Surgical treatment of cancer of the cervix

H. M. SHINGLETON

Summary: Evolution of surgical treatment, the interplay between treatment modalities and specific recommendations for the type and radicality of surgery necessary for the cure of cervical cancer are presented. The place of surgical staging in the management of large volume tumors is addressed. Computerized tomography (CT scans) and Magnetic Resonance Imaging techniques are unlikely to replace surgical staging in the near future due to their lack of sensitivity and specificity, yet these techniques combined with fine needle aspiration (FNA) of suspicious abdominal or pelvic lymph nodes can assist the oncologist in determining the necessity for extended field radiotherapy. In the absence of positive findings by FNA, young healthy patients with large volume tumors should be offered extraperitoneal surgical staging to aid in treatment planning.

Radical surgery for early Stage (IB, IIA) tumors is as likely to result in cure as surgery combined with radiotherapy or chemotherapy, although the availability in the future of more sensitive chemotherapeutic agents may allow such systemic adjuvant therapy to play a larger role. Exenterative surgery still has a place as salvage therapy in this disease but as radiotherapy becomes more effective, its role diminishes.

Key words: Cervical cancer; Diagnosis; Therapy.

It is almost one hundred years since the introduction of radical surgery as treatment of cancer of the cervix. The operation we now call radical hysterectomy was first performed in the United States by John G. Clark in 1895 (1). Shortly thereafter, Ernst Wertheim in Germany began performing a similar operation; his report of 1912 (2) summarized the operative mortality on his first 500 cases. The overall mortality was 19% (Table 1).

Prior to the advent of such curative surgery and the introduction of radiation treatment, cervical cancer was a universally fatal disease. The discovery of external radiation (X-rays = Roentgen 1895) and radium (the Curies 1898) made possible a non-invasive treatment, which was rapidly applied to cancer in general, and cervical cancer in particular. Radium was first used for this purpose in 1903, and the first radium hospital, The Radiumhemmnett, opened in Stockholm in 1910. As a result of these developments, contrasted with the high mortality from radical surgery, radiation treatment gained ascendency. Two decades elapsed after Wertheim's report before Bonney (1932) (3) reported encouraging 5-year survivals for early stage disease, using Wertheim's operation.

His belief was that radiation therapy, while safer, was not curing many patients.

In 1951, Meigs (4) published a larger series showing dramatic cure rates. By midcentury, therefore, improvements in anesthesia and the availability of antibiotics and blood banking had reduced the operative morbidity and mortality drama-

Chairman,
Department of Obstetrics & Gynecology
University of Alabama
at Birmingham Medical Center
Birmingham, Alabama

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Table 1. – *Operative mortality.*

Abdominal radical hysterectomy		
First	100 cases	30%
Second	100 cases	22%
Third	100 cases	17%
Fourth	100 cases	9%
Fifth	100 cases	15%
	500 cases	19%

Ernst Wertheim 1912 (2).

Table 2. – *Prognosis after operation for Stage IB SCC cervix according to nodal status.*

	No. Pts.	5 year survival	
		Neg. Nodes	Pos. Nodes
Wertheim (1912) [2]	184	70%	12%
Bonney (1932) [3]	339	50%	24%
Meigs (1951) [4]	85	88%	26%
Martimbeau (1982) [5]	562	92%	53%
Alvarez (1991) * [6]	401	90%	68%

* University of Alabama at Birmingham

tically. The work of Bonney in London and Meigs in Boston thus reestablished the place of radical surgery for early stage disease. Recent reports demonstrate the excellent 5-year survivals even in presence of pelvic nodal metastases (Table 2).

Surgery for Microinvasive Cancer

Two definitions of microinvasive squamous cell cancer of the cervix exist, one selected over the other by individual surgeons in various world centers. The 1985 FIGO definition (Table 3) limits depth of invasion to 5 mm and includes a second dimension, horizontal spread (limit 7 mm). It also distinguishes minimal stromal invasion (the so-called "single tongue" of invasion extending a mm or less into the stroma) from microcarcinoma. Prior to this recent change in the FIGO definition, the Society of Gynecologic Oncologists of the United States (1974) defined microinvasion as stromal invasion no more than 3 mm from the base of the epithelium; excluded from this definition were individuals who had lymph-vascular space (LVS) invasion. It is known that lesions invading beyond 3 mm but within the 5 mm depth of invasion limit of the FIGO definition have an appreciable (almost thirty-six-fold) increase in node metastasis (7). For this reason, most American gynecologic oncologists prefer the SGO definition over the FIGO. In addition, previous reports have demonstrated another disquieting fact: surgical pathologists are not remarkably accurate in measuring reproducibly depth of stromal invasion; adding a second measurement (of lesion width) would not be expected to improve their accuracy. My own recommendations for treatment of microinvasive carcinoma (Table 5) are that squamous lesions invading to 3 mm without LVS invasion may be treated by conization of the cervix or total hysterectomy without consideration of the nodes. When lesions invade between 3 and 5 mm (without LVS invasion), pelvic node dissection should be a part of the surgical treatment, yet since the parametrial tissues

Table 3. – *FIGO definition of Stage I carcinoma of the cervix (1985).*

Stage 1A. Preclinical carcinomas of the cervix, that is, those diagnosed only by microscopy.

Stage IA1. Minimal stromal invasion.

Stage IA2. Measurable lesions to a depth of 5 mm from the base of the epithelium. A second dimension, the horizontal spread, must not exceed 7 mm.

SGO definition of microinvasive carcinoma (1974)

Invasion of the stroma in one or more places to a depth 3 mm from the base of the epithelium without lymph-vascular space (LVS) involvement.

Table 4. – *Incidence of pelvic lymph node involvement in relationship to depth of stromal invasion (*).*

Authors	Depth of stromal invasion: 3 mm or less — Positive Cases	Nodes	3.1 to 5 mm — Positive Cases	Nodes
Foushee *et al.* (1969)	16	0	13	1
Roche and Norris (1975)	9	0	21	0
Leman *et al.* (1976)	32	0	3	0
Seski *et al.* (1977)	37	0	–	–
Taki *et al.* (1979)	55	0	–	–
Yajima and Noda (1979)	90	0	–	–
Nasumi *et al.* (1980)	106	1	29	4
van Nagell *et al.* (1983)	52	0	32	3
Simon (1986)	43	0	26	1
Total	440	1 (0.2%)	124	9 (7.3%)

* As reported in a series thought to be without biasing factors.

Shingleton (7), 1990 (with permission).

are not involved by direct spread in such small lesions, radical removal of these tissue need not occur.

Because LVS involvement is still viewed as a bad prognostic sign and in order to accumulate further data on this finding, we perform a Type II radical hysterectomy (8) (Fig. 1), as well as a pelvic node dissection.

While adenocarcinoma in situ of the cervix is reasonably well defined, the same cannot be said for microinvasive adenocarcinoma. Conization of the cervix or total hysterectomy might be selected as treatment for the former; however, definite evidence of invasion has led us to perform Type II radical hysterectomy for the latter.

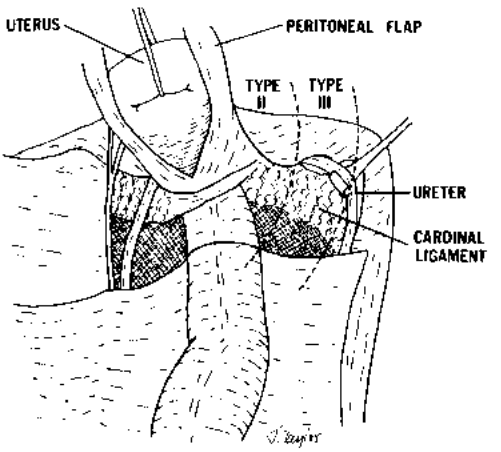

Fig. 1. — Types of radical hysterectomy (after Piver 8). (From Shingleton and Orr 10, with permission).

Surgery for Adenocarcinoma of the Cervix

Adenocarcinoma of the cervix or mixed adenosquamous tumors are treated, stage by stage, in a manner identical to the squamous cancers. While some have argued that adenocarcinoma patients with pelvic node metastases have a poorer survival than matched patients with squamous cell cancer, this has not been our experience.

Table 5. – *Recommendations for microinvasive carcinoma.*

	Positive nodes	
Lesions invading to 3 mm	0.4%	Total hysterectomy or conization
Lesions invading 3-5 mm	<8.0%	Total hysterectomy and pelvic node dissection
Lesions with lymph-vascular space involvement	Good data not available	Type II radical hysterectomy and pelvic node dissection

Surgical Staging

Many investigators have shown (Table 6) that paraaortic node metastases increase in each clinical stage [9]. Significant numbers of women with bulky Stage II or Stage III lesions have extrapelvic disease and thus are not offered a chance of cure with conventional pelvic radiation therapy. Extended field radiation for paraaortic node metastases offers a chance of 5-year survival of 23% to 40% of individuals so treated [10]. Because of the known complications associated with radiation following transperitoneal surgical staging operations (9% to 20% even in those whose radiotherapy doses are held within the 40-51 gray range), current recommendations are that surgical staging should occur through an extraperitoneal approach, which dramatically decreases complications and allows the patient to begin radiation therapy only a few days following the procedure. The technique of Schellhaus [11] (Fig. 2) is recommended by this author. Candidates for surgical staging are those otherwise healthy women who have enlarged aortic nodes but negative fine needle aspirations; normal sized aortic nodes but bulky Stage IB or small Stage IIB lesions; or women with bulky, later stage disease and normal-sized aortic nodes but in whom pelvic control by radiation has been demonstrated. Surgical staging still has a place, since CT scans and MRI scans lack sensitivity and (in the case of MRI) specificity (Table 7).

Table 6. – *Surgical staging.*

Incidence of para-aortic nodal metastases in invasive cervical cancer.

	No. Pts	No. Metas.	Percent
Stage I	259	22	8
Stage II	216	44	20
Stage III	162	48	30
Stage IV	13	3	23
	650	117	18

Collected Series (Averette, Buchsbaum, Nelson, Lagasse, etc.) in Cavanagh, 1985 [9] (with permission).

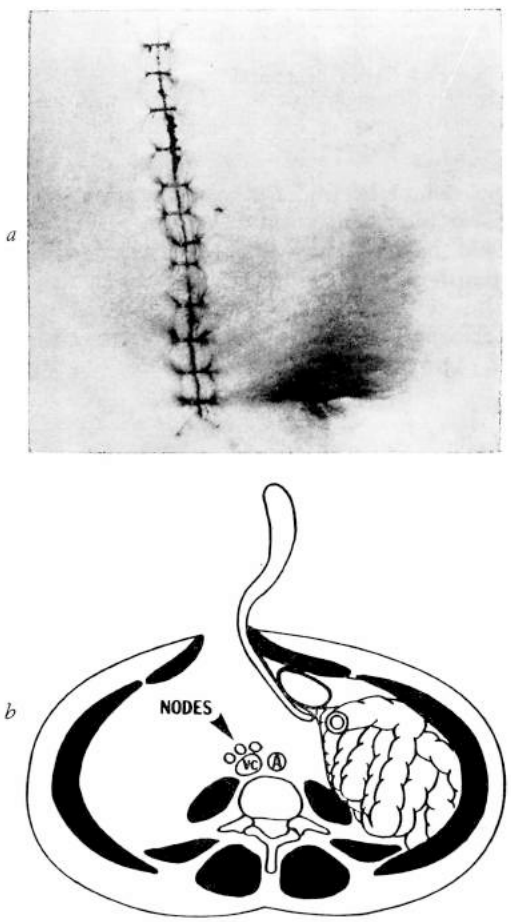

Fig. 2. — Extraperitoneal approach to aortic nodes (after Shellhas [11]). From Shingleton and Orr [10], with permission).

Is laparoscopy useful in treating this malignancy?

Recent developments in laparoscopic techniques and instrumentation hold promise to reduce the need for laparotomy

Table 7. – *Mt. Sinai Study pelvic CT and MRI vs. surgical staging.*

	Sensitivity	Specificity
CT	14%	100%
MRI	28%	64%

Conclusion:
These studies are not individually or collectively better than clinical staging.

Brodman ([12]), 1990 (with permission).

in treating many abdomino-pelvic diseases. Using these techniques, one can easily identify extrauterine spread of disease; intraperitoneal seeding is present in 5%-34% of individuals with advanced stages of cervical cancer and, if present, changes the treatment goals from cure to palliation ([13]). Pelvic nodes can be dissected laparoscopically but no one has to date advocated dissection of aortic nodes in this fashion, perhaps due to difficulty of exposure and risk of severe hemorrhagic complications through vena caval injury. Since the majority of therapy for cancer of the cervix (all stages) is radiotherapeutic, there is little need to ascertain whether pelvic nodes are positive as they are included in the pelvic field and (unless grossly enlarged) presumably receive tumoricidal dosages of radiation. Thus at this writing it is unclear as to what laparoscopic procedures offer that will affect survival in most patients with cancer of the cervix. Clearly, in those individuals who are treated primarily by surgery, lymphadenectomy will be done through a laparotomy incision. It is unlikely that the extended Wertheim-Meigs type hysterectomy can be performed by laparoscopic techniques; the requirement to dissect the ureter and bladder away from the surgical specimen and to achieve hemostasis in the deep pelvis would speak against this.

Considerations for combined surgery and irradiation

Certain situations lead to consideration of combining radiation and surgery in an attempt to cure cancer of the cervix. There is no clearcut evidence, however, that such combined therapy improves survival. Radiotherapy performed prior to radical hysterectomy has been shown to increase urologic complications ([14]) and has not been shown to offer a superior survival rate. Radiotherapy followed by conventional hysterectomy for bulky or barrel-shaped lesions has gained popularity in the last two to three decades and does indeed decrease pelvic recurrences, however has not been shown statistically to improve long term survival; this combination may simply change the pattern of recurrence. Whole pelvic radiotherapy given following radical hysterectomy in which there are pelvic nodal metastases or close margins may also result in decrease in pelvic recurrences, but has not been shown to significantly alter survival rates.

Neoadjuvant chemotherapy

It is known that untreated cervical squamous cell cancers respond to chemotherapy ([15]). It has also been shown that

Table 8. – *Considerations for combined surgery/irradiation.*

Situations	*Comment*
Radiotherapy Radical hysterectomy	Increases urological complications Does not alter survival
Radiotherapy Conventional Hysterectomy (Bulky/barrel shaped lesions)	Decreases pelvic recurrences Does not alter survival
Radical hysterectomy Postoperative radiotherapy (nodal spread; close margins)	Does not alter survival

Table 9. – *Neoadjuvant chemotherapy for cervical cancer.*

	No. Pts	Stage	Agent	Rx	Response	Comments
Friedlander [15] (1983)	35	Adv.	VB Bleo CDDP	NS	18% CR 48% PR	Ca Cx responsive to chemotherapy
Sardi [16] (1986)	33	Loc. Adv.	VC Bleo CDDP	Surg.	NS	Converts inoperable to operable
Kirsten [17] (1987)	47	Loc. Adv.	VB Bleo CDDP	Surg. or RT	66%	Longer recurrence free interval in responders
Rustin [18] (1987)	12	Adv. 10-Stage IV	VC MTX Bleo CDDP	Surg. or RT	60% CR 20% PR	2pts-no tumor in specimen
Kim [19] (1988)	35	Ib, II >4 cm	VB Bleo CDDP	Surg.	46% CR 43% PR	7pts-no tumor in specimen
Benedetti Panici [20] (1988)	33	Loc. Adv. >4 cm	CDDP Bleo MTX	Surg. Surg.	12% CR 63% PR	4pts-no tumor in specimen
Kim [21] (1989)	54	IB, II >4 cm	VB CDDP Bleo	Surg.	81%	22pts microscopic or no tumor in specimen 2yr survival 94%

one can convert inoperable tumors to operable ones [16]. The recent literature (Table 9) demonstrates these facts. While the use of neoadjuvant chemotherapy prior to surgery is promising, one cannot conclude at this time, due to lack of long term follow-up, that it will improve long term survival, even in those who have demonstrated an initial response.

Surgical treatment of radiation failure

It is known that given modern and adequate radiation therapy, very few individuals with cervix cancer will fail only in the central pelvis. This group of women, representing less than 10% of those so treated, are candidates for exenterative surgery as a final attempt to cure their disease. Operative mortality and 5-year survival rates for recent series of pelvic exenterations (Table 10) demonstrate the curative potential of such operations which have been perfected in a few centers. Recent improvements in exenterative surgery have included use of omental flaps for pelvic closure, myocutaneous flaps for va-

Table 10. – *Operative mortality rates and 5-year survival for recent series of pelvic exenterations.*

Authors	No. Pts	Operative mortality	5 years survivors
Ketcham (1970) [22]	162	7 %	38.0%
Brunschwig (1970) [23]	165	8 %	19.9%
Symmonds (1975) [24]	198	8.1%	33.0%
Rutledge (1977) [25]	296	13.5%	42.1%
Averette (1984) [26]	92	10.4% *	37.0%
Shingleton (1989) [27]	143	6.3%	50.0%

* Last 33 patients.

(From Shingleton [27], with permission)

ginal reconstruction, stapled rectal reanastomoses to obviate the need for colostomies, transverse colon and continent urinary conduits, and hyperalimentation, with has reduced operative mortality rates. In the United States, however, continuing improvements in radiation therapy equipment and techniques and the availability of well-trained radiation therapists in most locations have made the candidate pool for exenterative surgery dwindle such that the majority of training centers in the country have too few operable patients to teach the technique to trainees. Pelvic exenteration is thus a vanishing operation compared to the days of orthovoltage radiation, and may be offered to fewer and fewer patients in the future.

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Address reprints requests to:
H. M. SHINGLETON
Dept. Obstet. Gynec.
University of Alabama
Birmingham Medical CTR
Birmingham Alabama 35233-7333 (USA)