

**Special radical surgical techniques in the management
of cervical carcinoma**

Doctoral (PhD) theses

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Introduction

Radical hysterectomy (RH) with pelvic lymph node dissection is the standard treatment for most early stage cervical carcinoma. For locally advanced cervical cancer (LACC), however, guidelines suggest radical chemo-radiotherapy as primary treatment based on randomized trials demonstrating overall and disease-free survival advantages for concomitant chemoradiation compared to radiotherapy alone. In a recent review, Kyrgiou and Shafi reported that “Surgery with curative intent is not possible in women with advanced stage (stage IIB–IV) of disease. The available treatment modalities that offer potential of cure are radical radiotherapy and chemo-radiation.” As for recurrent cervical cancer, most authors favor chemo-radiation in women initially treated with surgery, and for those who primarily received radiotherapy or chemo-radiation, they believe that pelvic exenteration provides the only potential for cure in central recurrences without distant spread. There is general consensus that the treatment of sidewall or advanced recurrent tumors is palliation.

Since the introduction of RH by Wertheim in 1912, several modifications have been reported worldwide resulting in a spectrum of surgical interventions under the name of RH or Wertheim procedure or Wertheim RH. To compare treatment results there was a need to classify RHs mostly based on their radicality. The first classification was reported by Piver et al. in 1974, which is called Piver-Rutledge or Piver or classical classification of RHs. They separated five classes/types of RHs as shown in table 1. Due to shortcomings of this classification, Querleu and Morrow proposed a new classification system, and recently Trimbos reported a TNM-like classification. In spite of the proposed novel classifications, the classical one by Pivar et al is still in use mostly.

Piver type V RH is defined as removal of a portion of the bladder or ureter in addition to RH (type II, III or IV). We also include RH plus bowel resection into this group. In the literature, there is a paucity of articles dealing with this type surgery. We report our experience with classical type V RH performed in curative intent as primary treatment for LACC in 45 patients. The aim of

this retrospective review was to study the feasibility and to analyze the complications of the combined approach of RH with elements of bladder/ureter or bowel surgery in LACC treated in primary setting. To the best of our knowledge, this is the first report of this kind.

Methods

Surgical techniques used

Standard radical hysterectomy (sRH)

The sRH in our institution includes resection of all external iliac, common iliac, obturator and pre-sacral, as well as the gluteal superior and ilio-lumbal nodes. At completion, the vessels are entirely free of fatty tissue all around their circumference. The obturator nerve is visualized, posterior until its retro-psoas portion, and the fatty tissue around the obturator nerve is entirely removed such that the superior branch of the sacral plexus is apparent. In removing the parametrium all the visceral branches of the internal iliac vessel are sectioned, allowing removal of the entire connective tissue between the medial surface of the parietal branches of the internal iliac vessels and the uterus. This procedure can be classified as classical type III-IV RH.

Laterally extended parametrectomy (LEP)

The essence of the LEP is dissecting the parietal branches of the internal iliac vessels They are clipped and divided at the point where they leave or enter the pelvis. Thus, the entire hypogastric system is removed, and no connective tissue is left on the pelvic side wall. The technique has been described in details elsewhere.

Elements of bladder, ureter and bowel surgery

The procedures included:

- resection of the bladder wall adjacent to the uterine cervix with primary closure;
- vesicopsoas hitch (removal of a portion of the lower ureter (below the pelvic brim) and of the vesico-ureteric junction, followed by

- mobilization and fixation of the bladder to the psoas muscle and ureteral re-implantation – uretero-neocystostomy);
- ureteroileocystostomy (an isolated and resected segment of the ileum was interposed to bridge the gap between the end of the resected ureter and the bladder to ensure tension-free anastomosis;
 - partial or total cystectomy followed by urinary diversion (anterior supralelevator pelvic exenteration, ASLPE) with
 - orthotopic bladder replacement (Budapest-pouch)
 - Bricker conduit;
 - resection of the sigmoid colon with re-anastomosis.
 - removal of a segment of the ileum

Intraoperative histology of the pelvic nodes was utilized in all cases. Additional frozen sections were down when needed.

Staging

At diagnosis, patients were staged clinically according to the revised FIGO staging system. In this study, we report the pathologic stage based on histology of the surgical specimen, using the current TNM system .

Chemotherapy

For neoadjuvant chemotherapy patients received 2 cycles of CMVB (cyclophosphamide, methotrexate, vinblastin, bleomycin), with the exception of one woman receiving MPV – mitomycin, cisplatin, vincristin - 3 cycles). Postoperatively cisplatin monotherapy was given.

Radiotherapy

Preoperative radiotherapy consisted of two applications of high-dose rate vaginal afterloading radiation (AL) without external beam irradiation (EXT).

Postoperative full dose EXT was delivered with AL (mostly two applications) in the presence of inadequate surgical margins or for patients considered to be at high risk on individual bases.

Definitions used in this report

The spread of cervical carcinoma into the vesicovaginal space, the bladder wall or to the ureter tunnel is called anterior propagation, whereas the permeation into the sacrouterine ligament, Douglas pouch or to the sigma is called posterior extension.

Early and late complications were defined as any adverse event occurring intra-operatively or within and after 30 postoperative days, respectively.

Patients and treatment

Between January 1993 and June 2005, 2540 patients with invasive cervical cancer were referred to the Gynecologic Oncology Service of the Saint Stephen Hospital Budapest. In 1195 women the primary treatment was radiotherapy or chemoradiation. All other patients (1345) underwent surgery with curative intent. Of this, 1104 were treated with RH. During this 13 year period, our treatment policy changed. Before the introduction of the LEP in 1996, some patients with LACC received neoadjuvant chemotherapy or AL prior to surgery. After 1996, no preoperative treatment was given. Forty-five patients with LACC (pathologic stage IB2-IIB (pIB2-IIB); of whom 21 had pIIB disease) underwent classical type V RH. The mean age was 43,02 year (range: 28-62).

Indications of classical type V radical hysterectomy in 45 women with locally advanced cervical carcinoma

Indications	Number of patients
Tumor extension into the vesicovaginal space with infiltration of the adjacent perivesical connective tissue but not the bladder muscle, with or without parametrial or upper vaginal involvement	4
Infiltration of the bladder muscle (detrusor) without involvement of the bladder mucosa, with or without parametrial or upper vaginal involvement (in three of them the ureter tunnel was also involved and in one an ileal loop*)	6
Infiltration of the ureter tunnel without bladder wall involvement, with or without parametrial or upper vaginal involvement	8
Extention to the cul-de-sac peritoneum and parametrium	1
Endometriosis of the Douglas pouch and rectal wall	1
Intraoperative injury (2 bladder wall, 1 colon injury)	2
Clinically suspect, but histologically negative tissue change	23

* Direct infiltration of an ileal loop attached to retrocervix and the sigma

Distribution of surgical interventions in the 45 patients with locally advanced cervical carcinoma

Type of RH	Additional procedures	No of patients
Bilateral standard RH (21)	Bladder wall resection	3
	Bladder wall resection without bladder opening	1
	Bladder and ureter resection with vesicopsoas hitch	8
	Bladder and ureter resection with vsicopsoas hitch and PAO	1
	ASLPE with Bricker pouch and PAO	1
	ASLPE with Budapest pouch	5
	Sigmoid colon resection with end-to-end anastomosis	2
Standard RH + LEP (19)	Bladder and ureter resection with vesicopsoas hitch and PAO	8
	Bladder and ureter resection with vesicopsoas hitch	4

	Bladder wall resection	2
	Bladder wall resection and PAO	3
	ASLPE with Bricker pouch	1
	ASLPE with Budapest pouch and PAO	1
Bilateral LEP (5)		
	Bladder and ureter resection with vesicopsoas hitch	1
	ASLPE with Budapest pouch + sigma resection	1
	Bladder and ureter resection with esicopsoas hitch, PAO and loop colostomy	1
	Bladder resection with vesicopsoas hitch + sigma and ileum resection (end-to-end anastomosis)	1
	Ureter resection and re-anastomosis	1

ASLPE anterior supralelevator pelvic exenteration
PAO paraortic node dissection
LEP laterally extended parametrectomy

The LEP was indicated either in the presence of positive pelvic nodes on intraoperative frozen section examination or due to parametrial tumor spread or both. Para-aortic node dissection up to the renal vessels was carried out in patients with positive pelvic nodes.

Of the 45 patients, 16 patients received neoadjuvant chemotherapy (CMVB in 15 and MPV in 1) and five had preoperative AL. Four women had postoperative EXT + AL and one AL only. Cisplatin alone was given after surgery in one patient. Eighteen patients did not get adjuvant treatment.

Patients were followed up every 3-6 months, mostly in the referral institution with follow-up information available in all cases. Mean follow-up time was 73.3 months (range: 5-180 months).

RESULTS

Indications varied considerably thus the patient population is clearly heterogeneous with one or two patients in most categories. In 23 cases, however, the indication of performing additional surgical elements in conjunction with RH was clinically suspicious invasion, which was not proven histologically.

In addition to the parametrial infiltration, the most frequent site of

extracervical tumor spread in this cohort was the anterior propagation either into the vesicovaginal space involving the retrovesical connective tissue (4 patients) and further up to the bladder muscle (6 patients) or to the ureter tunnel (8 patients). Of these patients, the tumor infiltrated both the bladder wall and ureter tunnel in three cases. Consequently, bladder wall resection with primary closer and resection of the most distal ureter segment along with its intramural part followed by bladder mobilization and fixation to the psoas muscle (vesicopsoas hitch) with primary re-implantation of the ureter(s) were the most frequent surgical approaches (table 4). Of note, that none of the patients had involvement of the bladder mucosa, i.e. none had stage IVA cervical cancer. Of the 18 women with anterior extension of the cervical carcinoma, the parametrium was infiltrated in 12 cases, of which the upper third or fornix of the vagina was also involved in 6, upper vaginal spread without parametrial invasion occurred in five women and in 1 case the tumor extended directly to the sacrouterine ligament. It is interesting to note that anterior extension did not occur in the absence of either parametrial or upper vaginal tumor infiltration or both. Also of interest, that 11 of 18 women with anterior extension with or without posterior extension were node negative and had G2 squamous cell carcinoma (table 2).

Of the 9 patients with extension of the disease to the bladder and/or adjacent tissue, the tumor also involved the vagina in six, the ureter tunnel in 3, the lateral parametrium in 3 cases and the sacrouterine ligament in one patient.

PATHOLOGIC TNM STAGING (pTNM)

The pathologic stage of the primary tumor (pT) was IB1 in two cases, IB2 in 18, IIA in 5 and IIB in 21 patients. Thirteen patients had positive pelvic nodes (pN1) and none had positive para-aortic nodal metastasis. No distant metastasis (M0) occurred; the involvement of the ileal loop was direct permeation, therefore it was not considered distant metastasis.

HISTOLOGY

Thirty-nine patients had squamous cell carcinomas (one of them was large-cell non-keratinizing). Adenocarcinomas occurred in 6 cases (one adenoid, two glossy cell, one mucoepidermoid and two endocervical type adenocarcinoma). Of 43 patients with squamous cell or adenocarcinomas (one adenoid, mucoepidermoid and two endocervical type

adenocarcinoma) the histologic grade was G1 in four, G2 in 29 and G3 in 10 cases.

SURVIVAL AND RECURRENCE

Overall survival and recurrence (n = 45)

Because of the heterogeneity of the patients' population, statistical survival analysis in terms of comparing groups based either on indication or treatment modality (surgical method, adjuvant therapy) was limited. Overall, of the 45 patients 25 were alive >5 years (range 5-17 years) with no evidence of disease (NED), of them one woman had successfully treated local recurrence. Sixteen patients died of their disease (DOD), 2 of them after 5 years, two women died due to other primary cancer, one succumbed to apoplexy and one to late complications. The 5-year overall survival was 55.6% and the recurrence-free survival 53.3%.

Of the 17 cases of recurrence, 11 recurred within the first 2 years (6 in the first year), two at 3 and 1 at 4 years, and 3 after 5 years (range 7-12 years). The recurrence occurred locally in 16 patients and there was only one distant failure, however, this patient also suffered of primary breast cancer as well, and the distant metastasis might be due to that.

Of the 13 women with pN1 tumor, 6 had NED (46%) and recurrence occurred in 7 (53.8%) (6 of them DOD (46%), one woman was salvaged with irradiation). This compares unfavorably with 31,3% mortality rate (10 DOD of 32 pN0 patients) of the node negative women. Of the 10 patients with G3 tumor, 7 had NED >5 years (70%), two DOD (20%) and one died of primary breast cancer. Of 29 G2 cases, 14 had NED >5 years (48.3%) (the recurrent tumor was successfully treated in one), 12 patients DOD (41.3%), one died of late complications, one of apoplexy and one of primary hepatic cancer. Of 4 patients with G1 cervical cancer two DOD and two had NED >5 years. Of the 6 women with adenocarcinomas, including two cases of glossy cell tumors, only one DOD, this patient had adenoid cancer.

Patients with anterior and/or posterior tumor spread (n = 19)

Of the 16 patients with anterior tumor propagation (vesicovaginal space/bladder wall, ureter tunnel) and parametrial or upper vaginal, or both

involvement, 7 (44%) were alive >5 years, 7 died of recurrent cervical carcinoma, one succumbed to late complications and one to metastatic primary breast cancer. In this cohort, of 3 with vesicovaginal space involvement two had NED and one DOD; of 5 with bladder muscle involvement three had NED, two DOD; and of 8 with ureter tunnel without vesicovaginal space or bladder muscle involvement 4 DOD, one died due to late complications and one of primary breast cancer, one had NED and one had successfully treated recurrence and was alive >10 years. Of the 16 patients with anterior extension, two women had both bladder muscle and ureter tunnel involvement, one of them DOD, the other had NED (7 years).

Three patients had posterior tumor propagation. Two of them DOD (one had vesicovaginal space and sacrouterine ligament involvement and the other had direct tumor infiltration to the ileum attached to the retrocervix). One of the 3, who had tumor spread to the parametrium and the Douglas pouch, was alive >5 years with NED.

Of 12 patients with pT1B associated with anterior tumor spread, 6 had NED >5 years (50%), 4 DOD, one recurred but was successfully treated, one died of primary breast cancer.

Of 19 patients with anterior and/or posterior tumor spread, 7 (36.8%) had positive pelvic nodes (pN1); in four cases of them the cancer recurred with fatal outcome in three.

Patients without histologically proven anterior or posterior tumor spread (n = 26)

Of the 26 patients with histologically not proven anterior or posterior tumor spread, 17 (65.3%) had NED >5 years (three were N1), 7 (26.9%) DOD (three were N1), one succumbed to primary hepatic cancer and one to apoplexy. In this cohort, of 8 women with pT1B, 5 had NED >5 years (two were pN1), one died due to apoplexy and two DOD (one with N1).

Patients with parametrial invasion (pT1B; n = 21)

Of the 21 patients with parametrial invasion, 13 had NED (62%) and 8 DOD. One of the 13 women with NED recurred but salvaged with radiation therapy. Of them, 6 underwent LEP and 6 were treated with sRH. Of the 8 patients who DOD, 5 had LEP and 3 sRH. Twenty four patients had no

parametrial propagation, of them 12 had NED (50%), 8 DOD and four died of other reasons.

Endometrial involvement

Propagation of the cervical carcinoma to the endometrium occurred 13 cases. Of them, 8 had NED and 5 DOD.

External beam irradiation (EXT)

Four patients received EXT in combination with afterloading application (AL). All died; one of them secondary to complications, one due to apoplexy and in two the recurrence was the cause of death.

Neoadjuvant chemotherapy

Of the 17 women with neoadjuvant chemotherapy 8 (47%) had NED, 6 (35.2%) DOD, one died of primary hepatic cancer and one who also received EXT+AL succumbed to complications. All patients responded to neoadjuvant chemotherapy, but there was no complete response.

One patient died of complications (perforation of the repaired bladder followed by abdominal abscess, septic fever and intestinal obstruction) 9 months after the RH. In this case, partial bladder wall resection was carried out without opening the bladder and the patient received 2 cycles of CMBV preoperatively, and postoperative EXT+AL irradiation.

No complications were observed in 20 patients and their urinary function resolved spontaneously.

Hemorrhage

Serious bleeding was not encountered however, every patients required blood transfusion.

Injuries

During mobilization of the ureter from its tunnel in rather fibrotic tissue, the lower segment of the ureter was injured in two cases. The damage was

detected immediately and vesico-psoas hitch was performed. One woman suffered a sigmoid damage requiring temporary colostomy.

Postoperative fever

Five patients had immediate postoperative fever (three due to urinary infection), all well responding to combined antibiotic therapy. Abdominal abscess developed in the early postoperative period in one woman and resolved by combined antibiotic therapy and puncture of the abdominal cavity.

Fistula formation

Two women developed vesico-vaginal fistula in the early postoperative period. In one of them the fistula occurred between the orthotopic bladder and the vagina and closed spontaneously on the 10th postoperative day. The other woman, who underwent vesicopsoas hitch procedure secondary to intraoperative bladder injury, developed an uretero-vaginal fistula as a result of ureteral necrosis and was managed by orthotopic urinary diversion. She died of recurrence at 11 years later. One patient developed vesico-vaginal fistula in the second postoperative month, needing suprapubic catheterization for four months in which ureter stenosis developed. She was managed by ureteroileocystostomy.

Lymphocysts and lymphedema

Lymphocyst occurred in two women. One of them had unilateral lower extremity lymphedema as a consequence of her abscessing lymphocyst and was successfully treated with antibiotics and cyst aspiration. The lymphocyst in the other patient caused bowel obstruction managed by temporary colostomy. Permanent mild lower extremity lymphedema was encountered in two other women, in one of them it was secondary to recurrence, and an early abdominal abscess formation (lymphocyst?) might be the cause in the other. Severe unilateral lymphedema developed in one patient who underwent ASLPE with orthotopic bladder and had hydronephrosis.

Impaired bladder sensation

Insensitivity of bladder to filling in conjunction with difficulty in initiating micturition occurred in 9 patients. Most women needed to use abdominal straining to initiate micturition and/or emptied their residual urine by pressing the abdominal wall, two self-catheterised and in two suprapubic catheterization was necessary for 5 months.

Urinary incontinence

In 6 cases mostly nocturnal urinary overflow incontinence was observed, and one woman suffered from urge incontinence.

Peroneal nerve paresis

In 3 cases, unilateral peroneal nerve paresis occurred after LEP, which resolved with conservative therapy in one woman. The lower extremity pain lasted for 10 months in the other patient and in the third case the pareses resolved only partially with residual symptoms including pain and walking difficulties.

Arterial thrombosis

Due to iatrogenic injury to the external iliacal artery intraoperativ embolectomy was needed and performed as distally as the popliteal region in one woman, complicating immediate postoperative care (mobilization and exercise). One patient with unilateral LEP developed femoral artery thrombosis on the 2nd postoperative day and was managed by embolectomy successfully.

Ureteric stenosis and obstruction

One woman treated by ASLPE with Budapest pouch and sigmoid resection developed lymphedema and unilateral hydronephrosis with diminished renal function due to ureteric stricture. She refused percutaneous nephrostomy. In 3 patients with vesico-psoas hitch, we observed ureteric obstruction with pyelectasy and hydronephrosis. Percutaneous nephrostomy to drain the kidney was placed in two, in one of whom dialysis was also needed, and all three patients were successfully treated with ureteroileocystostomy.

Ureteric obstruction was common in women with recurrent disease, needing percutaneous nephrostomy drainage as palliation.

Mild dilation of ureters was observed 8 years after surgery in one patient secondary to partial ureteric stricture but no treatment was needed.

Ileus

The only patient who developed bowel obstruction died of operative complications. Paralytic ileus developed in three cases. Surgical exploration was necessary in one of them 4 weeks after the RH. The adynamic bowel function occurred in the 6th postoperative day in the other and 8 years following RH in the third one and resolved on conservative therapy in both.

Others

In one patient a large bladder calculus was found and removed via laparotomy in the second postoperative month. When removing the calculus the bladder was seriously injured, needing temporary urinary diversion with Bricker pouch, which was connected to the bladder 3 months later.

In one case, temporary percutaneous nephrostomy was needed during the early postoperative period due to slippage of the ureteric drains from the conduit into the urinary bladder.

Rectal bleeding occurred in one woman, which was due to hemorrhoids, however, following treatment permanent rectal incontinence developed.

One patient underwent abdominal hernia reconstruction, and another required treatment for deep venous thrombosis of the lower extremity.

Discussion

Our study demonstrates the feasibility of performing elements of bladder, ureter and bowel surgery in association with standard RH or LEP, the procedure, however, is extensive and is not without significant associated risk of complications.

In our series, one patient died of complications. Following neoadjuvant chemotherapy she underwent bilateral sRH and partial bladder wall resection without bladder opening and received full course EXT+AL 2 months postoperatively. In association with the radiotherapy ureter stenosis developed secondary to bladder wall necrosis, requiring bilateral percutaneous nephrostomy. Four months later she had septic peritonitis leading to a series of bowel obstruction and bowel surgery finally leading to death. One might speculate that the fatal bladder wall necrosis resulted from the joint effect of surgery and postoperative radiotherapy.

Postoperative EXT+AL was given to other high risk women (the tumor growth was near to the surgical margins). Two of them succumbed to recurrent cancer and the third patient died of apoplexy 1 year after operation. Our finding appears to suggest that full course postoperative irradiation is not beneficial in women undergoing such an extensive surgery. The inefficacy of radiation to kill the remaining cancer cells in this setting might be explained by the diminished tissue oxygenation in the irradiation field. Similarly, neoadjuvant chemotherapy did not appear to have any effect on survival and surgical complications in our patient material; the number of cases, however, is not enough for any firm conclusion in this context. Ki et al. reported 72.5% clinical response (13.7% complete response) to a quick course with vincristin, bleomycin and cisplatin in 51 bulky stage IB-IIA cervical cancer without significant survival advantage.

Impaired bladder sensation and consequent overflow or urge incontinency were the most common complications in our material, which was not surprising as bladder dysfunction has been reported commonly in all studies on RH and is likely resulting from disruption of the nerve supply to the bladder during parametrectomy. Lymphedema, lymphocyst and peroneal nerve paresis were infrequently demonstrated. They are most probably attributed to the extensive clearance of the connective tissue from the pelvic wall (sRH, LEP). Most were manageable with conservative treatment.

Intraoperative or immediate postoperative femoral artery thrombosis has been reported in women subjected to LEP. We noted femoral artery thrombosis only in one patient following LEP. She was successfully treated with embolectomy.

We observed adynamic bowel function infrequently, most resolved on conservative treatment. In one case, however, exploration was needed. Of interest, is that in of the three cases the paralytic ileus developed 8 years after primary surgery. Previous studies have shown that some bowel dysfunction invariably occur, particularly in long-term cervical cancer survivals, undergoing RH.

Complications most likely caused by the associated PE procedures include ureteric stenosis and obstruction with consequent pyelectasy and hydronephrosis and probably vesico-vaginal fistulas. The risk of ureteric stricture is particularly increased in women with vesicopsoas hitch and it is most likely resulting from the diminished blood supply at the anastomosis site. These findings suggest that patients who underwent vesicopsoas hitch should be followed up regularly for many years with abdominal ultrasound examination to diagnosis ureter dilatation and pyelectasy prior to irreversible renal damage develops. Conservative management options are limited, urinary diversion with orthotopic pouch is probably the best treatment. In the presence or ureter stenosis it is clinically important to rule out recurrent disease as ureter obstruction is a common finding in local recurrence.

In the present cohort, the incidence of fistula formation (6.7%) is higher than in our RH and/or LEP patient material and it is related to the additional bladder surgery. Early series of RHs reported utero-vaginal fistula rates between 5 and 10%, the prevalence in more recent ones is significantly less, around 1%. The explanation of the high incidence in this series might be the extensive tissue resection around as well as the dissection of the bladder and lower ureter with resulting compromised blood supply and edema. Again, women with vesicopsoas hitch are more at risk of developing vesico-vaginal fistula. If the fistula does not resolve spontaneously or on conservative therapy (suprapubic catheterization), urinary diversion or ureteroileocystostomy is needed.

It is of note that lower sigmoid resection with primary anastomosis was not associated with complication in our patients.

Approximately 50% of the patients with tumor permeation anterior towards or into the bladder wall but not to the bladder mucosa with (pT1IB disease) or without parametrial involvement can be managed with surgery without adjuvant therapy (5-year survival ~50%). This figure is not known in women

primarily treated with radiotherapy (chemoradiation) for this kind of tumor spread is rarely if ever diagnosed in irradiation setting. Consequently comparing our survival data with those obtained by chemoradiation in LACC is invariably biased. Less than one third of our patients had positive pelvic nodes, but none harbored positive para-aortic nodes. Pelvic node metastasis seems to be a negative prognostic determinant (46 vs. 31,2% DOD rate). On the contrary, tumor grade and histologic subtype as well as endometrial invasion had no significant impact on outcome, neither the histologically proven parametrial involvement (pTIIIB case). The number of patients with posterior tumor propagation towards rectum is too small (3 women) to draw any conclusion.

Our study demonstrates recurrence rate in the order of 50%, most tumor recurring in the first two years, late recurrence (after 5-10 years), however, is not exceptional. Almost all recurrent disease was local. This finding emphasizes the importance of long-term follow-up.

Paucity of literature does not allow comparison of our experience with that of others as most reports on exenterative procedures in managing patients with LACC discuss the role of pelvic exenteration (PE) in FIGO stage IVA disease. Per definition, however, none of our patients had stage IVA cervical carcinoma. Tumor extension to the adjacent tissue to or marginal permeation of the bladder or rectum wall by cervical cancer is neither included in the current FIGO nor in the TNM staging system. Similarly, Piver V RH cannot be considered as PE on definition, although the definition of PE varies in the literature. Originally, anterior PE was defined a combination of radical cystectomy, RH, and vaginectomy; and posterior PE as a combination of abdominal perineal resection of the rectosigmoid, RH, and vaginectomy, whereas total PE is the combination of the two, i.e. exenteration is an en-block resection of pelvic organs with surgical reconstruction. Since the introduction of low rectal anastomosis and orthotopic bladder the radicality of PE lessened with preservation a part of the bladder, most of the rectum and vagina in many cases. With this in mind, lower sigmoid resection with anastomosis in association with RH might be considered as posterior PE, but removing a segment of the bladder and the distal ureter in connection with RH hardly can be defined as anterior PE.

Currently, most authors would abandon RH in the presence of unexpected tumor growth beyond the cervix into the bladder or rectal wall or surrounding connective tissue in favor of chemoradiotherapy. This practice

invariably carries the risk of devastating psychological consequences: the patients being disappointed with the unsuccessful surgery, fear of inoperable disease, fear of radiation and chemotherapy etc. All of which can be avoided by completing surgery utilizing bladder, ureter and less frequently rectosigmoid resection with re-anastomosis in association with RH. The surgical principle is to ensure adequate tumor-free margins.

The parametrium, which is actually the lateral paracervical connective tissue, extending from the uterine cervix to the pelvic wall, represents the major route not only for direct tumor propagation but for lymphatic drainage as well. In our series, parametrial invasion does not seem to be an adverse prognostic factor, and LEP apparently has no impact of survival in women with pT1B disease.

The weakness of our study includes its retrospective nature and the fairly heterogeneous patients' population.

In conclusion, albeit the data are limited and comparative survival analysis was not possible; our findings reveal that radical surgery is an alternative treatment in LACC with acceptable survival rate and quality of life. This compares favorably to radical radiotherapy or chemoradiation, particularly in terms of long-term sequelae associated with irradiation. Our observation may be of particular helpful in decision making for surgeons encountering unexpected extracervical tumor spread of cervical carcinoma during RH. Postoperative irradiation apparently makes more harm than good and neoadjuvant chemotherapy is probably has no place in this setting, nevertheless the number of patients is too small for firm conclusions.

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