Original Articles

Nerve-sparing radical hysterectomy for Stage IA2-IIB cervical cancer: 5-year survival of 501 consecutive cases

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Summary

Objective: The purpose of this study was to assess the 5-year survival and morbidity in cases with radical hysterectomy and pelvic lymphadenectomy with pre- and postoperative irradiation performed to treat Stage IA2-IIB cervical cancer.

Methods: During a 10 1/2-year period between July 1990 and December 2000, 501 consecutive radical hysterectomies with bilateral pelvic lymphadenectomy were performed by the same gynecological surgeon in Stage IA2, IB, IIA and IIB cervical cancer. The patients were treated by pre- and postoperative irradiation as well.

Results: Apart from recurrence, perioperative complications were minimal with no long-term morbidity. The absolute 5-year survival rates for the patients in Stage IA2, IB1, IB2, IIA and IIB were 94.4%, 90.7%, 84.1%, 71.1%, and 55.4%, respectively. The respective 5-year survival rates for patients without or with lymph node metastasis were 94.5% and 33.3% in Stage IB2, 81.7% and 48.7% in Stage IIA and 70.2% and 36.5% in Stage IIB, respectively.

Conclusions: Nerve-sparing radical hysterectomy with pelvic lymph node dissection and pre- and postoperative irradiation remains the treatment of choice for most patients with early-stage and even Stage IIB cervical cancer. The radicalism and extent of lymph node dissection and parametrial resection should be individualized and tailored to tumor- and patient-related risk factors.

Key words: 5-year survival; Cervical cancer; Nerve-sparing radical hysterectomy; Pelvic lymphadenectomy; Pre- and postoperative irradiation; Wertheim operation.

Introduction

Cervical cancer takes an annual toll of 200,000 women worldwide. Hungary has a "share" of 500 cases among them. Pelvic tumors rank third among the most common female malignancies in the industrially developed countries, while they are at the top in developing countries [1].

Until now, it has been an established practice all over the world to rely on conization in stage "0" and to apply simple hysterectomy in Stage IA1, while radical hysterectomy with or without preoperative irradiation is recommended in early invasive cervical cancer (Stages IB and IIA) [2]. The reason for these solutions is the absence or minimal (1%) chance of lymph node metastases in preinvasive (Stage "0") and microinvasive (Stage IA1) cancer [3]. In the case of Stage IA2 patients, there is no uniform practice. Some physicians perform simple hysterectomy, while others suggest a radical solution. Similarly to Stage III cases, Stage IIB patients with locally advanced disease are given primary radiotherapy or chemoradiation, while others are recommended to undergo surgery [4].

Considering the above, we decided the following in 1990 in order to compare the efficiency of interventions in all of the women with Stage IA2, IB, IIA and IIB cervical cancer hospitalized in our department. The operations would be performed by the same gynecologist, postoperative histological investigations would be done by the same histopathologist, and radiotherapy would be provided by the same oncoradiologist for several years.

The present publication gives an account of the observations in 501 Wertheim operations (radical abdominal hysterectomy with pelvic lymphadenectomy) performed over ten and a half years.

Material and Methods

Between July 1, 1990 and December 31, 2000, 501 consecutive Wertheim operations were performed in non-selected women suffering from cervical cancer. Table 1 shows the distribution of women according to the stage of the disease. Staging was based on the clinical practice guidelines by FIGO [4], the diameter of the tumor and the involvement of the parametrium were assessed via vaginal and rectal examinations, routine cystoscopy and, if necessary, selective urography were performed. Abdominopelvic ultrasonography was also done routinely, CT and MRI were performed in selected cases only, while no PET investigations were done at all. Patients were referred to the oncology ward by the outpatient unit of our own department, as well as from various gynecological units and clinical wards, because of positive cytological and/or colposcopic screening tests done, or because of manifest cervical cancer. The presence of cervical cancer was confirmed by conization or biopsy in each case. In case these interventions had been done by the referring physician, we accepted the histological findings issued by an external pathologist.

Figure 1 shows the age distribution of the patients in each stage of the disease. It can be concluded that the incidence of

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Table 1. — *Distribution of the 501 cases according to stage.*

Stage	no.
IA2	36
IB1	75
IB2	88
IIA	121
IIB	168
III and IV	13
Total	501

the disease increases until 35-40 years of age in each stage, which is followed by a decrease in the age group of 41-45 years, and after 56-60 years of age another (usually mild) rise in the frequency of the disease is noted.

Patients were given preoperative intracavital high-dose-rate afterloading (HDR-AL) brachytherapy on two occasions (2 x 5.5 Gy). Operations were done two weeks after the second irradiation. Depending on the histological findings of the surgical specimens, postoperative local HDR-AL brachytherapy was given, and in case the tumor was still detected in the cervix, and/or lymph node metastases were found, the latter also was treated by teletherapy.

The operation was performed with antibiotic prophylaxis after the required investigations and preparations. Following the insertion of a Foley catheter after epidural anesthesia, lower midline laparotomy was performed by lengthening the incision beside the umbilicus (on the left side) by 3-4 cm, in intratracheal narcosis. In 18 cases, at the patients' special request and/or if the abdominal wall was extremely thin, an elongated Pfannenstiel cross section was applied. Having isolated the intestines, we lifted the uterus. Having entered the uterovesical fold and pushed down the bladder, we opened up the peritoneum covering the lesser pelvis medially, alongside the course of the ovarian vessels. The ureter was pushed medially, and the infundibulopelvic and round ligaments were clamped, cut and ligated. If preoperative histology was suggestive of the tumor being other than adenocarcinoma, at least one of the ovaries in young women (< 40 years old) was preserved and attached to the peritoneum at the level of the anterior superior iliac spine in 23 patients. (At least one ovary was "rescued" in 8, 11, 3, and 1 cases in Stages IA2, IB, IIA and IIB, respectively.)

The great blood vessels lateral to the pararectal and paravesical spaces were mobilized and the networks of lymphatic vessels and lymph nodes accompanying the common iliac artery were removed along the blood vessel as high as the bifurcation of the abdominal aorta and downward the vessel as low as Poupart's ligament, to the opening of the deep iliac circumflex vein.

Next, the obturator fossa was explored to allow for the removal of the lymph nodes situated in it. After that, the uterine artery and vein were cut between the ligatures. Having transected the peritoneum lining the Douglas pouch, we clamped, cut and ligated the sacrouterine ligaments. After clamping, cutting and suturing the uterovesical ligament, the ureter was mobilized as low as its opening into the urinary bladder. We paid attention to the blood supply to the ureter by maintaining its relationship with its surroundings. We also paid special attention to the intactness of connective tissue extending between the lateral wall of the sacrouterine ligaments and the medial wall of the ureter, containing autonomic nerve fibers of the hypogastric plexus. We also made it sure to spare the posterior wall of the uterovesical ligament while clamping off and cutting it. Having clamped off, cut and ligated the lateral edge of the parametrium and paracolpium, and removing varying portions of the vagina (usually the third including the vaginal fornix), we processed the whole uterine specimen and the lymph nodes of the different regions (making notes of their site of origin) in the histology laboratory of the department.

The vaginal stump and the edges of the uterine wall were closed and peritonized with absorbable knotted and simple running sutures, respectively. Redon drains were introduced into the retroperitoneal space and led through the abdominal wall, and the edges of the peritoneum were stitched together. (In the period of 1997-1999, retroperitoneal suction drainage was substituted by drainage of the abdominal cavity via a Pezzer catheter through the vagina in 128 consecutive cases). The Foley catheter was removed after seven days, while Redon drains and the Pezzer catheter were removed after 24-48 hours.

In 80% of the procedures, one or two units of intra- or postoperative blood transfusion were necessary. Three patients required larger amounts of transfusion.

Parallel to the Wertheim operation, appendectomy was performed in 24 cases, primarily because of signs of inflammation or closeness to the surgical site. Because of a major or an expected major hemorrhage, the hypogastric arteries were ligated at their origin in 34 patients [5]. Omental resection was performed in 14 cases. Five and four Wertheim operations were performed in the first and third trimester of the pregnancy, respectively. In the former cases, total removal of the pregnancy was performed, while in the latter cases, we delivered the fetus by cesarean section and then performed the Wertheim operation.

The extension of surgeries performed by us corresponds to class IV, according to the classification recommended by Piver *et al.* [6]. Similarly to other authors [7, 8], we also considered it essential to radically remove the parametrium.

Table 2. — *Intraoperative complications emerging in 501 Wertheim operations.*

Complication	no.	(percentage)
Injury of the common or external iliac veins	4	(0.8%)
Hemorrhagic shock	3	(0.6%)
Injury of the urinary bladder	1	(0.2%)
Damage of the obturator nerve	1	(0.2%)
Ureteral injury	0	(0.0%)
Intestinal injury	0	(0.0%)
Total	9	(1.8%)

Table 3. — *Early postoperative complications (emerging within one week) after the 501 Wertheim operations.*

Complication	no.	(percentage)
Urinary infection	24	(4.8%)
Subileus	13	(2.6%)
Fever of unknown origin	13	(2.6%)
Lymphocyst	12	(2.4%)
Pyelectasia	9	(1.8%)
Ureteral occlusion	5	(1.0%)
Gastric atony	4	(0.8%)
Abdominal wall hematoma	4	(0.8%)
Nerve pain	4	(0.8%)
Lower extremity lymphedema	3	(0.6%)
Phlebitis	3	(0.6%)
Thromboembolism	3	(0.6%)
Bladder atony	1	(0.2%)
Wound sepsis	1	(0.2%)
Toxic shock	1	(0.2%)
Postoperative hemorrhage	1	(0.2%)
Total	101	(20.2%)

Table 4. — *Late postoperative complications (emerging within 3 months) after 501 Wertheim operations.*

Complication	no.	(percentage)
Lymphocyst	21	(4.2%)
Post-irradiation ileus	12	(2.4%)
Hydronephrosis	9	(1.8%)
Post-irradiation bowel necrosis	6	(1.2%)
Ureteral occlusion	6	(1.2%)
Prolapse of the vagina	5	(1.0%)
Post-irradiation (vesical or rectovaginal) fistula	5	(1.0%)
Lower extremity lymphedema	4	(0.8%)
Narrowing of the vaginal orifice	4	(0.8%)
Post-irradiation proctitis	2	(0.4%)
Urinary incontinence	0	(0.0%)
Total	74	(14.8%)

Results

Tables 2, 3, and 4 sum up intraoperative, early, and late postoperative complications.

Among intraoperative complications (Table 2), little millimeter damage to the common and external iliac veins was observed in two cases each, which was repaired by suturing. Also, damage to the bladder was closed with a few stitches in one case. There were no complaints of symptoms from the patient with the injury of the obturator nerve. No damage was done to the ureters or the bowels in any of the cases. In three cases, hemorrhagic shock was observed which was controlled by lifting the hypogastric arteries and giving blood transfusions. There were no intraoperative deaths.

Early postoperative complications emerging within a week (Table 3), accompanied with fever and hemorrhage were controlled. Urinary dysfunction (15 cases) regressed spontaneously in eight cases in a week or two, while temporary percutaneous nephrostomy had to be performed in seven cases. Early removal or slip of the drains (within a few hours) could be detected in the background of 12 lymphocysts arising in the early postoperative period. Repeated puncture usually made them disappear. Four cases of gastric atony could be controlled by conservative treatment, while eight of the 13 patients with subileus had to undergo laparotomy. There were only temporary cases of phlebitis and neuropathy, two of the three thromboembolic patients were rescued, but the third one died on the second postoperative day.

Among late postoperative complications (within 3 months after surgery), radiotherapy-related consequences were significant (Table 4). Lesions (ileus, intestinal necrosis, proctitis and fistula) were thought to be related with irradiation in a total of 25 cases (5%). Ileus and/or intestinal necrosis required multiple surgeries in some cases, seven patients among them died within one year after the Wertheim operation. The rest of the postoperative complications (6 cases of ureteral occlusion and 9 cases of hydronephrosis) were solved by urological interventions such as ureter implantation, nephrectomy, and temporary or permanent percutaneous nephrostomy in four, three, four and four cases, respectively. Invasive intervention was necessary in 21 cases of lymphocysts, which had caused compression symptoms of varying severity. In 16 cases, laparotomy was performed and the "detachable" portion of the lymphocyst was removed; the rest was treated using a solution containing polycresulene (Vagothyl, Polfa, Poland). The cavity of the lymphocyst was drained via the abdominal wall using a Redon drain with an external diameter of 6 mm. The area was under suction for at least a week. In the other five cases, percutaneous lymphocystostomy was performed under ultrasonographic control and the drain was under suction for one to two weeks. All five patients have recovered.

Of the 12 early and 21 late lymphocysts, eight and 14 occurred in the group in which abdominal drainage alone was applied, four and seven patients, respectively, underwent retroperitoneal suction drainage. Accordingly, the incidence of lymphocysts was 17.2% (22/128) and 2.9% (11/373) in the groups treated with abdominal Pezzer drainage and retroperitoneal Redon drainage, respectively.

Plastic surgery helped the majority of patients suffering from a prolapsed vaginal wall or constricted vaginal orifice. Lymphedema in the lower extremities decreased spontaneously after the disappearance of the lymphocysts in all four cases. There was no sign of urine incontinence in any of the cases at all.

Data of 5-year survival were based on presence at annual follow-up examinations and on the dates of deaths obtained from the National Registry Office. Based on the above, 142 of 501 patients (28.3%) died within five years following the Wertheim operation. Among them, 93 patients (65.5%) died within two years after surgery (Table 5).

Lymph node metastases were most commonly found in the right obturator fossa (71 cases), followed by the surroundings of the left external iliac artery and vein (61 cases). Either the left obturator fossa or the region along the right iliac vessels contained at least one affected lymph node in 57 and 42 patients, respectively (Table 6).

Table 5. — *Time of the patients' death according to stage.*

Death	IA2	IB1	IB2	IIA	IIB	III-IV
Within 1 week	–	–	–	1	–	–
2-4 weeks	1	–	–	–	1	–
1-6 months	–	–	–	–	5	–
0.5-1 year	1	1	3	12	28	2
1-2 years	–	1	3	10	19	5
2-3 years	–	3	6	6	16	–
3-4 years	–	–	–	4	3	–
4-5 years	–	2	2	2	3	2
Total	2	7	14	35	75	9

Table 6. — *Incidence of lymph node metastases according to location.*

At least one lymph node metastasis	Right side	Left side
Along the common iliac artery and vein	25	20
Along the external iliac artery and vein	42	61
In the obturator fossa	71	57
Total	138	138

Histologically confirmed metastases were found in 25 cases at the level of the right common iliac artery and vein and in 20 cases on the left side. Five-year survival was at its lowest (32-35%) if positive lymph nodes were found in either the obturator fossa or along the left common iliac artery and vein. If both obturator fossae contained metastases, survival rates decreased to 24%.

Absolute and tumor-free five-year survival rates are presented in Table 7. Stage-independent, absolute 5-year survival was 71.7%, while tumor-free survival was somewhat less, at 69.5%. Independent of lymph node metastasis state, absolute survival decreased with progression of stage, as follows, Stage IA2, 94.4%, IB1, 90.7%, IB2, 84.1%, IIA, 71.1%, IB, 55.4%, III-IV, 30.8%. Absolute and tumor-free survival was almost identical. Among patients still alive after five years, only one woman in Stage IA2 was not tumor-free five years after the Wertheim operation, while the corresponding figures in the other stages were as follows: IB1, two patients, IB2, three patients, IIA, three patients, IIB, two patients. All of the surviving patients in Stages III and IV were tumor-free at that time. If there was no lymph node metastasis, absolute and tumor-free survival was 84.2% and 81.7%, respectively, while in the case of one positive lymph node alone, absolute survival decreased to half (41.1%) and tumor-free survival dropped to 39.7%. This significant difference was also clearly found in the individual stages. Table 8 shows the distribution of the individual histological types. Histological type had no effect on survival.

Considering cases with negative postoperative histological findings (no tumor tissue, only occasional in situ carcinoma found in the cervix), it can be concluded that only nine out of the 115 patients died in this group within five years, the survival rate therefore being 92.2% (Table 9). Patients with a negative postoperative histological finding constitute 23.0% of all cases (Table 9). In 107 women out of 115 with negative histological findings, lymph nodes were also found negative, while at least one lymph node turned out to be metastatic in the remaining eight patients (Table 9). Five of them are still alive but three died within five years after the operation. Five-year survival rate was found to be 94.4% (101/107) if both the postoperative cervical and lymph node histological findings were negative.

After five Wertheim operations done parallel to the termination of pregnancy in the first trimester, one patient died within two years, another passed away within four years, while three women are still alive. Four patients had to undergo Wertheim's operation after cesarean section, one of whom died within a year, another one in ten years, and two are still alive.

Table 7. — *5-year absolute and tumor-free survival according to stage, depending on and independently of lymph node metastasis.*

Stage	At least one lymph node metastasis	5-year survival [tumor-free survival]	No lymph node metastasis	5-year survival [tumor-free survival]	5-year survival independent of lymph node metastasis [tumor-free survival]
IA2	0	–	36	34 (94.4%) [91.7%]	94.4% (34/36) [91.7%]
IB1	5	5 (100.0%) [100.0%]	70	63 (90.0%) [88.6%]	90.7% (68/75) [88.0%]
IB2	15	5 (33.3%) [33.3%]	73	69 (94.5%) [90.4%]	84.1% (74/88) [80.7%]
IIA	39	19 (48.7%) [46.2%]	82	67 (81.7%) [79.3%]	71.1% (86/121) [68.6%]
IIB	74	27 (36.5%) [35.1%]	94	66 (70.2%) [69.1%]	55.4% (93/168) [54.2%]
III and IV	13	4 (30.8%) [30.8%]	0	–	30.8% (4/13) [30.8%]
Total	146	60 (41.1%) [39.7%]	355	299 (84.2%) [81.7%]	71.7% (359/501) [69.5%]

Table 8. — *Distribution of histological results in specimens removed during radical hysterectomy.*

Histological type		
Non-keratinizing planocellular carcinoma	235	(46.9%)
Keratinizing planocellular carcinoma	60	(12.0%)
Adenocarcinoma	43	(8.6%)
Microcellular carcinoma (basaloid carcinoma)	27	(5.4%)
Adenosquamous carcinoma	7	(1.4%)
Glassy-cell carcinoma	4	(0.8%)
Papillary (transitional) carcinoma	3	(0.6%)
Adenoid cystic carcinoma	2	(0.4%)
Verrucous carcinoma	2	(0.4%)
Leiomyosarcoma	2	(0.4%)
Carcinoid	1	(0.2%)
Carcinoma in situ	14	(2.8%)
Chronic ulcer caused by irradiation	101	(20.2%)
Total	501	(100.0%)

Table 9. — *Tumor-free postoperative findings (115 cases) (with only occasional in situ carcinoma) and 5-year survival.*

Stage	Alive	Dead	Negative postoperative histological findings in % of cases	Survival rate among patients with tumor-free postoperative findings
IA2	29	2	31/36 (86.1%)	93.5%
IB1	28	1	29/75 (38.7%)	96.6%
IB2	24+2*	2+1*	29/88 (33.0%)	89.7%
IIA	10+1*	0	11/121 (9.1%)	100.0%
IIB	9+2*	1+2*	14/168 (8.3%)	78.6%
III and IV	1	0	1/13 (7.7%)	
Total	101+5*	6+3*	115/501 (23.0%)	92.2%

* with at least one lymph node metastasis present.

Discussion

Freund was the first to use the radical approach in operating on a patient with cervical cancer in 1878, and in addition to hysterectomy, he also removed lymph nodes from the lesser pelvis [9]. Although mortality stood at 50%, there was no other choice at that time. It was considered a great step forward when, in the modern sense of the word, Wertheim performed radical abdominal hysterectomy and pelvic lymph node dissection in 1898,

although mortality was close to 20% [10]. In 1901, Schauta [11] argued for radical vaginal hysterectomy, but he had fewer followers than Wertheim, owing to a great disadvantage of the technique proposed by the former, the removal of lymph nodes, and the exploration and survey of the parametrium and abdominal organs could not be complete.

The Wertheim operation gained grounds in Japan and the USA owing to the "promotion" activities by Okabayashi and Meigs, respectively [12, 13]. The importance of sparing pelvic autonomous nerves was first emphasized by Kobayashi, later, colorectal surgeons, urologists and various gynecologists also called attention to this issue [14-16]. Recently, Höckel *et al.* [17, 18] have attracted attention; they base the removal of the "mesometrium" on their embryological observations.

After the discovery of radium, radiotherapy has been used since the first half of the 20th century, perfected via a later combination of surgery and radiotherapy. Applying (primary) radiotherapy alone, Perez *et al.* [19] and Mayer *et al.* [20] achieved 5-year survival in 68% of their patients operated on for Stage IIB cervical cancer. Other publications have reported lower survival rates [4]. A recent prospective randomized study found radical hysterectomy and primary radiotherapy equally effective, the size of the tumor being thought to be the most important factor for survival [21].

It emerged in 1997 that neoadjuvant chemotherapy contributed to the operability and improved the chances of survival [22, 23]. Benedetti-Panici *et al.* [23] randomized the treatment of 441 patients, comparing Wertheim's operation following neoadjuvant chemotherapy with external-internal radiotherapy applied alone. In the first group, 5-year survival was found to be 58.9% (IB2-IIB, 64.7%), while in the second group it was 44.5% (IB2-IIB, 46.4%). According to the findings by Keys *et al.* [24], extrafascial hysterectomy performed after preoperative irradiation or neoadjuvant chemotherapy in the case of Stage IB2 patients ("bulky" Clarke tumor with a diameter exceeding 4 cm) improved the results significantly compared with non-operated patients. Decker *et al.* also rely on this type of surgery [25].

Having combined the Wertheim operation and radical vaginal approach (Schauta operation) in Stage IA2, IB and IIA patients, Kenter *et al.* [26] found that the 5-year survival rates independent of the presence of lymph node metastases, in the case of positive lymph nodes and lymph nodes free from metastases, were 87.5%, 65% and 94%, respectively. Long-term urination problems were reported by 40.8% of the patients, while fistulae developed in 6.7% of them. In a larger study, they found these figures at 32.0% and 7.8%, respectively [27]. Despite the above innovation, the results did not improve. Moreover, surgery took much longer than a classic Wertheim operation, so the authors accepted that there was no point in insisting on the abdominovaginal solution [27].

Lately, laparoscopy-assisted radical vaginal hysterectomy and lymphadenectomy [28, 29] and laparoscopic radical hysterectomy and lymphadenectomy [30, 31] have been on the rise. The results are also promising with regard to fertility-preserving radical trachelectomy and lymphadenectomy in highly selected cases, in the early (IA1, IB1) stages of the disease. According to reports to date, the rate of recurrence is 4%, and in pregnancy, early rupture of membranes has been seen more frequently [3, 32].

When in 1990 we decided to assess the efficacy of a several-decade-old solution (preoperative irradiation + Wertheim operation + postoperative local and external irradiation) in a large number of unselected patients, all in Stage IA2 and IIB of the disease, first of all, we thought of the advantages of comparability and care of the same level associated with identical therapeutic conditions, such as the same highly experienced surgeon, histologist and radiologist. In addition, another impetus was the availability of a patient registration and follow-up system, based on the patients' personal codes, which allowed for long-term follow-up.

The comparability of therapeutic results in the individual stages was possible because the same physician performed the staging and operation of each patient, and because all patients up to stage IIB were operated on without selection. Primary irradiation was given in Stage III, while in Stage IV, palliative treatment was recommended and provided. In a few selected cases among Stage III and IV patients (13 women) we found that Wertheim's operation would be of advantage, although we were convinced of a very poor prognosis. Their future history was also followed-up. When, after almost ten and a half years, we exceeded the 500-case "record" (the number of cases Wertheim reported in his own practice [10]), we decided to give an account of our experience obtained with 501 patients after the 5-year survival period.

Covens *et al.* were the first to emphasize the importance of the operating surgeon's skills and preparation in performing Wertheim operations [33]. They compared eight gynecologic surgeons' achievements in doing Wertheim operations, and found significant differences among them, as far as the quantity of intraoperative blood loss, need for transfusion, duration of hospitalization, and, most importantly, vesical dysfunctions were considered.

In our own cases, the operating surgeon, experienced in ligating the hypogastric artery [5], presumably operated with the same quantity of blood loss and, owing to his technique, the incidence of vesical dysfunction was really low. The importance of ligating the hypogastric artery in Wertheim operations was also highlighted by Gharoro [34].

In our sample, the incidence of intraoperative, early, and late complications was minimal.

According to the literature, the proportion of intraoperative complications falls in the range of 1.1-7.4%, while ureteral injuries are found at 0.6-1.7% [3, 26, 35]. In our sample, there were four vascular injuries, one vesical injury, and one obturator nerve injury (1.2%). Neither ureteral nor rectal injuries occurred. The complications could be controlled, and damage to the obturator nerve did not result in disturbed adductor innervation.

In the literature, early postoperative complications such as urinary tract infections (10-16%), vesical dysfunction

(up to 70%), wound infections (4-6%) and thromboembolism (0.3%) are mentioned in the first place [3, 26, 35, 36, 37]. In our sample, there were 24 cases of urinary tract infections (4.8%), vesical atony and wound infection in one case each (0.2-0.2%), and lethal thromboembolism in one case (0.2%).

Incontinence problems, which are often mentioned in the literature, may be due to the injuries of the sympathetic and parasympathetic nerves of the pelvis [26, 37]. Dysfunction of the anorectum may also be attributed to injury of the hypogastric plexus. Therefore, more and more reports are published about "nerve-sparing" Wertheim operations [17, 38, 39, 40]. Interventions done in our department have always been nerve-sparing ones, which is why we have not encountered cases of postoperative vesical and anorectal innervation problems. We have always paid attention to the autonomous nerve plexus running along the lateral side of the sacrouterine ligament and the posterior wall of the uterovesical ligament. Also, we have always tried to spare the vascular supply of the ureters, and never separated the vessels from their immediate surroundings composed of connective tissue. In the 501 Wertheim operations, there were no intraoperative ureteral injuries, but postoperative complications including 11 cases of ureteral occlusion and 18 cases of pyelectasia or hydronephrosis developed, possibly because of local ischemia and tumor propagation. They could be managed by performing temporary percutaneous nephrostomy or urological surgery.

Postoperative lymphocysts should be discussed separately. The removal of the network of lymph vessels and nodes (lymphadenectomy) running along the great blood vessels interferes with the lymph circulation from the lower extremities and, according to the literature, thin-walled lymph-filled sacs (lymphocysts) develop, their bases being attached to the iliac vessels and the psoas muscle, in 0-35% of the cases. They cause pain, and owing to the compression they exert on the great vessels, disturb circulation in the lower extremities with subsequent lymphedema. Suction drainage applied at closure of the retroperitoneum can prevent the development of lymphocysts. Some authors have observed that, if reperitonization is omitted, the accumulation of lymph can also be prevented without suction [26].

In our sample, we compared the efficiency of retroperitoneal Redon drainage and transvaginal intraabdominal Pezzer drainage. In the first group, lymphocysts developed much less frequently (2.9%) than in the second one (17.2%). Based on this finding, we still use and recommend retroperitoneal Redon drainage [41]. In a few cases, spontaneous absorption of lymphocysts is observed, whereas in other cases they are successfully treated by exploration or percutaneous lymphocystostomy and the use of prolonged suction drainage.

The most severe late complications included postirradiation damage such as intestinal necrosis, ileus and fistulae. Seven of the patients in this group (1.4%) were lost in one year after surgery.

The role of pathological prognostic factors has been examined by several authors [42, 43]. Its importance has not yet been clearly established. We have not found any significant relationship between survival and the histological picture of the patients in our sample as yet. This also applies to the relatively high incidence of our adenocarcinoma cases. Similar experience was reported by Grisby *et al.* [44] and Kleine *et al.* [45] if primary treatment involved surgery. These observations contradict the generally accepted idea, according to which adenocarcinomas are of poorer prognosis than squamous cell carcinomas [46], especially in cases of irradiation being the primary treatment [45]. This may be attributed to the fact that adenocarcinomas exhibit lower radiosensitivity. A similar explanation can account for poorer survival rates in keratinized squamous cell carcinomas as compared to cases of the non-keratinized type, although the latter is less mature and less differentiated histologically [47]. We have found no difference in survival between the keratinized and non-keratinized types.

Special mention must be made of our nine cases complicated with pregnancy. In pregnancy, conization has been an established practice in cases of cervical intraepithelial neoplasia [48]. If histological findings confirm an invasive process (> IA1), the treatment of carcinoma is given priority in early pregnancy, while in midtrimester pregnancies, a six to 12 week delay can be allowed for reaching the highest possible fetal maturity. This should always be discussed with the patient, of course, as we did in our cases. We performed five Wertheim operations to terminate pregnancies in toto in the first trimester, and four operations were done after cesarean section in the last trimester. In both groups, three women survived for longer than five years.

Recently, it has been increasingly recommended to preserve the endocrine function in young women by preserving the ovaries and transposing them in order to protect them from the harmful effects of irradiation. This has been supported by ensuring the possibility for surrogate pregnancies, and also the fact that cervical carcinoma does not give metastases to the ovaries. It must be remembered, however, that, unlike squamous cell carcinoma, adenocarcinoma metastasizes to the ovaries more frequently (in 10% of cases) [49]. These issues were considered with regard to the preservation of the ovaries when we discussed the situation with our patients. In one of these cases, a surrogate mother helped a patient to have a genetic child.

Finally, it seems worth evaluating our results in view of the data in the literature. According to our data, stage-independent, absolute 5-year survival was 71.7%, while tumor-free survival was 69.5%. In Stage IA2, 5-year survival was still 94.4%, but survival rates gradually declined with the progression of the stage of the disease. The same tendency could be observed if cases with lymph node metastasis and the ones free of metastasis were examined separately. Our results are no worse and are even better than the latest figures in the literature. Benedetti-Panici *et al.* [23] observed 64.7% and 46.4% survival rates following neoadjuvant chemotherapy com-

bined with Wertheim operations in Stages IB2-IIB and after primary radiotherapy, respectively. This proportion was 67.1% in our sample. According to the literature, 5-year survival in Stage IB in a wide sample from the period of 1955-1988 fell in the range of 78.4%-91.4% [50], our rate being 87.1%.

In the report by Lee *et al.* [35], 5-year survivals following 438 Wertheim operations were as follows: Stage IB, 86,1%, Stage IIA, 71.7%, and Stage IIB, 60.1%. Survival in lymph node metastasis-free patients was 87.7%, while in cases of positive lymph nodes, it was 73.1%. In Stage IIA, figures were 79.8% and 40.9%. These results almost completely coincide with our data.

Independently of one another, lymph node involvement, tumor size and the depth of invasion (i.e., stage of disease) were the most important factors of prognosis in our cases as well. According to the literature, metastases most often affect the obturator lymph nodes [43]. In the majority of our patients the tumor metastasized to the right obturator fossa, and the five-year survival was 35% in these cases. If lymph node metastases were found in both obturator fossae, the chances of survival were reduced to as low as 24%. Based on our results, it was concluded that metastases in the obturator fossae (especially the right one) present a very poor prognosis.

The survival rates of our patients receiving preoperative and postoperative irradiation are similar to those in the literature. The low incidence of complications, however, suggests that we not only helped the patients to survive longer, but also their health was preserved in the majority of cases. It could be attributed to the fact that, similarly to other cases, the extension of Wertheim's operation was always tailored to the patient, with due consideration of the factors of risk in the tumor given, and within the limits of sensibility [51-53]. We always spared the hypogastric plexus and the blood supply to the ureters and as a result, the majority of our patients became free of symptoms and complaints.

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