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(Laterally) Extended Endopelvic Resection: Surgical treatment of locally advanced and recurrent cancer of the uterine cervix and vagina based on ontogenetic anatomy

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HIGHLIGHTS

► Ontogenetic anatomy of the female pelvis provides the basis for (Laterally) Extended Endopelvic Resection ((L)EER).
► (L)EER achieves excellent local tumor control in patients with advanced and recurrent cervicovaginal cancer.

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ABSTRACT

Objective. Pelvic exenteration is mainly applied as a salvage operation for a subset of patients with persistent and recurrent cervicovaginal cancer. The procedure can also cure locally advanced primary disease not suitable for radiotherapy. However, high operative abortion and intralesional tumor resection rates significantly limit its clinical benefit. To improve locoregional tumor control we have proposed to establish cancer surgery on ontogenetic anatomy and, consequently, we have developed the (Laterally) Extended Endopelvic Resection ((L)EER).

Methods. (L)EER is clinically and histopathologically evaluated with a monocentric prospective observational study. Patients with advanced and recurrent cervicovaginal cancer are treatment candidates if distant metastases and tumor fixation at the region of the sciatic foramen can be excluded.

Results. 91 patients with locally advanced primary (n = 30) and recurrent or persistent (n = 61) carcinoma of the cervix and vagina were treated with (L)EER. 74% of the tumors were fixed to the pelvic wall. No (L)EER treatment was aborted, R0 resection was histopathologically confirmed in all cases. (L)EER definitively controlled the locoregional cancer in 92% (95% CI: 85–99) of the patients. Five year overall survival probability was 61% (95% CI: 49–72).

Conclusions. The results of (L)EER treatment confirm the concept of cancer surgery based on ontogenetic anatomy. In patients with locally advanced and recurrent cervicovaginal cancer (L)EER achieves locoregional tumor control both with central disease and with tumors fixed to the pelvic side wall except at the region of the sciatic foramen.

Introduction

For selected patients with persistence or pelvic recurrence of cervicovaginal cancer, particularly in an irradiated pelvis and those with locally advanced primary cancer not suitable for radiation pelvic exenteration is a treatment option with curative potential. The surgical principles of pelvic exenteration introduced more than 60 years ago have remained essentially unchanged [1]. This “ultraradical” operation aims at excising the tumor with microscopically free margins by resection of the female genital tract en bloc with adjacent pelvic organs such as the distal urinary tract (urethra, bladder, ureters) and/or the anorectum. Several types of pelvic exenteration have been defined to tailor the multivisceral surgery for the individual tumor situation [2]. Significant improvements have been achieved in the reconstruction of the pelvic organ functions [3]. However, in spite of the progress in pelvic imaging exenteration remains to be a surgical *attempt of tumor removal* leading to abortion of the operation and/or to intralesional resection in up to 50% of the cases [4,5]. These failures spoil patients' hopes and waste considerable resources.

We have set up the compartment theory of locoregional spread of malignant tumors and provided several lines of evidence that a new principle of surgical radicality, namely the resection of developmental compartments, is superior to the conventional treatment concepts and techniques [6]. The translation of these insights into the surgical therapy of locally advanced and recurrent cancer of the lower female

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genital tract resulted in the development of procedures termed (*Laterally*) *Extended Endopelvic Resection* (*L*)*EER* [7–9]. These procedures achieve R0 resection and locoregional tumor control not only in patients which are regarded as suitable candidates for conventional pelvic exenteration but also in patients with pelvic side wall disease currently excluded from surgical treatment either pre- or intraoperatively. With this report we present the outcome of a 13-year prospective observational study of the treatment of locally advanced and recurrent cervicovaginal cancer.

Methods

Ontogenetic anatomy of the female pelvis

A current synopsis of the ontogenetic anatomy of the female pelvis with special consideration of the (Laterally) Extended Endopelvic Resection is given in the online supplement, including Table S1.

(Laterally) Extended Endopelvic Resection

A brief description of the surgical principles and the nomenclature of the procedures is given in the online supplement. The step-by-step surgical techniques have been published earlier [10].

Patient evaluation and selection

All patients with cancer of the uterine cervix and/or the vagina admitted to our center for treatment received a high-resolution MRI series of their pelves which was on display during the gynecologic examination under anesthesia. During that investigation also site-directed core biopsies were taken. Cystoscopy and rectoscopy were performed if physical and MRI findings indicated a risk of tumor infiltration of these hollow organs. Patients with primary disease in stages II(B), III(A,B) and IVA as well as patients with persistent and recurrent cancer were staged for distant metastases until 2009 with CT and isotope bone scan, thereafter with PET-CT.

Patients with carcinomas of the uterine cervix and vagina stages I(B) to II(B) without evidence of bladder involvement were offered treatment by Total Mesometrial Resection (TMMR) [11,12]. Patients with stage II(B), with evidence of bladder involvement, with stage III(A, B) and IVA primary disease and those with tumor recurrence following surgical treatment alone were regarded as candidates for chemoradiation unless the radiotherapist voted for or the patient requested surgical treatment. Patients with a tumor persistence and recurrence after radiotherapy and patients with tumor-induced fistulae between the genital and urinary tracts and/or anorectum were candidates for (L)EER if the following conditions were met preoperatively:

- exclusion of distant metastases,
- no tumor fixation at the site of the sciatic foramen,
- patient's physical and mental fitness adequate for the megaoperation.

For recurrent tumors in addition:

- verification of local disease, i.e. intersection of the tumor mass with the domain of the Müllerian compartment,
- clinical exclusion of multifocal disease.

If the postradiation recurrent tumor was characterized as regional disease, macroscopical extracapsular spread was assessed. Surgical treatment of postradiation regional recurrence without extracapsular spread consisted of metastasectomy with supplementing therapeutic lymph node dissection. Both TMMR and metastasectomy are not considered in this report.

Treatment

Patients underwent surgical treatment with (L)EER for *local* tumor control.

For *regional* tumor control (L)EER was supplemented by therapeutic lymph node dissection based on ontogenetic anatomy as described for early cervical carcinoma [13].

Vital organ functions lost by the resective procedure were substituted adhering to the following principles:

- choosing the optimal procedure from several reconstructive options considering the patient's preference,
- setting surgical safety over patient comfort in case of doubt,
- strictly avoiding irradiated tissue for reconstruction.

All reconstructive urinary procedures were performed by colleagues from the Department of Urology, University of Leipzig. Preoperatively, the patients had been advised by the urologists regarding the individual options for continent and incontinent urinary diversion.

Complications during the in-house postoperative period were documented as early events, those occurring after discharge as late treatment morbidity. Complications were classified and graded according to the Franco-Italian Glossary [14].

Neither neoadjuvant nor adjuvant radiotherapy was administered supplementing (L)EER. From 2005 onwards patients with ≥ 2 lymph node metastases were treated with adjuvant chemotherapy (cisplatin 75 mg/m^2, six cycles every 3 weeks).

Histopathology

Topographically defined lymphatic tissue, distal resection margins of the ureters and macroscopically assured closest tumor resection margins in the (L)EER specimens were examined intraoperatively by frozen section. For the definitive histopathological report the tumor's location and extension within the en bloc specimen were assessed. Tumor size was recorded in 3 dimensions. Resection margins were specified and measured. Tumor involvement was documented regarding the following anatomical structures: uterus, vagina, vulva, urogenital mesentery; bladder, ureter, urethra; pubo-, iliococcygeus and coccygeus muscle; and internal iliac vessels. The numbers of overall examined and metastatic nodes were reported. pTNM-staging was documented using the prefix “r” for recurrent tumor and “y” after multimodal non-surgical therapy.

Follow up and statistical analysis

Patients were prospectively followed up to 10 years. After-care visits were scheduled every 3 months during the first 2 years and every 6 months up to 5 years postoperatively. Thereafter, patients were asked for a yearly visit. At the follow-up visits patients were interviewed and physically examined. In case of a suspicious finding or indicative symptoms radiologic investigation with pelvic MRI and CT thorax and abdomen, bone scan or PET-CT was done. Locoregional tumor progression had to be proven histopathologically. Disease-free, pelvic disease-free and overall survival probabilities were calculated with the Kaplan–Meier method using SPSS Statistics version 20. For the analysis of *locoregional tumor control* pelvic only recurrences without synchronous distant metastases were considered as events. Kaplan–Meier curves were compared with the log rank test. Cox regression analysis was applied to identify independent prognostic features.

Results

From 3/1999 to 3/2012 91 consecutive patients with locally advanced primary and with recurrent or persistent carcinomas of the

uterine cervix or of the vagina have been treated with (L)EER for local tumor control. Patient, pretreatment and tumor characteristics are given in Table 1. During the study period 5 patients were excluded from the treatment with curative intent due to the intraoperative diagnosis of distant metastases. Four of these patients had peritoneal carcinomatosis, and in one patient liver metastases were found which had not been detected by preoperative imaging.

The majority of tumors (74%) were local disease fixed to the pelvic side wall with or without hydronephrosis, 26% was central disease. 92% of the recurrent tumors had a radiotherapeutic primary treatment component. In 53% of the patients the original pelvic anatomy had been distorted by previous surgery. In 43 patients with recurrent disease the primary tumor had been treated with radical hysterectomy (n = 26) or with simple hysterectomy (n = 17). Three patients with primary vaginal carcinoma had a history of radical hysterectomy for cervical cancer; another two had undergone simple hysterectomy for CIN and myoma. Table 2 demonstrates the types of (L)EER performed for local tumor control and the reconstructive procedures to restore or substitute the pelvic organ functions. Since the surgical intention was aimed at regional tumor control as well, therapeutic pelvic lymph node dissection was performed in all patients who had not undergone surgical and/or radiotherapeutic therapy of the lymph node regions before and in those whose previous treatment for lymph node metastases was incomplete as realized intraoperatively. Two of the three patients treated for cervical cancer with radical hysterectomy developing vaginal carcinoma as a secondary primary cancer had a complete pelvic lymph node dissection before, and in the other one the remaining pelvic lymph nodes had to be removed. Therefore, 28 of 30 patients with primary disease received a pelvic lymph node dissection. In 24 of the 61 patients with recurrent/persistent disease pelvic lymph node dissection was carried out. 23 patients with primary cancer and 49 patients with recurrent/persistent cancer had a paraaortic lymph node dissection. The median duration of the complete procedure was 11.5 h (8–19.5), and the median number of blood transfusions was 4 units (0–16). Postoperatively, patients were kept in the intensive care unit for a median time of 2 days (1–4). The median overall hospitalization period was 23 days (18–42).

Tumor progression following (L)EER treatment occurred only in the pelvis in 6 patients, in the pelvis and at distant sites simultaneously in 12 patients and only at distant sites in 16 patients. The findings of the histopathological investigations are summarized in Table 3. R0 resection was confirmed in all cases. All tumors infiltrated the Müllerian compartment. Of the non-Müllerian compartments the bladder was the favored site of tumor infiltration, and rectal infiltration was less frequent. Rectal involvement was detected more often with recurrent disease than with primary cancer, particularly after previous pelvic surgery. Although infiltration of the urogenital mesentery was frequent (97%) tumor involvement of the parietal pelvis was rare and occurred only in one patient with recurrent cancer. 48% of the patients with primary carcinoma and 10% of the patients with recurrent/persistent carcinoma had pelvic lymph node metastases. Paraaortic metastases

Table 1
Patient, tumor and pretreatment characteristics.

	Primary carcinoma n = 30	Recurrent/persistent carcinoma n = 61
Age of patient, median (range)	53 years (27–78)	51 years (28–76)
Tumor entity		
Cervical carcinoma	21	54
Vaginal carcinoma	9	7
Histologic type		
Squamous cell carcinoma	23	46
Adeno(squamous) carcinoma	7	14
Neuroendocrine carcinoma	1	
Clinical tumor size, median (range)	6 cm (3–15)	4 cm (1–8)
Tumor location		
Central	12	12
Pelvic wall	18	49
FIGO stages		
II (B)	9	n.a.
III (B)	11	n.a.
IV A	10	n.a.
Previous pelvic treatment		
(Chemo)radiation	1+	18
Surgery and radiation	3+	38
Surgery	3+	5

+Patients were treated for previous benign or malignant pelvic disease.

Table 2
Types of (Laterally) Extended Endopelvic Resection and reconstructive procedures.

(L)EER type (n = 91)	25	Abdominal, anterior
	28	Abdominal, total
	15	Abdominoperineal, anterior
	1	Abdominoperineal, posterior
	21	Abdominoperineal, total
	1	Perineal, posterior
LEER type (n = 83)	66	Caudal
	2	Rostral
	15	Caudal and rostral
Reconstruction of urethrovesical function	44	Colon conduit
	19	Ileum conduit
	19	Colon pouch
	5	Ileum neobladder
Reconstruction of anorectal function	46	Colostomy
	4	Colorectal anastomoses
	2	Rectal J pouch
Reconstruction of vaginal function	6	Sigma neovagina
	4	Pudendal thigh neovagina
	3	Gluteal thigh neovagina
	1	Rectus abdominis neovagina
Pelvic lymph node dissection	52	
Paraaortic lymph node dissection	72	

Table 3
Histopathological results.

Feature	Primary carcinoma n = 30	Recurrent/persistent carcinoma n = 61
Tumor size, median (range)	5.0 cm (2.5–15.8)	3.3 cm (0.5–8.7)
Tumor stage		
(y,r)pT1b	2	1
2(a,b)	14	19
3(a,b)	5	29
4	9	12
# of tissues resected/infiltrated[1]		
uterus	24/20	17/12
vagina	29/23	62/49
vulva	4/1	11/4
urogenital mesentery[2]	29/28	62/60
bladder, ureter	29/22	60/35
urethra	24/4	55/10
rectum	6/3	48/20
anus	5/0	18/1
pubococcygeus muscle	23/0	39/2
iliococcygeus muscle	21/0	56/1
coccygeus muscle	2/0	12/0
internal iliac vessels	5/0	12/0
Nodal stage		
pN1	14	6
pN0	9	28
pM1(LYM)	3	4
pM0	20	47

[1] For the indicated anatomical structure the total number of (L)EER specimens of which it was a part and its number infiltrated by the local tumor is given.
[2] Mesometrium and mesocolpium included.

Table 4
Moderate and severe complications.

Complication	Early			Late		
	G2	G3	G4	G2	G3	G4
Cardiopulmonary[1]	2					
Cutaneous[2]	8			3		
Gastrointestinal[3]	6	3		4		
Neurologic[4]	2					
Urinary[5]	6	1	1	1	1	
Vascular[6]	8			3		

[1] Pneumonia, pulmonary edema.
[2] Laparotomy dehiscence, partial flap necrosis, donor site dehiscence, perineal hernia.
[3] Bowel obstruction, anastomosis insufficiency, bowel fistula, generalized peritonitis, rectum stump dehiscence, pelvic abscess, parastomal hernia.
[4] Temporary paresis of femoral and sciatic nerve.
[5] Anastomotic insufficiency, ischemic necrosis of conduit, pouch neobladder; stenosis of urostoma, pouch incontinence, hydronephrosis.
[6] Postoperative bleeding, deep venous thrombosis, pulmonary embolia, infected lymphcyst, leg edema.

were present in patients with primary and recurrent disease in 7% and 6%.

45 patients had no or only grade 1 complications. Complications of grades > 1 are specified in Table 4. The patient who developed fatal sepsis had been treated in the early study period (1999). Most complications were associated with reconstructive procedures. One patient was lost for follow up, two patients died due to intercurrent disease, 4 patients died without clinical signs of tumor but were not autopsied to rule out a disease-related cause of death.

Representative Kaplan–Meier curves for survival are shown in Fig. 1. At a median observation time of 34 months (1–158) five year overall and recurrence-free survival probabilities were 61% (95% CI: 49–72) and 57% (95% CI: 45–69) for the whole group. Survival of patients with advanced primary disease was not significantly different from those with recurrent disease (66% (95% CI: 46–86) and 58% (95% CI: 44–72). Survival was also similar in patients with central disease as compared to those with tumors fixed to the pelvic side wall. Likewise, the histologic type of the carcinoma (squamous cell vs. adeno) had no impact on survival. Both tumor size and nodal state influenced survival. Overall survival at five years was 63% (95% CI: 47–79)) for patients with tumors ≤ 5 cm and 43% (95% CI: 14–71) for patients with tumors measuring > 5 cm (log rank p = 0.029).

Five year overall survival probabilities were 67% (95% CI: 54–79) for pN0 and 31% (95% CI: 0–61) for pN1 (log rank p = 0.057). Cox regression analysis identified nodal status as the only significant independent prognostic factor (p = 0.038; Table S2 online supplement). (L)EER definitively controlled the locoregional disease in 92% (95% CI: 85–99) of the patients.

Discussion

Thirteen years of experience with surgical treatment of locally advanced and recurrent carcinoma of the cervix and vagina by (Laterally) Extended Endopelvic Resection confirm the compartment theory of locoregional tumor spread and substantiate the principle of cancer surgery based on ontogenetic anatomy. According to the compartment theory of local tumor spread a malignant neoplasm is initially confined to its permissive ontogenetic compartment [6]. Transgression into adjacent compartments from different embryonic precursor tissues necessitates phenotype changes which are generally associated with advanced malignant progression. Transgression follows a developmental hierarchy. The probability of a tumor to infiltrate an ontogenetically different compartment by local permeation depends on the degree of developmental kinship between the two compartments which can be estimated from the ontogenetic pathway. The adult Müllerian compartment verges on the bladder, ureters, urogenital mesentery, rectum and mesorectum. Due to the concave shape of the subperitoneal Müllerian compartment both in the axial and sagittal planes the area bordering the (meso)rectum is larger than the

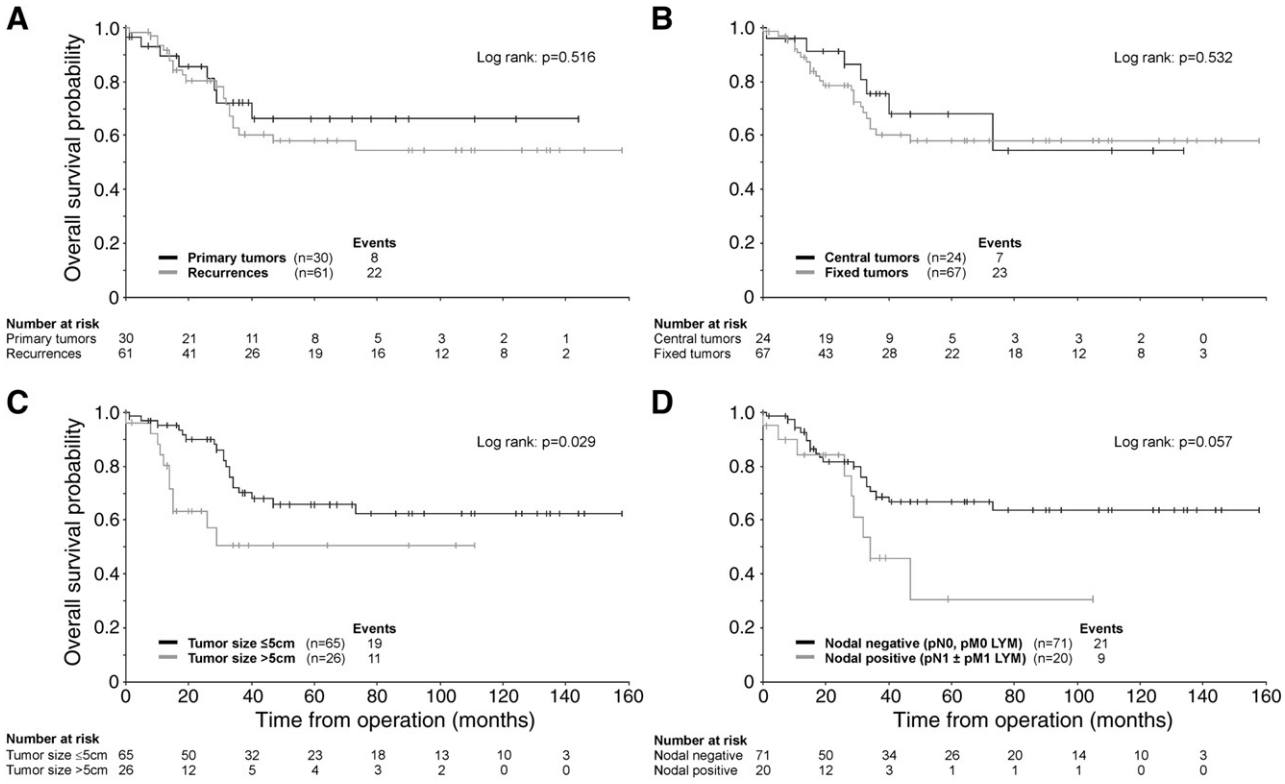

Fig. 1. Kaplan–Meier plots of overall survival for patients with cervicovaginal carcinoma treated with (L)EER. A) Patients with locally advanced primary tumors vs. patients with recurrent tumors. B) Patients with central disease vs. patients with pelvic side wall disease. C) Patients with tumors ≤ 5 cm vs. patients with tumors > 5 cm. D) Patients with nodal negative (pN0, pM0 LYM) tumors vs. patients with nodal positive (pN1 ± pM1 LYM) tumors.

contact area to the bladder. Yet, tumor transgression into the (meso) rectum was less frequent than tumor transgression into the bladder (rectum: 17%, bladder: 67%) in the anatomically naive pelvis. Ontogenetically, the Müllerian compartment and the bladder trigone are derived from the same metacompartment and share the mesonephric ducts and the primitive urogenital sinus as tissues involved in their development (see online supplement). The (meso)rectum differentiates from a different metacompartment. The structure shared in the development with the Müllerian compartment is the cloaca which is ontogenetically more distant than the urogenital sinus. The Müllerian compartment is thus ontogenetically more akin to the bladder than to the rectum which is concordant with the pattern of tumor transgression.

Pelvic trauma and surgery destroy and alter compartmental borders by the loss of original tissue and by scarring which is thought to weaken their tumor suppressive action. Accordingly, rectum infiltration was comparatively more frequent in the surgically pretreated pelvis (33%) but still less than bladder infiltration (57%). The Müllerian compartment and the urogenital mesentery belong to the same metacompartment as they are derived from the urogenital ridge, whereas the parietal pelvis represents a different metacompartment. Consistently, local tumor propagation within the urogenital mesentery was histopathologically manifested in almost all cases of advanced cervicovaginal cancer, whereas infiltration of pelvic wall structures (striated muscles, fascia) was detected in only one patient. The fact that locally advanced and recurrent tumors firmly fixed to the pelvic wall very rarely invaded parietal structures was among our first observations leading to the development of LEER [7]. The fixation may be explained by an inflammatory reaction accompanying the tumor front and producing the fibrotic adherence of the tumor to adjacent compartments which are not infiltrated yet. As the compartment bordering zone of the caudal subperitoneal urogenital mesentery is attached to the pelvic floor, the inclusion of the underlying pubo-, ilio- and coccygeus muscles as part of the LEER procedure guarantees the complete extirpation of the tumor fixed to the pelvic side wall at that site (Fig. 2). However, the cranial bordering area of the urogenital mesentery towards the pelvic wall is spatially complex involving the internal iliac vessel system and the sacral plexus. By including the internal iliac artery and vein in the LEER specimen wide tumor excision at the cranial subperitoneal urogenital mesentery is possible in selected cases. When the tumor reaches the plane of the internal iliac vessels at the sciatic foramen, wide excision is no longer possible. Consequently, this feature – clinically proven by sciatic pain and discerned by pelvic MRI irrespective of patient's symptoms – remains a contraindication for surgical treatment.

(L)EER results confirm the relevance of pelvic lymph node metastases as prognostic factor. Both in locally advanced and recurrent cervicovaginal cancer the presence of pelvic lymph node metastases with or without paraaortic lymph node metastases approximately halved the curative chance in accordance with previous reports of pelvic exenteration [4]. However, a five year overall survival of patients with pelvic and/or paraaortic lymph node metastases was still 30%, the presence of these metastases should not be considered a

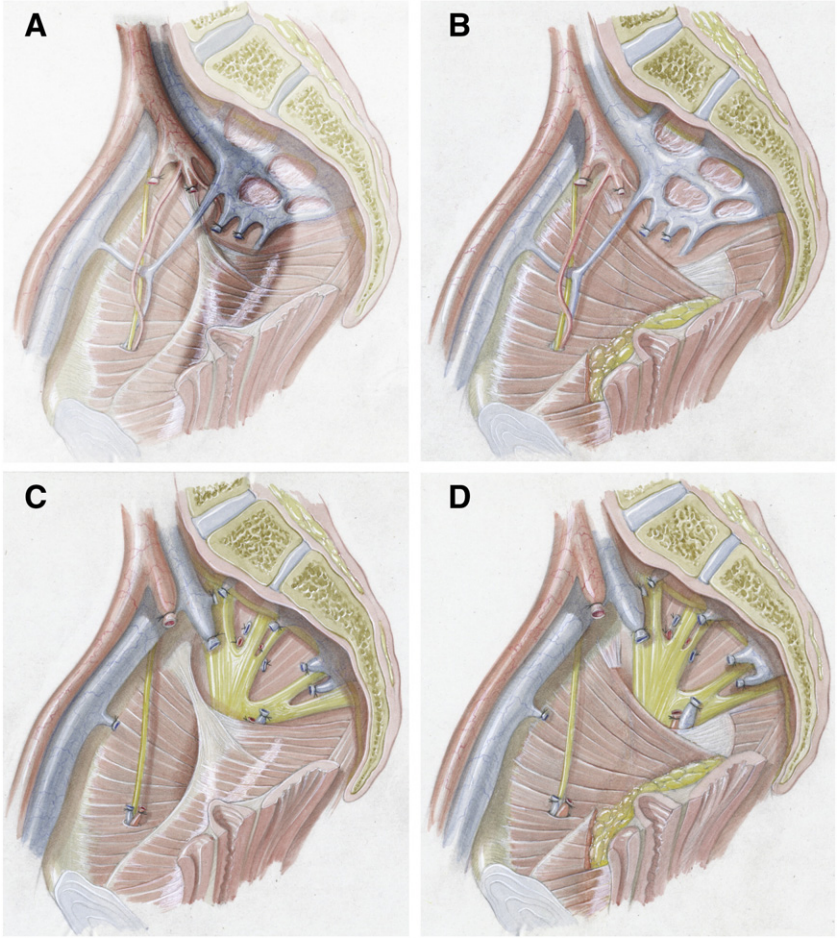

Fig. 2. Surgical anatomy of the right pelvic side wall for (L)EER. A) Contact zone (dark field) of the urogenital mesentery. B) Dissection of the caudal part of the distal urogenital mesentery including the pubo-, ilio- and coccygeus muscles into the LEER specimen. C) Dissection of the rostral part of the urogenital mesentery including the internal iliac vessels into the LEER specimen. D) Dissection of the complete urogenital mesentery including the pubo-, ilio- and coccygeus muscles and the internal iliac vessels into the LEER specimen.

contraindication for extended surgical treatment. Certainly, the detection of multiple paraaortic lymph node metastases indicates an ominous prognosis. None of the patients in our series with 3 and more paraaortic lymph node metastases survived her disease.

The application of the concept of compartment resection for the surgical treatment of locally advanced and recurrent cervicovaginal cancer demanded the en bloc extirpation of the Müllerian compartment, the urogenital mesentery, the bladder and distal ureters in all cases except in one patient with distal vaginal cancer. Inclusion of the (meso)rectum was considered mandatory in 59%, the urogenital sinus compartment in 42%, and parts of the vulva in 17%. (L)EER thus achieved a 100% R0 resection rate without abortion of any procedure during the resective phase, which was never reported with traditional exenteration. R0 resection has been proven to be the most important factor for pelvic tumor control and cure [4,5,15]. Locoregional tumor control and overall survival were 92% and 61% in our patient cohort including 79 tumors fixed to the pelvic side wall which are usually not considered for exenterative treatment at all. Because patients with advanced and recurrent cervicovaginal cancer treated with extensive surgery are usually selected in an uncontrolled manner, a comparison of the reported survival data is not meaningful. Nevertheless, our R0 resection and locoregional tumor control rates prove the principle of cancer surgery based on ontogenetic anatomy for compartment-transgressing tumor states and at the same time question the traditional concept and practice of pelvic exenteration.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2012.07.120.

Conflicts of interest statement
The authors declare to have no conflicts of interest.

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References

[1] Brunschwig A. Complete excision of pelvic viscera for advanced carcinoma. Cancer 1948;1:177-83.
[2] Magrina JF. Types of pelvic exenterations: a reappraisal. Gynecol Oncol 1990;37:363-6.
[3] Salorn EM, Mendez LE, Schey D, et al. Continent ileocolonic urinary reservoir (Miami pouch): the University of Miami experience over 15 years. Am J Obstet Gynecol 2004;190:994–1003.
[4] Höckel M, Dornhöfer N. Pelvic exenteration for gynaecologic tumours: achievements and unanswered questions. Lancet Oncol 2006;7:837-47.
[5] Schmidt A-M, Imesch P, Fink D, Egger H. Indications and long-term clinical outcomes in 282 patients with pelvic exenteration for advanced or recurrent cervical cancer. Gynecol Oncol 2012;125:604-9.
[6] Höckel M. Cancer permeates locally within ontogenetic compartments: clinical evidence and implications for cancer surgery. Future Oncol 2012;8:29-36.
[7] Höckel M. Laterally extended endopelvic resection: surgical treatment of infrailiac pelvic wall recurrences of gynecologic malignancies. Am J Obstet Gynecol 1999;180:306-12.
[8] Höckel M. Laterally extended endopelvic resection: novel surgical treatment of locally recurrent cervical carcinoma involving the pelvic side wall. Gynecol Oncol 2003;91:369-77.
[9] Höckel M. Laterally extended endopelvic resection (LEER) — principles and practice. Gynecol Oncol 2008;111:S13-7.
[10] Höckel M. Laterally extended endopelvic resection. In: Smith JR, DelPriore G, Coleman PL, Monaghan JM, editors. An atlas of gynecologic oncology investigation and surgery. 3rd ed. London: Informa Medical Books; 2009. p. 120-6.
[11] Höckel M, Horn L-C, Fritsch H. Association between the mesenchymal compartment of uterovaginal organogenesis and local tumour spread in stage IB–IIB cervical carcinoma: a prospective study. Lancet Oncol 2005;6:751-6.
[12] Höckel M, Horn L-C, Manthey N, et al. Resection of the embryologically defined uterovaginal (Müllerian) compartment and pelvic control in patients with cervical cancer: a prospective analysis. Lancet Oncol 2009;10:683-92.
[13] Höckel M, Horn L-C, Tetsch E, Einenkel J. Pattern analysis of regional spread and therapeutic lymph node dissection in cervical cancer based on ontogenetic anatomy. Gynecol Oncol 2012;125:168-74.
[14] Chassagne D, Sismondi P, Horiot JC, Sinistero G, Bey P, Zola P. A glossary for reporting complications of treatment in gynecological cancers. Radiother Oncol 1993;26:195-202.
[15] Andikyan V, Khoury-Collado F, Sonoda Y, et al. Extended pelvic resections for recurrent or persistent uterine and cervical malignancies: an update on out of the box surgery. Gynecol Oncol 2012;125:404-8.