



Peritoneal Mesometrial Resection (PMMR) with Therapeutic Lymphadenectomy (tLNE) in Endometrial Cancer

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Introduction

PMMR (peritoneal mesometrial resection) is the surgical equivalent to TMMR (total mesometrial resection) in endometrial cancer and has first been described in detail in 2013 [1, 2]. Background and principles of compartmental surgery and differences of the surgical approach due to the different subcompartment of tumour origin are outlined in Chapter 14. In short, with respect to the tumour bearing subcompartment of uterine corpus, there is no drainage to the ligamentous mesometrium (i.e. sacrouterine ligament) and nodes of the sacrouterine and preischadic region [3]. Thus, neither the ligamentous mesometrium nor the preischadic nodes have to be dissected; on the other hand, there is drainage from the fundus along the mesonephric ovarian vessel system suggesting complete resection of these structures including the para-aortic mesenteric lymph nodes being first-order regional lymph compartments on the basis of the concept of compartmental surgery.

These differences in lymphatic drainage may be demonstrated functionally with injection of indocyanine green (ICG) into the uterine corpus prior to surgery. In Fig. 15.1 it is shown that there is no drainage along the ligamentous mesometrium, whereas the vascular mesometrium fully drains. The drainage along the fundus (Fig. 15.2) may be followed along the ovarian vessels (Fig. 15.3) up to the para-aortic nodes ventrally of the aorta and between aorta and caval vein (Fig. 15.4). The data with respect to local uterine drainage have been already summarized together with the results following cervical injection in [3].

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Technique of PMMR

Following inspection and coagulation of fallopian tubes in endometrial cancer, the peritoneum is incised lateral to the right infundibulopelvic ligament, and if not primarily resected completely—which should always be done in complete PMMR—the ovarian vessels are coagulated and cut well above the adnexa. The peritoneum is divided to the right round ligament.

Step 1: The peritoneum is incised as shown in Fig. 15.3a that still covers the utero-ovarian vessel network which contains also the lymphatics (Fig. 15.3b) to be resected, first, following dissection of the round ligament ventrally along the border between Müllerian and bladder peritoneum to the cervicovesical fold. The bladder is pushed down to expose the vagina down at the level where it is planned to be resected.

Step 2: Second, the peritoneal incision is done similarly at the posterior peritoneal surface to open the rectovaginal space in the same way (Fig. 15.3c, d). This integral part of PMMR will be done for two reasons: first, to resect the embryologically “uterine peritoneum” completely and, second, not to dissociate the supplying and draining vascular and lymph vessel system of the Müllerian and mesonephric compartments.

Step 3: The umbilical artery will be prepared to its origin from the internal iliac artery and the branching of the uterine and the superior vesical artery will be identified.

Step 4: The vascular mesometrium will be exposed ventrally by detaching it from the bladder mesentery opening the avascular space between the uterine and superior vesical artery (Fig. 15.4a, b) and posteriorly by opening the avascular space between the ureter, the uterine artery and the internal iliac artery. In case of ICG labelling the lymphatic draining vessels will cross the umbilical artery at the origin of the uterine artery connecting to the iliac sentinel nodes (Fig. 15.5).

Step 5: The vascular mesometrium containing the uterine artery and vein will be coagulated and cut at the origin from

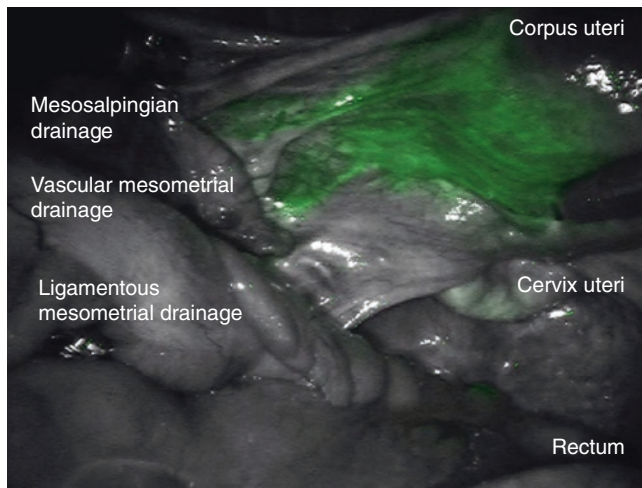


Fig. 15.1 Lymphatic corporal network in endometrial cancer (corporal injection of ICG)

the iliac vessels (Fig. 15.6) and lifted up together ventrally and medially to identify the ureter and its supplying vessels (Fig. 15.7).

Step 6: Connecting vessels from the vascular mesometrium to the ureter will be coagulated and cut.

Step 7: The uterovesical anastomosing vessels anteriorly to the ureter will be identified and cut (Fig. 15.8, so-called vesicouterine ligament). Now the ureter can be mobilized and pushed laterally caudally.

Step 8: The cervical venous drainage and the ligamentous mesometrium are now coagulated and cut paracervically to expose the vaginal wall.

Steps 1–8 will be repeated on the left side.

Step 9: Colpotomy and removal of the PMMR specimen along the vagina.

The fluorescence persists throughout the surgery as can be seen in Fig. 15.9.

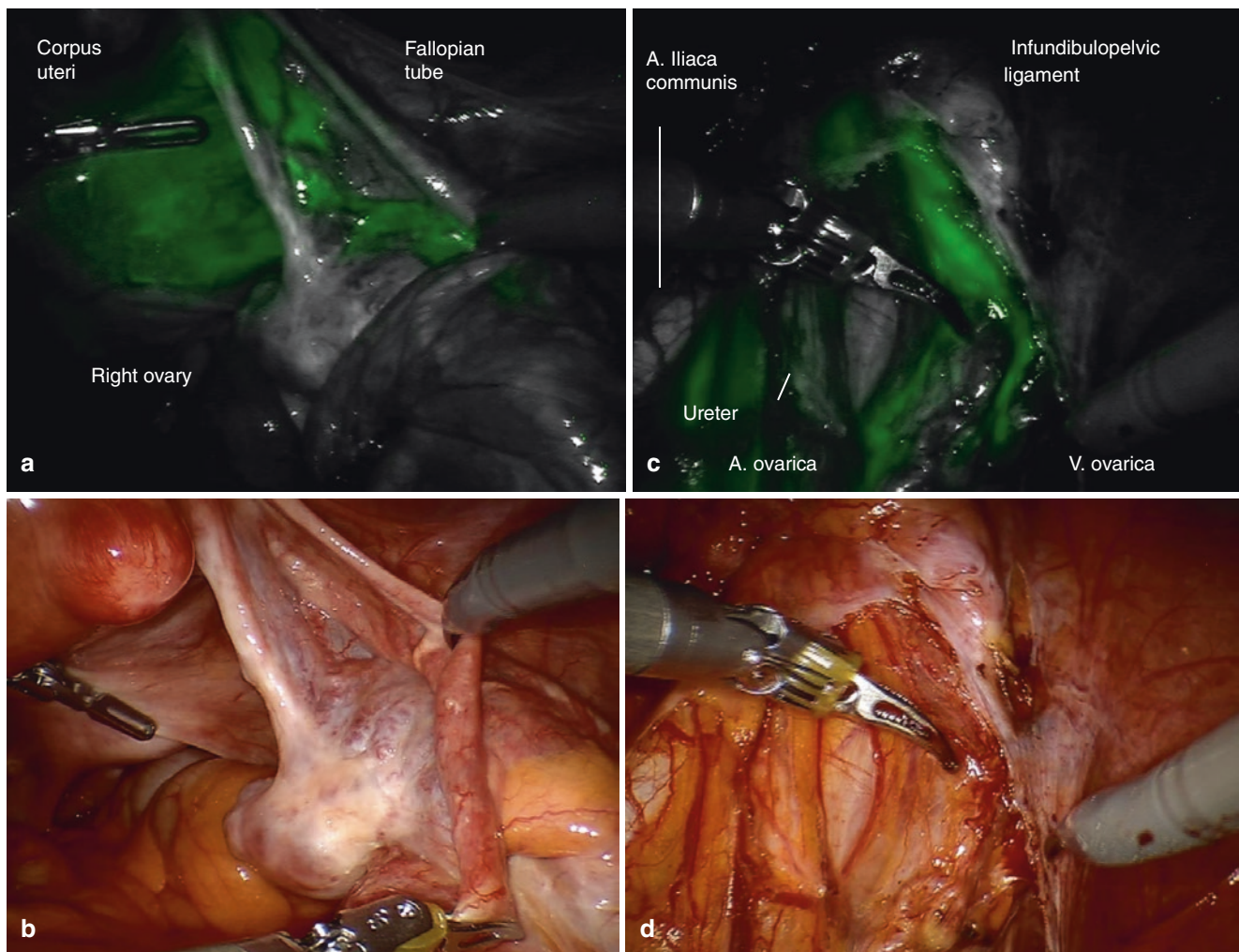


Fig. 15.2 Lymph drainage right infundibulopelvic ligament (ICG and real light comparison) [1]

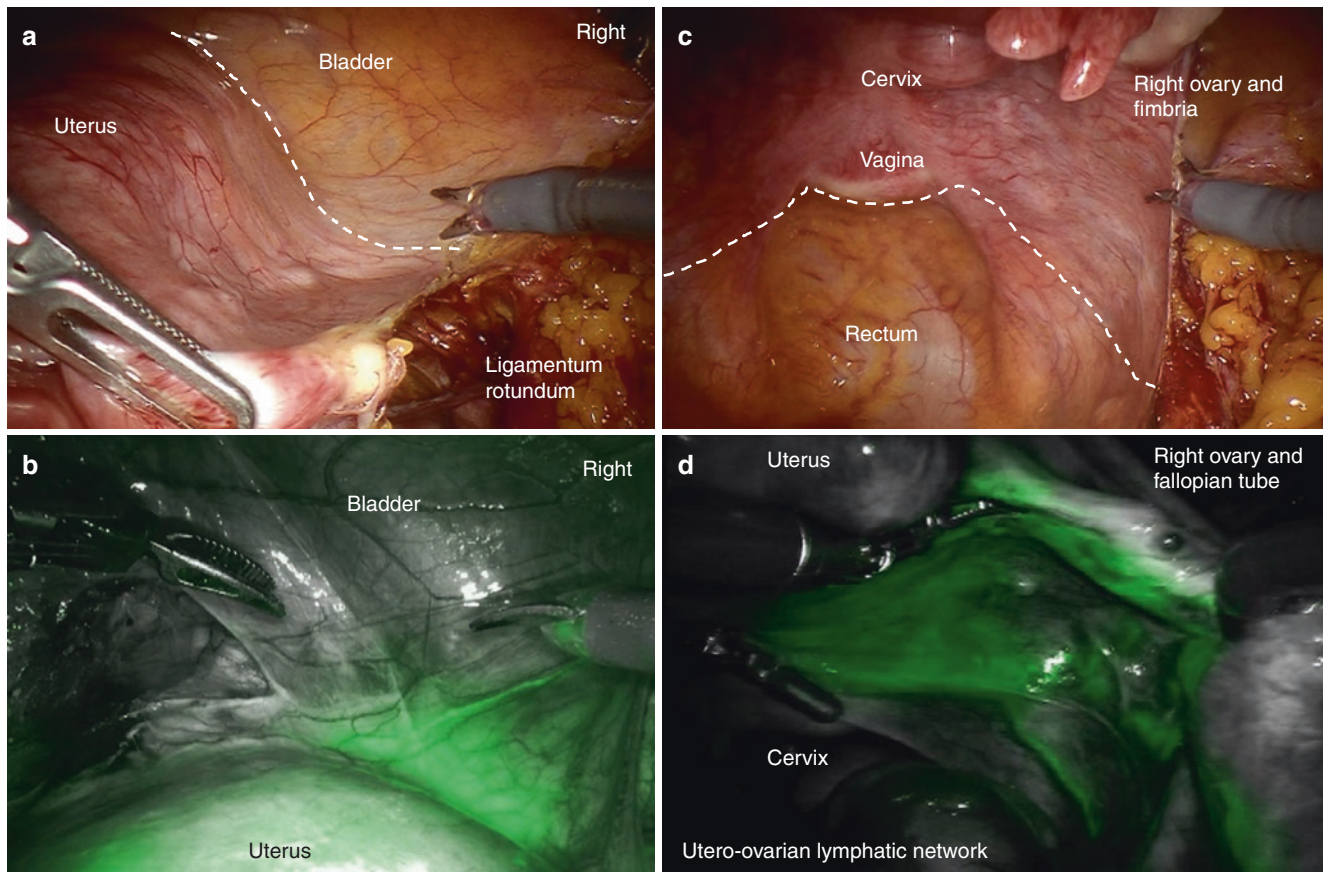


Fig. 15.3 Ventral (a, b) and dorsal (c, d) peritoneal incision in PMMR covering the utero-ovarian vessel network with (b, d) and without (a, c) intracorporeal ICG application [1, 2]

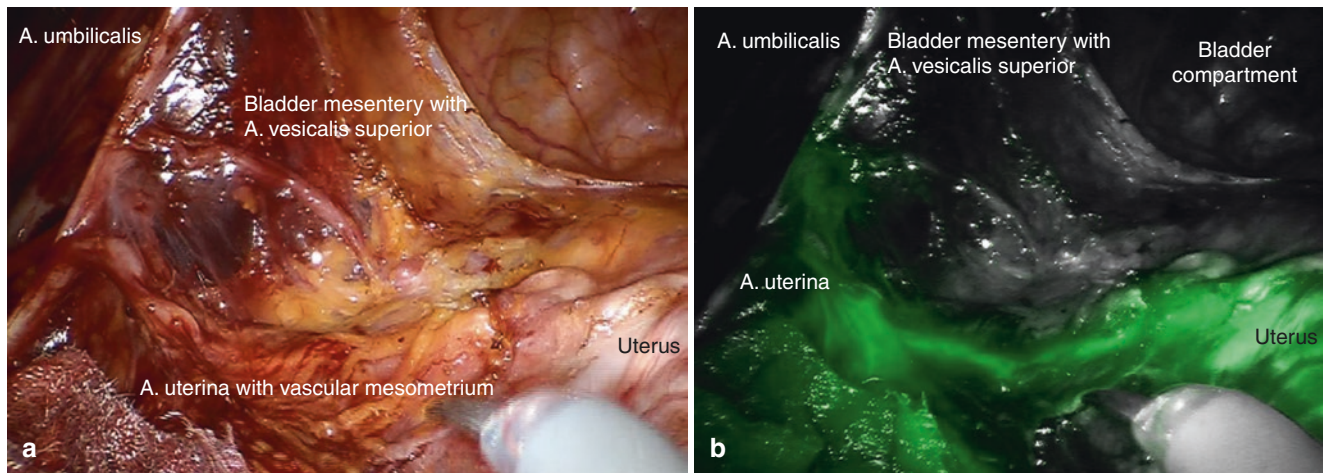


Fig. 15.4 (a) Preparation of the umbilical artery and identification of uterine and superior vesical artery (left) [3]. (b) Correspondent ICG lymphography of left vascular mesometrium [3]

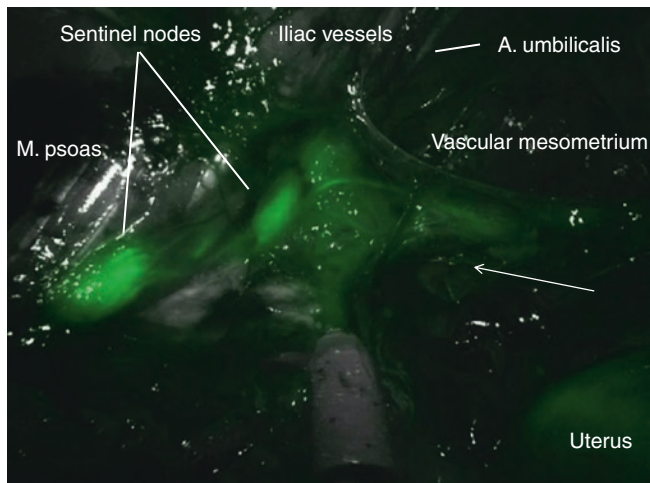


Fig. 15.5 Vascular mesometrium and iliac sentinel nodes on the left (ICG)

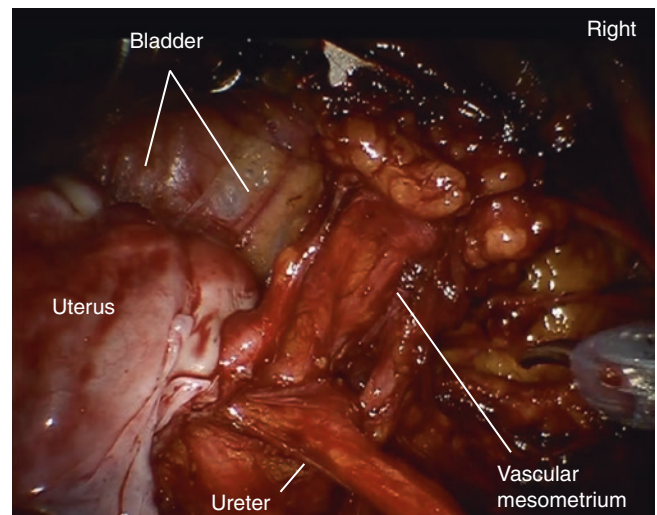


Fig. 15.7 Lifting up the entire vascular mesometrium including uterine vessels to identify the vesicouterine vessel anastomoses

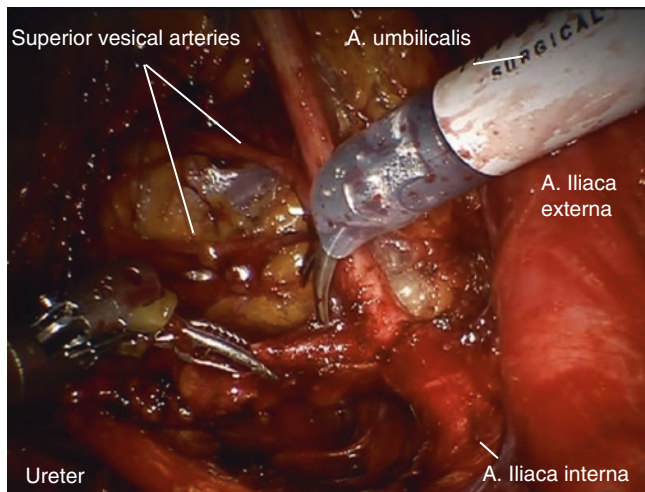


Fig. 15.6 Resection of entire vascular mesometrium including uterine vessels at the branching from internal iliac vessels on the right

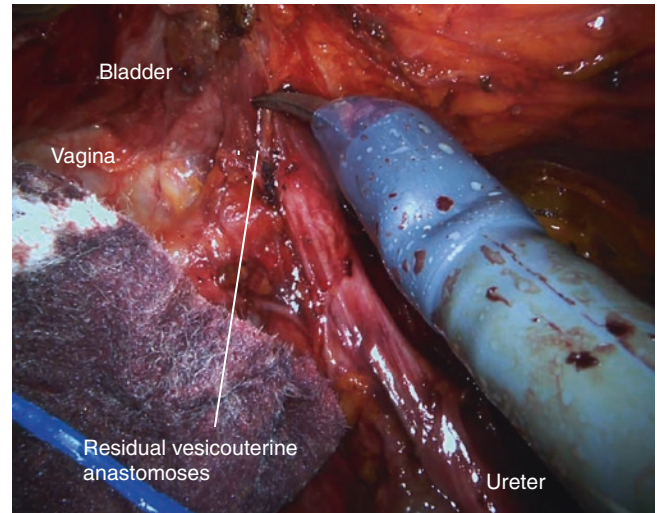


Fig. 15.8 Division of anterior vascular mesometrium anastomoses to free ureter and bladder from attachment to uterine compartment on the right developing the ureter on the right

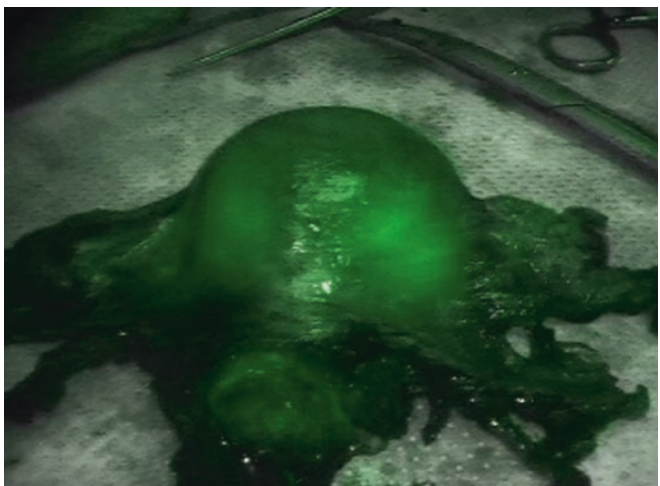


Fig. 15.9 PMMR specimen postoperatively, native and with ICG fluorescence [11]

Therapeutic Pelvic and Para-aortic Lymphadenectomy

Lymphadenectomy is done as outlined in Chapter 14 for cervical cancer with two important differences:

First, prespinal and preischial nodes do *not* have to be removed since they are not involved into the drainage of uterine corpus.

On the other hand, the para-aortic infrarenal lymph nodes together and in continuity with the draining ovarian lymph vessels “en bloc” *have to be* removed in all patients with indication for lymphadenectomy due to the “mesonephric” lymphatic drainage along this pathway.

The infundibulopelvic ligament containing the ovarian vessels (Fig. 15.10) will be followed dissecting the anastomoses to the colonic vessels (Fig. 15.11) as demonstrated in Fig. 15.12 for the right side. On each side up the ovarian vessels will be coagulated and cut close to their origin from the caval vein, aorta and left renal vein (Fig. 15.13). There are no direct lymph connections to the lumbar chain of para-aortic nodes. The connecting lymph vessels enter the mesenteric para-aortic lymph basin and end up around and above the inferior mesenteric artery on the right (Fig. 15.14a, b) and close to the renal vein on the left (Fig. 15.15a, b). As can be seen with ICG fluorescence, the lymphatic vessels run caudally and medially of the corresponding ovarian vessels, which is the reason why they join the para-aortic nodes lower on the right compared to the left side.

Thus the para-aortic nodal compartments may be resected in continuity with the mesonephric draining system, i.e.

infundibulopelvic ligaments, and may be resected together with the uterus entirely as shown in Fig. 15.16 for the right and Fig. 15.17 for the left side. The entire PMMR specimen with adjacent pelvic and para-aortic lymph compartments is shown in Fig. 15.18.

Although it is not mandatory to remove the whole organ and lymph compartments in physical continuity as shown, it should always be done functionally.

Nota Bene

The complete procedure of lymphadenectomy and PMMR can be studied in detail in several educational videos [4–9]; the preparation of para-aortic utero-ovarian “sentinel nodes” and ICG-guided left infrarenal para-aortic lymphadenectomy is demonstrated in [10].

First Results of PMMR and Therapeutic Pelvic and Para-aortic LNE in Intermediate and High-Risk Endometrial Cancer

Assuming that compartmental surgery exerts its effect similar to cervical cancer with respect to locoregional control by removing the soil for locoregional recurrence, the PMMR and therapeutic LNE should reduce the incidence of locoregional recurrence. In a first series we could show that locoregional recurrence was as low as 2.8%, which was expected to be at least fivefold with respect to the high number of intermediate-/high-risk tumours and the low rate of adjuvant

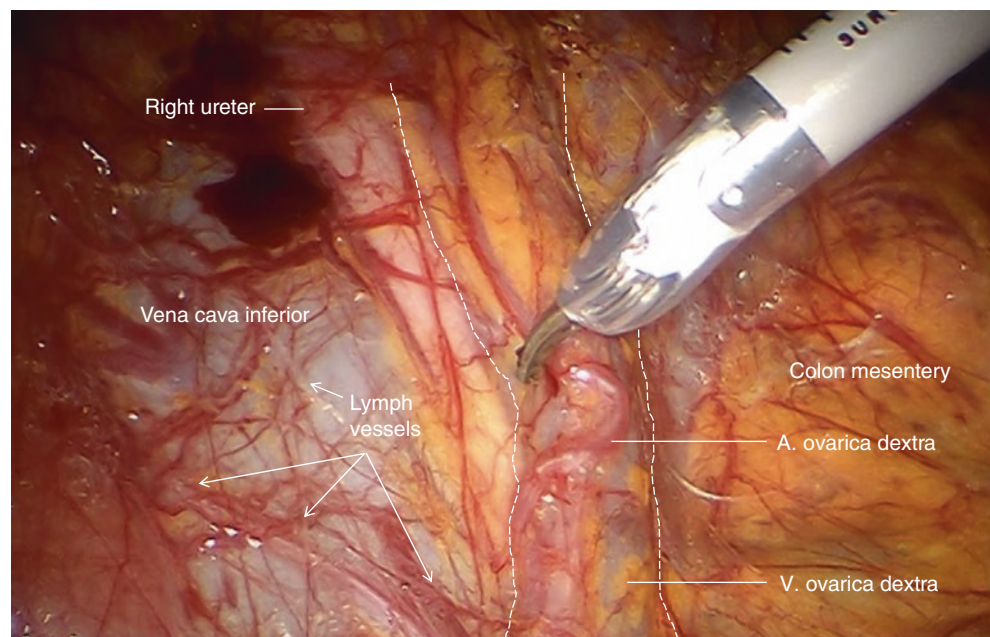


Fig. 15.10 Identification of right infundibulopelvic ligament, ureter and right colon mesentery [1]

Fig. 15.11 Separation of right infundibulopelvic ligament from right colon mesentery [1]

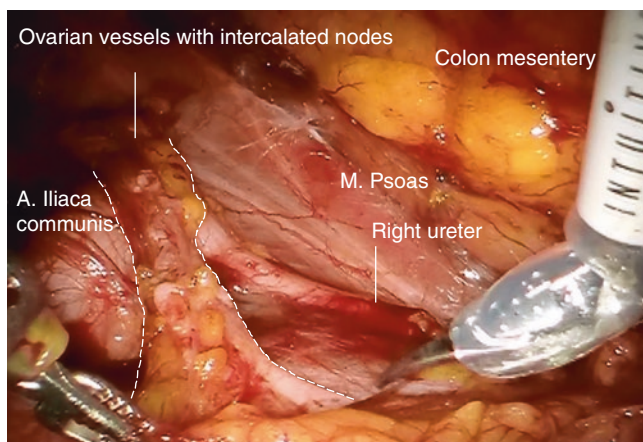
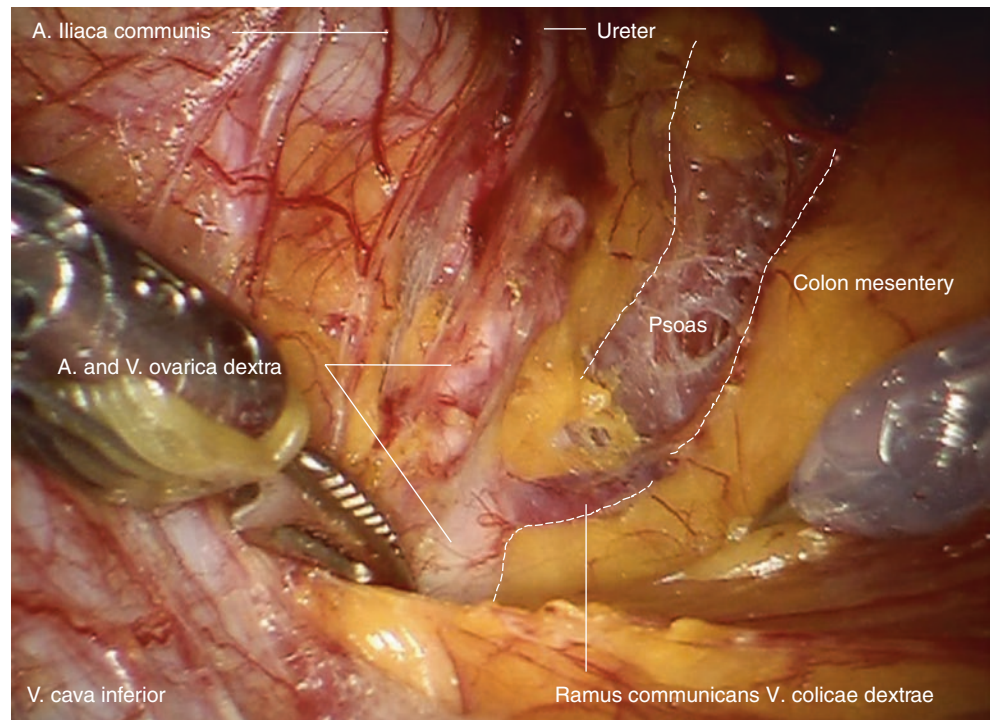


Fig. 15.12 Separation of ovarian vessel system from mesocolon, psoas muscle, ureter, and caval vein [1]

radiotherapy around 10% [11] at least encouraging further studies.

On the other hand, a lot of endometrial cancer patients experience high morbidity, and thus reduction of surgical risk could be beneficial especially by omitting para-aortic and even pelvic lymphadenectomy. Pelvic sentinel node excision has been widely investigated, and in fact, it seems reasonable to omit systematic lymphadenectomy in proven sentinel-negative patients, since the incidence of isolated positive para-aortic nodes is calculated to be about 1–2% [12–15]. This seems not to be true for pT1b, G2-3 tumours and to a lesser degree for non-endometrioid

histology with significantly higher rates of isolated para-aortic nodes [16]. In these patients still systematic para-aortic lymphadenectomy should be performed, which may also be replaced by para-aortic sentinel lymph node excision. Whereas for pelvic sentinel node excision cervical application of ICG seems to work equally well, this is known not to be true for para-aortic sentinels, which should be marked by intracorporeal application as demonstrated in [10].

Future Perspectives: PMMR and Pelvic Targeted Compartmental Lymphadenectomy (TCL)

With respect to current literature, it seems true that in the majority of the patients diagnostic pelvic and para-aortic lymphadenectomy may be safely replaced by pelvic sentinel lymphadenectomy which may significantly reduce surgical morbidity. However, there will still be some problems to be solved:

1. There is still a need for adjuvant irradiation due to enhanced risk of locoregional recurrence in case of risk factors increasing again morbidity.
2. There are 5–10% of patients with G1 tumours [16] having positive nodes not receiving a diagnostic lymphadenectomy because of an impaired balance of benefit/risk ratio but in fact being at risk.

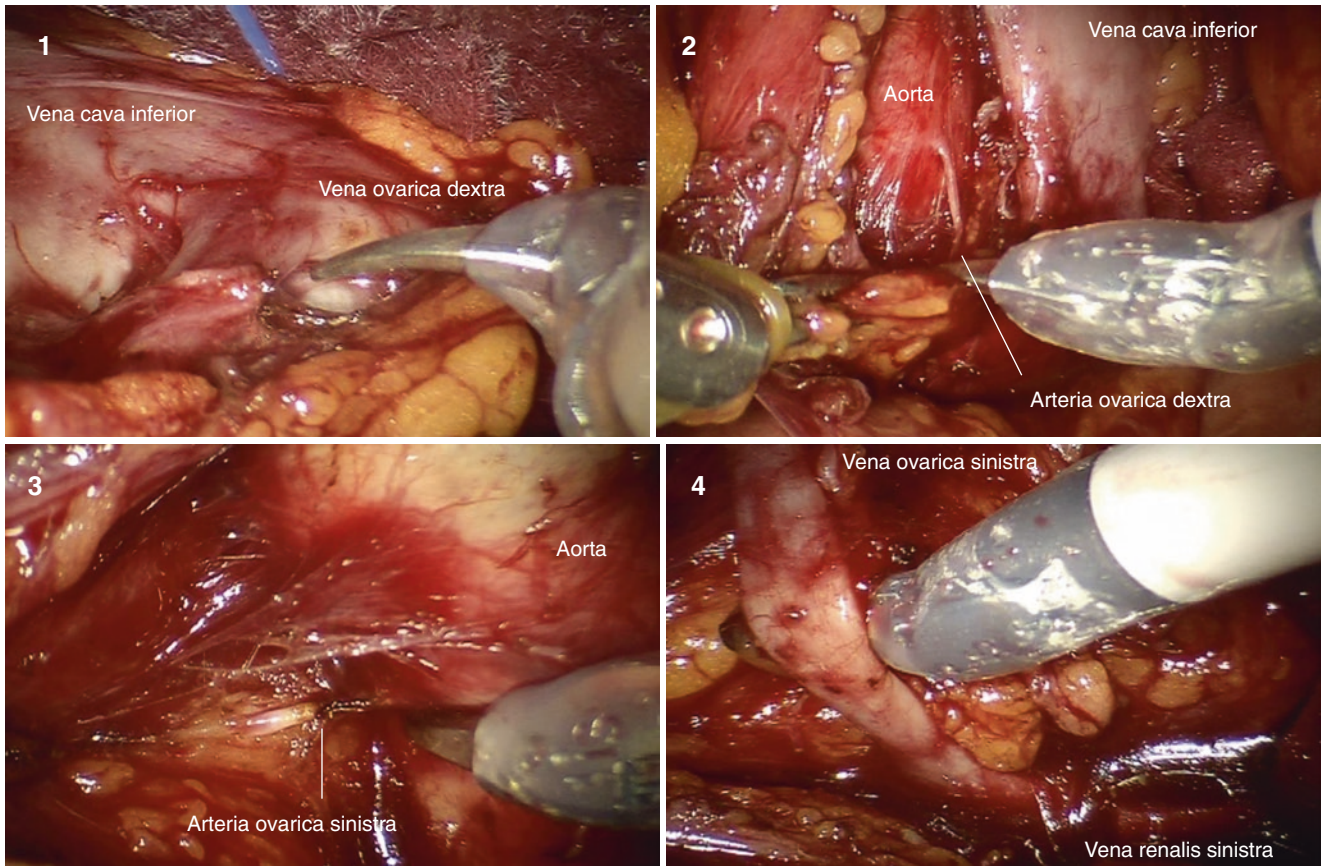


Fig. 15.13 Dissection of ovarian veins and arteries from caval and renal veins and aorta [1]

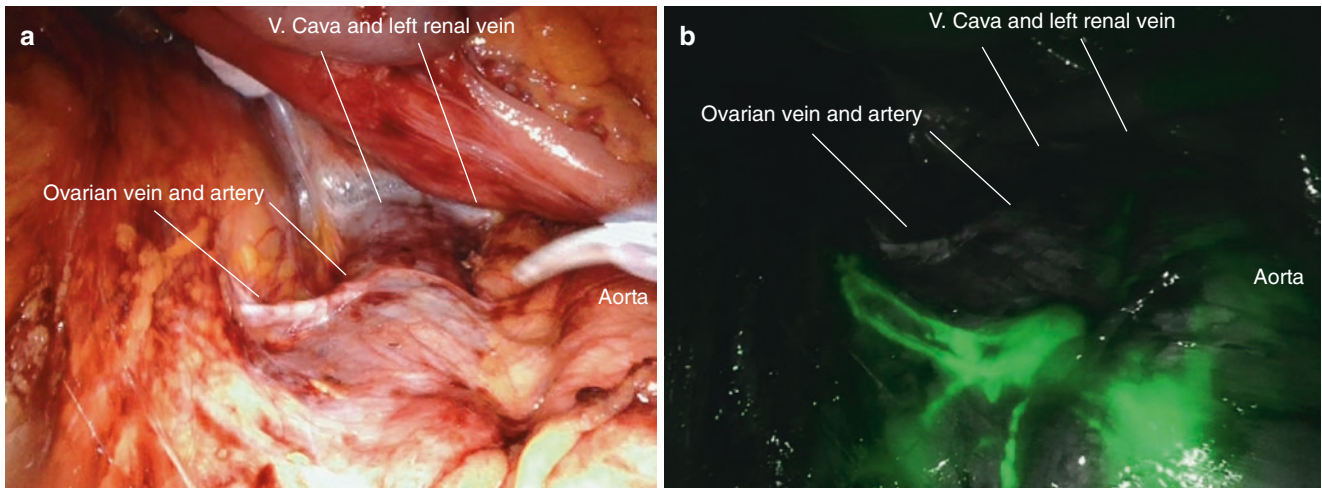


Fig. 15.14 (a) Right para-aortic node compartment with right ovarian vessels (normal light). (b) Right para-aortic node compartment with right ovarian vessels (ICG Fluorescence)

3. There are patients with up to 25% risk having isolated positive para-aortic nodes in negative pelvic sentinel, e.g. pT1b G2-3 and non-endometrioid tumours to a lesser extent

What could this procedure potentially achieve?

1. Locoregional recurrence usually occurs in the residual tissue of the Müllerian compartment including lymphatic

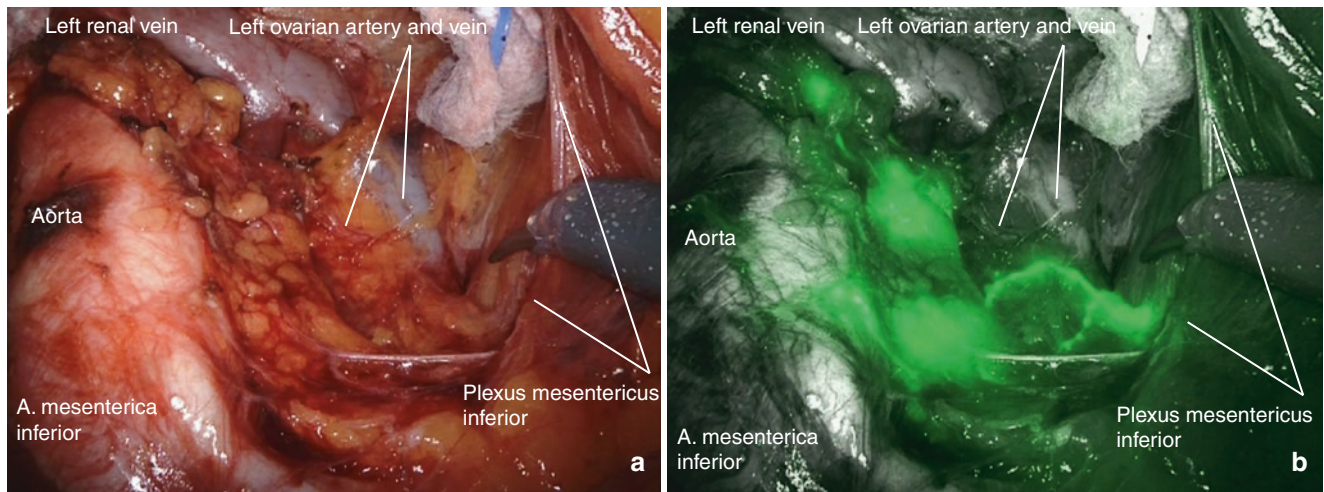
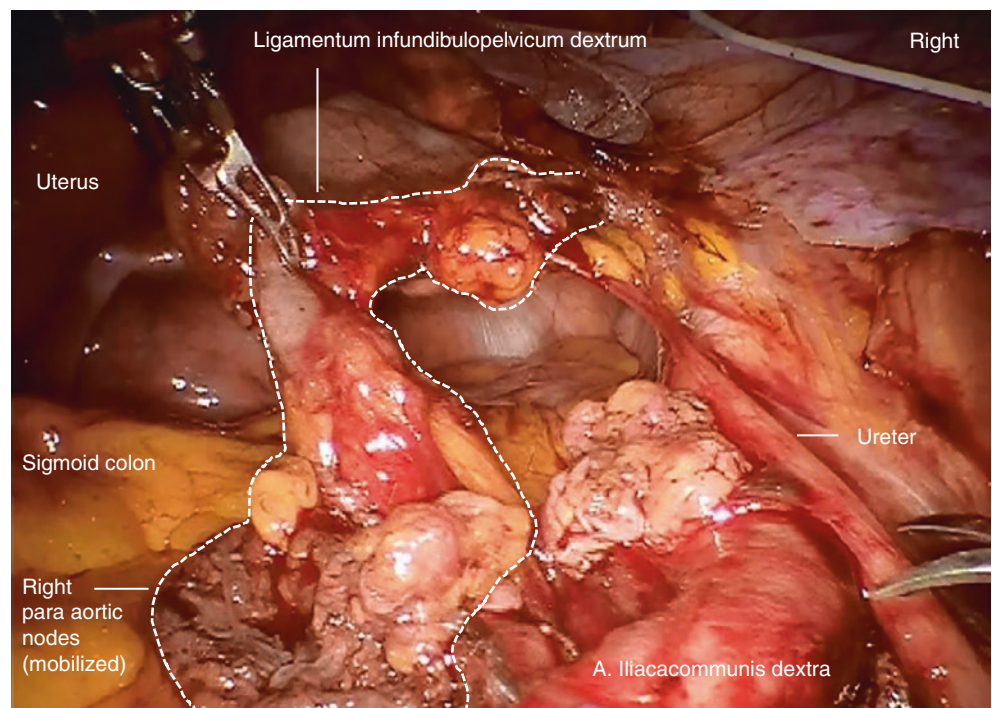


Fig. 15.15 (a) Left para-aortic node compartment with left ovarian vessels (normal light). (b) Left para-aortic node compartment with left ovarian vessels (IGC fluorescence)

Fig. 15.16 Completely mobilized right ovarian vessel system with right para-aortic nodes [1]



drainage area. Thus, complete resection of the compartment (and not hysterectomy and sentinel node only) as PMMR and targeted pelvic (sentinel) lymphadenectomy could achieve both locoregional control without radiotherapy and reduction of surgical morbidity due to omission of systematic lymphadenectomy in node-negative disease.

2. The same procedure could detect the 5–10% patients at risk with only slightly enhanced surgical morbidity which seems to be low in sentinel lymphadenectomy and PMMR only [11, 17].

3. Additional para-aortic sentinel lymphadenectomy [10] should have the potential to detect additional patients at risk with isolated para-aortic metastases without morbidity of systematic lymphadenectomy for all patients.

Thus there could be a new strategy in surgery of endometrial cancer as proposed in [18].

1. PMMR and pelvic TCL +/- para-aortic sentinel node excision in all patients and completion of node dissection when positive nodes are present alternatively

Fig. 15.17 Mobilized left ovarian vessel system entering the “sigmoid tunnel” [1]

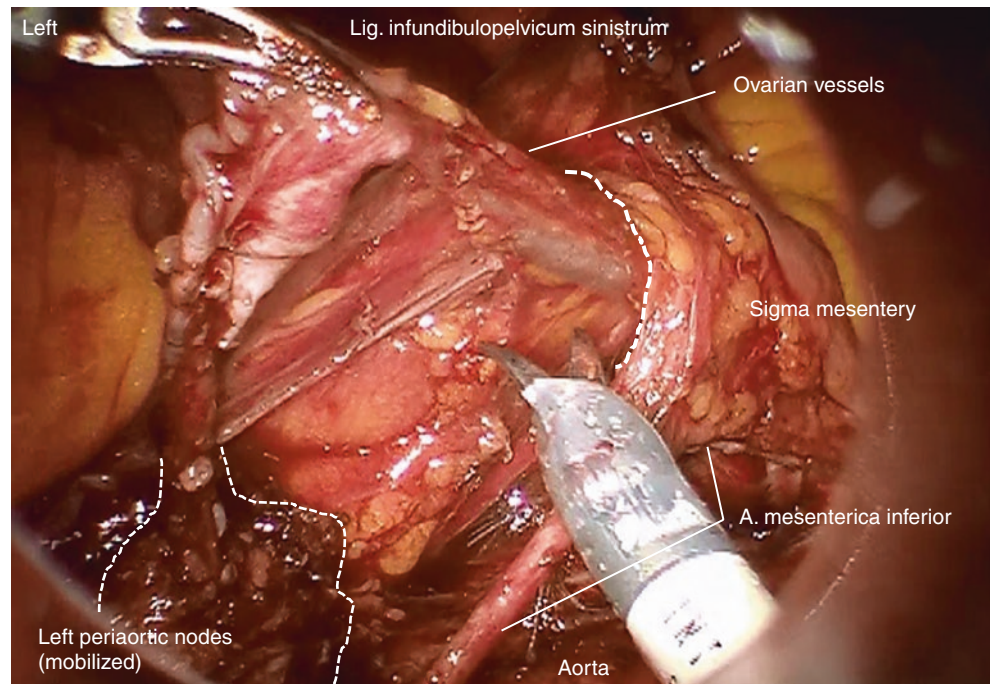
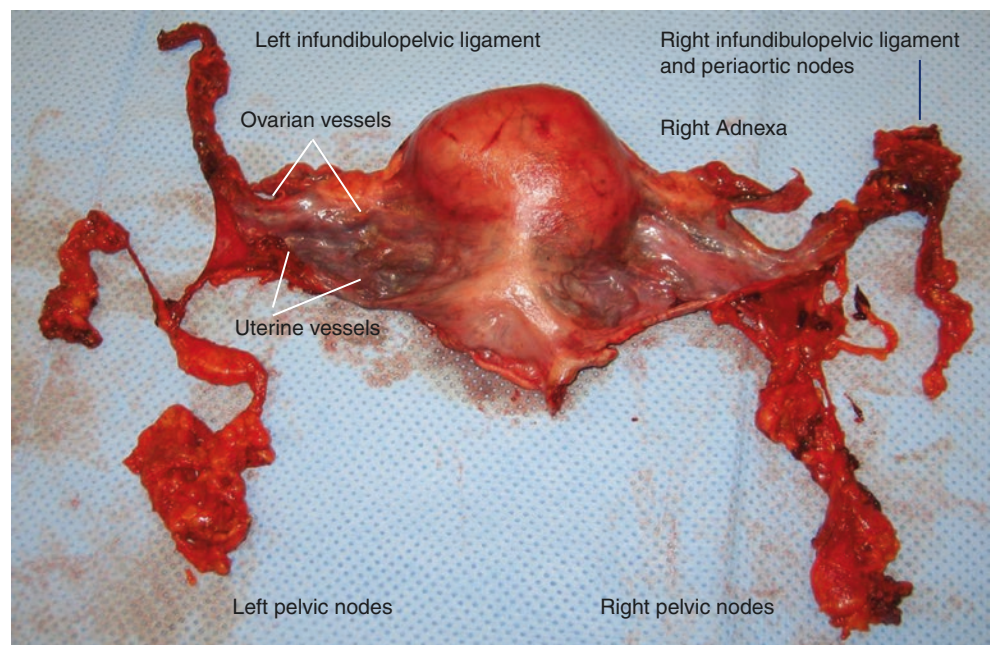


Fig. 15.18 Typical entire specimen following PMMR in endometrial cancer [1]



2. Hysterectomy and salpingo-oophorectomy only in apparently low-risk patients, if patients accept 5–10% of positive nodes not detected and eventually adjuvant radiotherapy
3. Complete lymphadenectomy pelvic and para-aortic in pT1b G2-3 tumours or non-endometrioid histology in apparently intermediate-/high-risk patients if they do not accept false-negative para-aortic sentinel nodes
4. Radio-chemotherapy instead of extended surgery in intermediate-/high-risk disease if further therapy is indicated

A prospective study is planned to evaluate the PMMR/TCL approach as a cohort study comparing with guideline-based best practice named “European collaborative multicenter study: Modular treatment with PMMR and targeted compartmental pelvic lymphadenectomy followed by therapeutic pelvic and paraaortic lymphadenectomy in node positive disease for locoregional control in endometrial cancer FIGO stages I-III”.

With this study, we hope to be able to add further evidence for the effect of limited compartmental surgery on the

locoregional outcome of uterine cancer; concomitantly surgical and radio-chemotherapy-induced morbidity should decrease not injuring patients' tumour-specific life expectancy.

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