measured using the Completeness Cytoreduction Score (CCS), which takes into consideration the residual tumor size as follows:

- CCS0 no macroscopic residual disease
- CCS1 residual disease sized less than 2.5 mm

- CCS2 residual disease between 2.5 mm and 2.5 cm
- CCS3 residual disease greater than 2.5 cm

In case of CCS0-1 HIPEC finds its best indication and is performed with curative intent. CCS2-3 usually contraindicate HIPEC, which in some selected cases is anyway performed but just with a palliative intent, as it is recognized to significantly reduce neoplastic ascitis in the terminal stage disease.

8.4. Cytoreductive Surgery (CRS) and peritonectomy

The surgical procedure of cytoreduction is now well standardized. Sugarbaker's classification is still the reference for abdominal oncologic surgery and goes under the definition of peritonectomy [21]. The surgical procedure was classified according to specific different areas of the abdominal cavity and it has been tailored by Milan's panel workshop, defining:

- Upper Right Peritonectomy: right diaphragmatic peritonectomy with Glisson's capsule dissection; lesser omentectomy, stripping of the omental bursa and cholecystectomy plus gastric antrectomy or total gastrectomy.
- Upper Left Peritonectomy: left diaphragmatic and parietal peritonectomy with splenectomy and greater omentectomy.
- Pelvic Peritonectomy: pelvic parietal peritonectomy, sigmoidectomy, hysterectomy and salpingo-oophorectomy.
- Right Parietal Peritonectomy, right/total colectomy; left parietal peritonectomy.
- Mesenteric implants on visceral surfaces could be removed surgically or by electro-surgical local dissection.

While performing cytoreduction for peritoneal tumor dissemination, not all the procedures are necessary and performed, usually necessitating one to three of the different peritonectomy procedures.

8.5. Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

After having made complete surgical cytoreduction with an absent or minimal residual disease (less than 2.5 mm tumor diameter), some catheters are inserted into the abdominal cavity and a perfusion of saline solution is made. Usually, depending on patient BMI, the quantity of saline solution perfused in the abdomen may vary between 2 and 6 l. After reaching a determined temperature, antineoplastic drugs are perfused. The most frequently used antineoplastic drugs include Mitomycin, Cisplatin, Oxaliplatin, Doxorubicin, and Taxol, which are chosen case by case depending on the origin of peritoneal carcinomatosis.

The peritoneal perfusion may last 30-90 minutes and it can be performed in condition of closed abdomen or open abdomen (coliseum technique) or a compromise between the two, with an abdominal wall small entrance suitable for the handling by the operator.

Hyperthermic perfusion can be obtained by heating the perfusion medium with a heat exchanger connected to the perfusion pump. The peritoneal cavity temperature considered

optimal in terms of antitumor activity and antiproliferative tumor tissue diffusion is 41.5-42.5 °C [23, 24]. It is of absolute importance to control the temperature of organs and bowels during the procedure. Excessive temperature of intraperitoneal tissue, more than 43 °C, is strongly correlated with lesions of the bowel wall and perforation, and also with necrosis of nerves, bladder or vessels. To prevent excessive intraperitoneal temperature multiple temperature probes are placed within the peritoneal cavity to monitor the temperature. At the end of the procedure the perfused medium is removed from the peritoneal cavity.

8.6. Outcomes of CRS and HIPEC in gynecologic malignancies

Among patients affected by ovarian cancer, the performance CRS and HIPEC has been recognized to correlate with better overall and disease-free survival. Two recently published systematic reviews, which analyzed almost all the available international literature, concluded that this comprehensive treatment modality is a viable option in the management of patients with advanced stage III-IV disease, with potential benefits comparable with the current standard of care (conventional secondary cytoreduction or systemic chemotherapy) [15, 25]. In particular, median overall survival for primary and recurrent disease extrapolated from the studies reviewed ranged from 22 to 64 months with a median disease-free survival from 10 to 87 months [25]. Most of the studies among those reviewed showed that patients with complete CRS had the greatest benefit, with a 5-year survival rate ranging from 12 to 66% [15, 25].

About uterine cancer, indeed, there is very poor data about the outcome after CRS and HIPEC. However, a recent study on thirteen patients demonstrated a significant survival time in selected patients, suggesting in the future a more extensive role of this procedure in women with peritoneal carcinomatosis of endometrial origin [16]

9. Conclusive summary

Radical hysterectomy is still an important surgical procedure in gynecologic oncology. New technologies are changing hysterectomy techniques and integrated treatments (e.g., cytoreduction associated with HIPEC) could expand the surgical indications in gynecologic oncology.

Despite the benefits of the minimally invasive (laparoscopic or robotic surgery) radical hysterectomy its adoption has been slow in cancer treatment [1]. In fact, both laparoscopic and robotic approaches showed favorable mobility profiles in comparison to open techniques. However, some issues have likely contributed to the slow adoption of these techniques. In general these cancer treatments are technically demanding procedures and the relatively uncommon diagnosis of cervical cancer have probably slowed the adoption of these techniques. Another issue is the cost of introducing robotic surgery in a gynecologic operative theater. Furthermore, data about oncologic long term outcomes of minimally invasive surgery are relatively sparse [1].

Acknowledgments

The authors would like to thank the whole collaborating staff of the Westfälische Wilhelms-Universität Münster (WWU), Università dal Friûl, and IRCCS CRO of Aviano.

In particular, we would like to thank Alexandra Woltering. In addition, we are also grateful to Prof. Diego Marchesoni and Dr Lorenza Driul for their help and suggestions.

Author details

Ambrogio P Londero^{1*}, Serena Bertozzi², Luca Martella², Giulio Bertola², Giorgio Giorda², Angelo Calcagno³, Arrigo Fruscalzo^{4,5}, Ralph J Lellé⁴

*Address all correspondence to: ambrogio.londero@gmail.com

1 Unit of Obstetrics and Gynecology, S. Polo Hospital, Monfalcone (GO), Italy

2 IRCCS CRO, Aviano (PN), Italy

3 Clinic of Obstetrics and Gynecology, University of Udine, Italy

4 Clinic of Obstetrics and Gynecology, University of Münster, Germany

5 Unit of Obstetrics and Gynecology, St. Franziskus-Hospital, Münster, Germany

References

- [1] Wright JD, Herzog TJ, Neugut AI, Burke WM, Lu YS, Lewin SN, et al. Comparative effectiveness of minimally invasive and abdominal radical hysterectomy for cervical cancer. *Gynecol Oncol.* 2012;**127**:11–17. .
- [2] Kim HS, Kim TH, Suh DH, Kim SY, Kim MA, Jeong CW, et al. Success factors of laparoscopic nerve-sparing radical hysterectomy for preserving bladder function in patients with cervical cancer: a protocol-based prospective cohort study. *Ann Surg Oncol.* 2014;.
- [3] Meigs JV. Removal of the pelvic lymph nodes in cancer of the uterine cervix; transperitoneal (taussig) and retroperitoneal (nathanson) dissection. *Gynecol Prat.* 1951; **2**:127–39.
- [4] Lellé RJ, Heidenreich W, Lück HJ, Schneider J. Morley inter-iliac transverse incision in gynecologic operations. *Geburtshilfe Frauenheilkd.* 1995;**55**:695–698.
- [5] Toussaint MN, Hillemanns HG. Graduated ruler for making a transverse suprapubic incision. *J Gynecol Obstet Biol Reprod (Paris).* 1989;**18**:99–101.
- [6] Lellé RJ, Schneider J. Intentional incision of the urinary bladder during complex gynecologic oncologic operations. *Zentralbl Gynakol.* 1996;**118**:228–231.
- [7] Roberts WH, Krashingner GL. Comparative study of human internal iliac artery based on Adachi classification. *Anat Rec.* 1967;**158**:191–196. .
- [8] Querleu D, Morrow CP. Classification of radical hysterectomy. *Lancet Oncol.* 2008; **9**:297–303. .

- [9] Patsner B. Closed-suction drainage versus no drainage following radical abdominal hysterectomy with pelvic lymphadenectomy for stage IB cervical cancer. *Gynecol Oncol.* 1995;**57**:232–234. .
- [10] Choi CH, Lee JW, Lee YY, Kim HJ, Song T, Kim MK, et al. Comparison of laparoscopic-assisted radical vaginal hysterectomy and laparoscopic radical hysterectomy in the treatment of cervical cancer. *Ann Surg Oncol.* 2012;**19**:3839–3848. .
- [11] Ditto A, Martinelli F, Bogani G, Gasparri ML, Di Donato V, Zanaboni F, et al. Implementation of laparoscopic approach for type B radical hysterectomy: a comparison with open surgical operations. *Eur J Surg Oncol.* 2015;**41**:34–39. .
- [12] Al-Shammaa HAH, Li Y, Yonemura Y. Current status and future strategies of cytoreductive surgery plus intraperitoneal hyperthermic chemotherapy for peritoneal carcinomatosis. *World J Gastroenterol.* 2008;**14**:1159–1166.
- [13] Glehen O, Schreiber V, Cotte E, Sayag-Beaujard AC, Osinsky D, Freyer G, et al. Cytoreductive surgery and intraperitoneal chemohyperthermia for peritoneal carcinomatosis arising from gastric cancer. *Arch Surg.* 2004;**139**:20–26. .
- [14] Chua TC, Yan TD, Saxena A, Morris DL. Should the treatment of peritoneal carcinomatosis by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy still be regarded as a highly morbid procedure?: a systematic review of morbidity and mortality. *Ann Surg.* 2009;**249**:900–907. .
- [15] Chua TC, Robertson G, Liauw W, Farrell R, Yan TD, Morris DL. Intraoperative hyperthermic intraperitoneal chemotherapy after cytoreductive surgery in ovarian cancer peritoneal carcinomatosis: systematic review of current results. *J Cancer Res Clin Oncol.* 2009;**135**:1637–1645. .
- [16] Delotte J, Desantis M, Frigenza M, Quaranta D, Bongain A, Benchimol D, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for the treatment of endometrial cancer with peritoneal carcinomatosis. *Eur J Obstet Gynecol Reprod Biol.* 2014;**172**:111–114. .
- [17] Bakrin N, Cotte E, Sayag-Beaujard A, Raudrant D, Isaac S, Mohamed F, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for the treatment of recurrent endometrial carcinoma confined to the peritoneal cavity. *Int J Gynecol Cancer.* 2010;**20**:809–814.
- [18] Bristow RE, del Carmen MG, Pannu HK, Cohade C, Zahurak ML, Fishman EK, et al. Clinically occult recurrent ovarian cancer: patient selection for secondary cytoreductive surgery using combined PET/CT. *Gynecol Oncol.* 2003;**90**:519–528.
- [19] Bharwani N, Reznick RH, Rockall AG. Ovarian cancer management: the role of imaging and diagnostic challenges. *Eur J Radiol.* 2011;**78**:41–51. .
- [20] Pasqual EM, Bertozzi S, Bacchetti S, Londero AP, Basso SMM, Santeufemia DA, et al. Preoperative assessment of peritoneal carcinomatosis in patients

undergoing hyperthermic intraperitoneal chemotherapy following cytoreductive surgery. *Anticancer Res.* 2014;**34**:2363–2368.

- [21] Sugarbaker PH. Peritonectomy procedures. *Ann Surg.* 1995;**221**:29–42.
- [22] Gilly FN, Carry PY, Sayag AC, Brachet A, Panteix G, Salle B, et al. Regional chemotherapy (with mitomycin C) and intra-operative hyperthermia for digestive cancers with peritoneal carcinomatosis. *Hepatogastroenterology.* 1994;**41**:124–129.
- [23] Sugarbaker PH, Chang D. Results of treatment of 385 patients with peritoneal surface spread of appendiceal malignancy. *Ann Surg Oncol.* 1999;**6**:727–731.
- [24] Sugarbaker PH. Observations concerning cancer spread within the peritoneal cavity and concepts supporting an ordered pathophysiology. In Sugarbaker PH. (ed.) *Peritoneal carcinomatosis: principles of management.* Springer US; 1996. p79–100.
- [25] Bijelic L, Jonson A, Sugarbaker PH. Systematic review of cytoreductive surgery and heated intraoperative intraperitoneal chemotherapy for treatment of peritoneal carcinomatosis in primary and recurrent ovarian cancer. *Ann Oncol.* 2007;**18**:1943–1950.

