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CERVICAL CARCINOMA STAGE I AND II TREATED BY PRIMARY RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY

320 Cases by the Method of Meigs-Taussig
and 350 by the Method of Okabayaschi

By

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Cervical Carcinoma Stage I and II Treated By Primary Radical Hysterectomy and Pelvic Lymphadenectomy

320 Cases by the Method of Meigs-Taussig and 350 by the Method of Okabayaschi

During the period 1953–1969 a total of 681 cases of invasive carcinoma of the cervix uteri, classified clinically as stages I and II, were treated by *primary* surgery in Bispebjerg Hospital, Copenhagen.

The primary procedure in 670 cases was radical Wertheim hysterectomy (67, 68) with pelvic node dissection as described by Taussig 1934 (61). 320 of these patients had the operation by the method of Meigs 1945 (39) and 350 by the method of Okabayaschi 1921 (51).

Eleven patients were excluded, 8 because they had only palliative operations and 3 because they were cystectomized owing to macroscopic invasion of the bladder.

The material does not include any stage 0 cases.

All the operations were carried out in a specialized gynaecological department, where the operative facilities and postoperative management were uniform throughout the period in question.

The present study was designed to compare the survival results and complication rates in the two surgical methods.

In addition, the clinical staging will be compared with the operative findings and microscopic reports. Errors in staging were also evaluated in relation to lymph-node metastases, determined both by step-section and by routine microscopy.

Preoperative pyelograms were compared with operative findings, lymph-node metastases, and survival.

In the various parts of this paper we are quoting the literature for comparison with the present results.

Clinical Material

670 cases of invasive carcinoma of the cervix uteri, clinical stages I and II, were treated primarily by radical surgery.

The diagnosis was confirmed histologically on the basis of biopsies, fractionated curettage, or conization of the cervix.

Out of the 670 malignant tumours 633 were diagnosed histologically as squamous-cell tumours, 31 as pure adenocarcinomas (4.6 %), and 6 as mixed tumours, viz. squamous-cell carcinomas with distinct adenomatous components (0.9 %).

Adenocarcinomas and mixed tumours are included in the total analysis, but will also be considered separately where lymph-node metastases and therapeutic results are concerned.

The material was divided into two groups by surgical method used:

Series 1

comprises 320 patients treated by radical Wertheim hysterectomy with pelvic node dissection according to the *Meigs-Taussig method during the period 1953–1960.* 272 of these patients were admitted direct to the department or referred from other gynaecological departments in the municipality of Copenhagen, while 48 were transferred from the Radium Centre, Copenhagen, as surgery was wanted instead of radiotherapy in order to preserve ovarian function in a number of

patients under 40 years of age. Besides, this latter group included cases with complicating, benign gynaecological disorders.

Series 2

comprises 350 patients treated by the *Okabayaschi operation during the period 1961–1969.* 286 of these patients are also included in a randomized clinical trial performed in collaboration with the Radium Centre, Copenhagen, during the period 1963–1969. The results of this trial are not yet available.

Clinical Staging

The clinical staging in its present form is based upon the League of Nations Classification from 1950, modified in part in 1961 by the introduction of the sub-groups: Ia, Ib, IIa, and IIb (2, 27).

In 1970, moreover, it was decided that cases of cervical carcinoma with radiological evidence of ureteral stenosis with non-functioning kidney were to be allotted to stage III (FIGO (3, 15)).

Table I. Definitions of the different clinical stages in carcinoma of the cervix uteri.
To be used from January 1, 1972.

Invasive carcinoma

Stage I Carcinoma strictly confined to the cervix (extension to the corpus should be disregarded).

Stage Ia — The cancer cannot be diagnosed by clinical examination, early stromal invasion, occult cancer.

Stage Ib — All other cases of stage I.

Stage II The carcinoma extends beyond the cervix but has not extended on the pelvic wall.
The carcinoma involves the vagina, but not the lower third.

Stage IIa — No obvious parametrial involvement.

Stage IIb — Obvious parametrial involvement.

(Annual report. Vol. 15.)

The clinical staging is of decisive importance in analysing and comparing therapeutic results and in planning treatment. It is based exclusively upon the clinical examinations carried out *prior to* the treatment, including cytological studies, colposcopy, biopsy, fractionated curettage, conization, pyelography, cystoscopy, and rectoscopy (Annual Report 1967 and 1973 (2, 3)).

Table II gives the clinical staging of the 670 cases.

Table II. Distribution of cases by clinical stage and operation.

Clinic. stage	No. of cases	Series 1. No.	Series 1. %	Series 2. No.	Series 2. %
I	463	243	75.9	220	62.9
II	207	77	24.1	130	37.1
Ia	67	9	2.8	58	16.6
Ib	396	234	73.1	162	46.3
IIa	127	54	16.9	73	20.9
IIb	80	23	7.2	57	16.2
Total	670	320		350	

In surgical series 1 the classification into sub-groups a and b was retrograde, based upon the clinical data in the case notes.

There is a difference in staging between the two surgical series. In particular, it will be noted that *stage Ia* accounts for 2.8 % in series 1, but for 16.6 % in series 2, presumably because the examination of cytological smears had been introduced in the period 1961–1969.

Stage II makes up 24.1 % of the cases in series 1, but 37.1 % of those in series 2. This increase seems reasonable, as our operative results and survival rates in series 1 were on a level with those of radiotherapy in Denmark (Clemmesen (16)).

Age Distribution

For the total material the mean age was 45.1 years:

Series 1: 42.3 years
Series 2: 47.7 years

Tables III and IV present the distribution of the patients by age and clinical staging.

Table III. Distribution of cases by age and stage in series 1.

Stage	Age group (years)						Total	
	<45		45 – 55		>55			
	No.	%	No.	%	No.	%	No.	%
I	156	65	64	26	22	9	242	76
II	44	56	23	30	11	14	78	24
I + II	200	63	87	27	33	10	320	100

Table IV. Distribution of cases by age and stage in series 2.

Stage	Age groups (years)						Total	
	<45		45 – 55		>55			
	No.	%	No.	%	No.	%	No.	%
I	103	47	73	33	44	20	220	63
II	45	35	37	28	48	37	130	37
I + II	148	42	110	32	92	26	350	100

Preoperative Investigations

The routine investigations done prior to the operation included:

Blood studies.
Electrocardiogram.
Chest radiography.
Pyelography.
Cystoscopy.
Urine analyses.

If indicated, supplemented with:

Rectoscopy.
X-ray examination of the colon.

All patients were assessed for complicating medical diseases and examined by an anaesthetist before surgery.

Among the operated patients 33 (4.9 %) were 20 % or more overweight, 3 had diabetes mellitus, 3 had pulmonary tuberculosis, and 8 were over 70 years of age.

Pyelography

Preoperative pyelography is of such great importance that it deserves special mention.

In 6.9 % of the 670 patients the *preoperative i.v. pyelography disclosed abnormalities without direct relation to the spread of the tumour.*

Twenty-nine patients (4.3 % of 670) had congenital anomalies of the urinary tract:

Renal aplasia in 1 case.
Unilateral double kidney in 1 case.
Bilateral double ureter in 4 cases.
Unilateral double ureter in 23 cases.

Knowing these anomalies is necessary for properly performing the surgical procedure.

Ureteral stenosis, with completely or partially abolished renal function, assigns a case to stage III (FIGO 1970) and thus does not occur in the present material.

Preoperative signs of mild ureteral obstruction and hydronephrosis spell a poor prognosis (cf. Dearing 1953 (17), Shingleton, Fowler & Koch 1971 (56)).

The present material includes 17 cases with mild to moderate preoperative ureteral obstruction and hydronephrosis. Three of these patients exhibited a demonstrable cause of the obstruction (a small ureteral concretion, pregnancy, and in the third case total vaginal prolapse). In the remaining 14 cases the preoperative cystoscopy was normal, and the ureters permitted the ureteral catheter. At operation it was not possible to demonstrate neoplastic infiltration or lymph-node metastases in direct contact with the ureters. Only 2 of the patients were found to have mild inflammation of the parametrium on the side of the mild preoperative obstruction.

Table V gives the distribution of the 14 cases showing preoperatively mild degrees of ureteral stenosis compared with the clinical stages, recurrence rate, and survival.

The 9 patients with preoperative ureteral stenosis who died of recurrence succumbed within the first 2 years. *5-year survival was obtained by 5 of the 14 pts. = 35,7 %,* which is half the 5-year survival in the total material.

Shingleton et al. have reported mild preoperative obstruction to occur in 5.6 % of stage II cases, with a 24 % 5-year survival.

Correspondingly, Dearing found a 33.4 %

one-year survival among 39 patients in clinical stage II having *mild* primary ureteral obstruction (radiotherapy in some cases supplemented with operation).

Table V. Mild degrees of urinary obstruction in relation to stage and survival.

Stage	Total No. of cases	Hydronephrosis			
		No.	%	Died of recurr.	Alive after 5 years
Ia	67	0	0	0	–
Ib	396	5	1.3	3	2
IIa	127	4	3.1	2	2
IIb	80	5	6.3	4	1
Total	670	14		9	5

Among the 14 patients listed in Table V, *three had lymph-node metastases.* One had unilateral mild ureteral obstruction and lymph-node metastases on the same side, and in 2 cases with bilateral nodal metastases there was bilateral mild obstruction. *Operation did not show direct contact between the ureters and lymph nodes in any of these cases.* The obstructive phenomena are presumably due to mild inflammatory processes and other tissue reaction induced by the tumour tissue, but it must invariably be interpreted as a poor prognostic sign.

Complicating Gynaecological Disorders

The operations on the 670 patients revealed a number of benign gynaecological disorders co-existing with the cervical carcinoma, often accidental, asymptomatic findings.

86 had fibromyomas and adenomyosis of the uterus,
3 had pyometra,
7 had simple ovarian cysts or dermoid cysts, and
3 had Brenner tumours.

Thirteen of the 670 patients with stage I and II carcinoma of the cervix uteri were pregnant.

Seventeen patients had carcinoma of the uterine stump.

Surgical Methods

As stated in the introduction, the radical hysterectomy was carried out by two different principles, described by *Meigs* and by *Okabayaschi.* Both are based upon the technique worked out by Wertheim, described in a paper from 1900 (67). The therapeutic results in the first 500 cases were published in 1911 (68).

Both modifications are more radical than the original method. Wertheim did only selective *lymphadenectomy,* whereas the Meigs as well as the Okabayaschi radical hysterectomy is always combined with extensive lymph-node dissection.

The pelvic lymphadenectomy has been described in detail by Taussig 1934 (61). Primarily, it was intended as a supplement to radiotherapy, the current therapeutic principle at the time.

Surgery had been largely abandoned because of the high operative mortality and the serious postoperative complications. However, a few stuck to surgery, among others Bonney (5) and Read (54) in England, Martius (35) in Germany, Werner & Sederl (66), and Antoine (4) in Austria, and Okabayaschi (51) in Japan.

Owing to the great advances in anaesthesiology and operative surgery from the late 30's, the risk of the operative procedures was reduced. During the subsequent years, therefore, the surgical treatment of cervical carcinoma was resumed.

In U.S.A. Meigs (39) of Boston and Brunschwig (7) of New York were the pioneers.

The *Meigs-Taussig radical hysterectomy* with pelvic-node dissection was described in 1939 (39, 40, 41). Its procedure is briefly as follows:

After opening the peritoneum in the utero-vesical pouch, the bladder is separated from the cervix and upper part of the vagina in the midline. The round ligament and infundibulo-pelvic ligament are cut on both sides. The

peritoneum is incised laterally to the ureters, exposing the pelvic wall with vessels and nodes. Thereafter, obligate, i.e. systematic pelvic lymph-node dissection is carried out, removing at the same time all fatty tissue and loose connective tissue around the iliac and hypogastric vessels as well as such tissues in the obturator fossa.

The uterine artery is ligated at its origin, and the ureters are exposed as far as the bladder. The vesicouterine ligaments and cardinal ligaments are resected, the latter as close as possible to the pelvic wall. After the peritoneum in the pouch of Douglas has been opened, the rectum is detached from the posterior vaginal wall. The sacrouterine ligaments are exposed and resected close to the sacral bone. The entire block of organs, consisting of the uterus, upper third of the vagina, ligaments, parametria, and adnexa, is removed *in toto*. After securing haemostasis, the peritoneum is closed over the open vagina, draining the cavity.

Okabayaschi's operation was first described in 1921 (51). This operation is started by exposing the pelvic wall and ligating the uterine artery. The rectovaginal pouch is opened and the rectum isolated from the vagina. Thereupon, the sacrouterine and cardinal ligaments are resected very close to the sacral bone and pelvic wall. Now, the uterus and vagina have been released, and the internal genitalia may be lifted up to the level of the abdominal wall. The ureters, now easily accessible, are freed in a way as atraumatic as possible to avoid injuring the *vascular adventitia which is left in a conus at the site where the ureter opens into the bladder.* The vesicouterine ligaments are resected close to the bladder wall.

The paravaginal column of tissue is ligated, the vagina is opened, sucked clean of secretion, and transected at the junction between its upper and middle third. After the organ block has been removed, the vagina is closed with knotted sutures. Now, the pelvic lymphadenectomy is carried out as in the Meigs operation. Before closing the abdominal wall, a rubber drain is inserted extraperitoneally and led out through the skin laterally in the coccygeal region on both sides.

A detailed description of the two operative methods should be superfluous, as the literature contains thorough descriptions accurately accounting for each individual phase.

Meigs' modification has been discussed in papers by Meigs 1954 (43), Tovell 1973 (63), and Held 1973 (22).

Okabayaschi's technique has been described in his original papers from 1921 (51) and 1929 and also by Yagi 1957 (69, 70).

The technique used in the present study differs from the descriptions only with regard to drainage. The operations were performed by experienced surgeons on the gynaecological staff.

Under general anaesthesia careful disinfection of the vagina was carried out prior to the operation. The bladder was kept empty by an indwelling Foley catheter throughout the procedure.

After the abdominal cavity was opened, the spread and fixation of the tumour were assessed, the parameteria were described. Metastases to other organs were recorded. The liver was palpated, and palpable nodes were described.

If the case was assessed as operable, the operation was performed, as described, by either of the two methods – Meigs-Taussig during the period 1953–1960, Okabayaschi during the years 1961–1969. In both methods the operation was done without inserting ureteral catheters, in accordance with Meigs, in order to avoid injury during the operative manipulations.

Before sending the removed block of organs for histopathological examination, the macroscopic spread of the tumour was described after opening the uterus and vagina by a vertical incision.

Histological examination of the specimens in the present material consisted in ordinary routine investigation of the organ block containing the uterus, vagina, parametria, and ligaments. The study of the lymph nodes was according to two different principles, as described below.

The *lymphadenectomy was obligate* and identical in both methods. In series 1 (Meigs) the dissection was done *before* the radical hysterectomy. In the Okabayaschi operation it was done *after* removal of the uterus, vagina, and adnexa with appurtenant ligaments. The Okabayaschi operation definitely affords a better view of the pelvic cavity and a greater possibility of radically excising fatty tissue with nodes. The latter has also been recommended by Ulfelder in comments to Tovell's description of the Meigs operation 1973 (63).

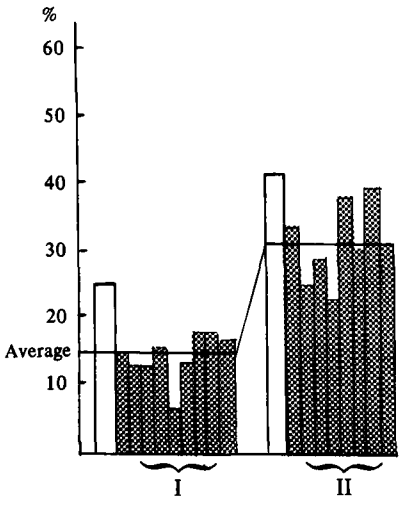
The lymph-node dissection comprises the common and external iliac, hypogastric, and obturator nodes.

Lymph-node Metastases

Metastases to the regional lymph-nodes are of the utmost prognostic importance in cervical carcinoma. Therefore, obligate lymph-node dissection is necessary to obtain the best possible cure.

The number of lymph-node metastases in the individual clinical stages depends primarily upon the *histological technique used.* If each node is isolated and cut into step or serial sections, the metastatic frequency may increase to twice that found by ordinary routine microscopy (Christensen and Lange 1955 (12), Ahrens and Tschoke 1961 (1)).

Table VI. Graphic presentation of the number of positive nodes in the Wertheim operation reported by a number of authors in relation to the number of serial sections after Ahrens & Tschoke 1961 (1).



The white column is serial section.

In collected statistics comprising 4390 cases from the literature, Reiffenstuhl 1967 (55) found 18.57 % nodal metastases in stage I and 33.26 % in stage II. All cases had been treated primarily by surgery, but the list contains a mixture of materials with routine as well as serial examination of the nodes removed by obligate pelvic-node dissection.

Apart from the histological technique and the clinical staging, the radicalness of the lymphadenectomy has a decisive influence upon the metastatic frequency.

If a case is classified into too low a clinical stage, the frequency of metastases in the stage concerned will become too high.

The radicalness of the procedure depends upon several factors, e.g. obesity, complicating gynaecological disorders, infection, disproportionately profuse bleeding during the operation, and not least the surgeon's experience.

Even under the most favourable conditions, one cannot expect to be able to remove more than 90 % of the regional lymph nodes without increasing the operative risk beyond what is ethically permissible.

In our material the nodes were dissected in 4 separate groups, 1 and 2 from the right pelvic wall, groups 3 and 4 from the left.

Group 1: Common and external iliac nodes from the bifurcation of the aorta to the inguinal canal and hypogastric node on the right.

Group 2: Right-sided obturator nodes.

Groups 3 and 4: As groups 1 and 2, but on the left side.

The histological examination of the removed lymph nodes was according to 2 different principles:

1) 158 cases from series 1 were examined histologically by Lange, using *step sections,*

and are included as part of the material of his thesis from 1960 (29).

As Lange started his study in 1950, and as the present study was not instituted until 1953, the patient material and the results are not quite identical.

2) 512 cases were examined histologically by the *ordinary hospital routine* in which only a few sections from each group of nodes are microscoped.

Table VII lists the series of 158 cases showing positive nodes in 28.5 %, distributed by clinical stage and node group.

62.5 % of the positive nodes belong to the iliac and hypogastric groups, 37.5 % to the obturator group.

Table VII. Distribution of metastases in the different groups of lymph nodes.
158 cases examined by *step section microscopy.*

Clinical stage	No. of cases	Positive lymph nodes		Groups of positive lymph nodes			
		No.	%	1	2	3	4
Ia	6	–	–	–	–	–	–
Ib	114	25	21.9	13	9	18	8
IIa	25	12	48.0	6	6	6	5
IIb	13	8	61.5	6	2	6	3
Total	158	45	28.5	25	17	30	16

There is a slight preponderance of left-sided metastases (52.3 %).

Table VIII gives the 512 cases studied by ordinary routine microscopy, which showed 78 cases with positive nodes = 15.2 %.

58.5 % of these nodes were from the iliac and hypogastric group, 41.5 % from the obturator group. Here too there was a slight preponderance of left-sided nodes (53.4 %).

Table VIII. Distribution of metastases in the different groups of lymph nodes.
512 cases examined by *routine microscopy.*

Clinical stage	No. of cases	Positive lymph nodes		Groups of positive lymph nodes			
		No	%	1	2	3	4
Ia	61	1	1.6	0	0	1	0
Ib	282	28	9.9	14	6	15	11
IIa	102	25	24.5	9	5	9	11
IIb	67	24	35.8	11	10	10	6
Total	512	78	15.2	34	21	35	28

Errors in Clinical Stagning

The clinical staging may carry considerable errors, the operative findings not always being consistent with what might be expected according to the clinical classification. The first

Table IX. Surgical and pathological classification of carcinoma of the uterine cervix.

Class	*Criteria*
0	Carcinoma in situ, also known as preinvasive carcinoma, intraepithelial carcinoma, microcarcinoma
A	Carcinoma is strictly confined to the cervix
A_0	After a positive biopsy of infiltrating carcinoma, no tumour is found in the cervix in the surgical specimen
B	Carcinoma extends from the cervix to involve the vagina, except the lower third. The carcinoma extends into the corpus. The carcinoma may involve the upper vagina and corpus. Vaginal and/or uterine extension may be by direct spread or be metastatic
C	Carcinoma has involved paracervical and/or paravaginal tissue by direct extension, by lymphatic vessels, or in nodes within such tissues. Vaginal metastases and/or direct extension into the lower third of the vagina
D	Lymph vessel and node involvement beyond paracervical and paravaginal regions. This includes all lymphatic vessels and/or nodes in the true pelvis, except as described in Class C. Metastasis to the ovary or tube
E	Carcinoma has penetrated to the serosa, musculature, or mucosa of the bladder, and/or to the colon or rectum
F	Carcinoma involves the pelvic wall (fascia, muscle, bone, and/or sacral plexus)

From Meigs, J. V., & Brunschwig, A.: Amer J Obstet Gynec **64**: 414, 1952.

studies done to elucidate the magnitude of this misinterpretation and its causes were performed by int. al. Döderlein & Baatz 1934 (18), Lauterwein 1947 (30), and Antoine 1952 (4).

Increasing use of surgery in the treatment of cervical carcinoma combined with histopathological examination of operative specimens gave rise to a surgical-pathological classification, finally worked out by Meigs & Brunschwig 1952 (44).

Mistakes in the clinical staging are due to several factors. For instance, it is difficult to distinguish stage Ib from IIa, as the junction of the portio and the vaginal mucosa is often vague and difficult to assess in the presence of hypertrophic, exophytic, or papillomatous types of tumour, preventing inspection of the transitional zone. In other cases the cancer may grow intra- or sub-epithelially down into the vaginal wall, so that it is not disclosed until at histological examination of the excised organs.

The parameterial tumour infiltrations in stage IIb may also be misinterpreted, as often they are masked by inflammatory changes and connective-tissue hyperplasia, which may at times be so marked as to make up the greater part of the palpated infiltrate in cervical cancer. In other cases the parameterial extension of the tumour is so slight that it is not disclosed until the histological examination.

Encroachment of the tumour upon the endometrium may also be difficult to assess preoperatively.

By definition cases with palpable lymph-node metastases on bimanual recto-vaginal examination are classified in clinical stage III, whereas cases showing only histologically demonstrated nodal metastases are included in stage I or II.

If a material of cervical carcinoma treated exclusively by surgery is tabulated by international clinical staging as well as by surgical-pathological grouping by the Meigs and Brunschwig system 1952 (44), it is possible to read directly how many cases have been classified correctly at the clinical examination as well as the mistaken assignment to the individual stages.

Modified Meigs-Brunschwig System

With a view to analysing the present material for errors in clinical staging, we chose a corresponding classification into surgical-pathological groups based *exclusively upon the localization of the primary tumour in the uterus, vagina, and parametria,* paying no regard to any positive nodes in the operative specimen.

Table X comprises 603 patients in clinical stages Ib, IIa, and IIb out of the total of 670 cases. The 67 cases in stage Ia are excluded in this connection, as all were correctly staged.

The surgical-pathological groups A, B, and C in Table X correspond to the definition in the Meigs-Brunschwig system. Group D, which comprises all cases with histologically positive nodes, is divided into 3 sub-groups,

Table X. Clinical error calculated in relation to the surgical-pathological extent of the primary tumour (error in heavy figures).

Clinical stage	No. of cases	Surgical-pathological classification									Clinical errors			
		A + DA			B + DB			C + DC			$I_b \leftrightharpoons II_a$		Parametrial infiltr.	
		A	DA	Total	B	DB	Total	C	DC	Total	No.	%	No.	%
Ib	396	320	29	349	20	9	**29**	3	15	**18**	29/396	7.3	18/396	4.5
IIa	127	7	10	**17**	81	18	99	2	9	**11**	17/127	13.4	11/127	8.7
IIb	80	0	5	**5**	14	4	**18**	34	23	57	–	–	23/80	28.8
Total	603			371			146			86				

DA, DB, and DC, by localization of the tumour in the uterus, vagina, and parametria.

Histo-pathologically the operative specimens were studied by ordinary routine microscopy, without the use of serial or step sectioning except for the lymph-node study by Lange (29).

By this means we obtain a uniform basis for calculating errors in clinical staging, as the groups by the two classifications are directly comparable.

The lymph-node error which cannot be recognized in the current clinical methods, can be calculated separately, but in our opinion this is not of the same practical significance in the staging.

Table X gives the following information:

Stage Ib: 396 patients.

349 of these cases were correctly staged (88.1 %).

In 29 patients there was encroachment of the tumour upon the vaginal wall or endometrium (7.3 %). In 5 of them the downgrowth into the vaginal mucosa was demonstrable only histologically. In 18 cases there was tumour tissue in the parametria (4.5 %).

Stage IIa: 127 patients.

99 cases were correctly staged (78 %).

In 17 cases there was no spread in the vagina or endometrium postoperatively. In 11 cases histological examination revealed carcinomatous tissue in the parametria which exhibited clinical changes (8.7 %).

Stage IIb: 80 patients.

57 cases were correctly staged (71.2 %).

In 23 cases there were no malignant changes in the parametria. 19 of these patients had been staged by radiologist as well as gynaecologist.

In 14 patients the infiltration was of inflammatory nature, without cancer tissue, 4 patients had small fibromas in the uterine wall, 2 had previously undergone gynaecological operation leaving scar tissue in the parametria, and in 3 cases there was no explanation of the erroneous staging.

Mitani et al. 1956 (45) have published the results of a comprehensive histological investigation using *serial sections of the parametria* and lymph-node specimens after radical hysterectomy with pelvic lymphadenectomy. In 31.5 % they found, unexpectedly, cancer tissue in the parametria in stages I and IIa, and in patients with stage IIb only cancer at the site of the palpated parametrial infiltration in 54.2 % of the cases. In the same material they demonstrated metastases to regional lymph nodes in serial sections from 30.9 % in clinical stage I and in 33.6 % in stage II.

Errors due to parametrial changes have also been reported by Bruntsch 1957 (10). In *step-section microscopy* of parametria from 115 patients subjected to radical vaginal hysterectomy he found parametrial cancerous changes in 15.5 % in clinical stages Ib and IIa. In stage IIb he demonstrated cancer tissue in only 31.8 %, whereas 41.0 % had merely inflammatory lesions and 27.2 % no pathological changes despite the findings in the bimanual examination.

Lohe, Bräunig & Zander 1969 (32) demonstrated a clinical misinterpretation in 54 %, 10 % of which had been overstaged and 44 % understaged. The limit between stage Ib and IIa, i.e. downgrowth of tumour into the vagina, had been erroneously estimated in 17 %. Despite negative findings in the bimanual examination in the same stages, 19 % were found to have tumour tissue in the parametria. In stage IIb (12 patients) *no* case was correctly classified. In the same material nodal metastases were demonstrated in 30 % by the step section method in stages I and II.

In the present material of 670 stage I and II cases routine microscopy (Table X) showed that the total clinical error in distinguishing between stage Ib and IIa was 46/523 = 8.8 %. Lohe et al. 1969 (32), using a special histological technique (Matuscka 1962 (38)), found the corresponding value to be 17 %.

Unrecognized *parametrial cancer* was found by routine microscopy in the present material in stages Ib and IIa in 29/523 = 5.5 %. Lohe et al. (32) found 19 %, Bruntsch (10) 15.5 % by step sectioning, Mitani (45, 46) 31.5 % by

serial sectioning, all in stages I + IIa.

Parametrial cancer in stage IIb was correctly classified in the present material in 71.2 %, in Mitani's in 54.2 % (serial sectioning), in Bruntsch's in 31.8 %, and in Lohe et al.'s (32) in 0 %.

The total error (including lymph nodes) according to the Meigs-Brunschwig surgical-pathological system, may be read from Table X, but in our material it was calculated separately for the group of 512 patients whose lymph nodes were studied by routine microscopy (Table XI) and the group of 158 having step-sectioning of the lymph nodes (Table XII).

Table XI. Meigs-Brunschwig's surgical-pathological classification of 512 cases from the material with *routine microscopy* of the nodes.
The total error (including lymph nodes).

Clinical stage	No. of cases	A_0	A	B	C	D	% pos. nodes	Total errors
Ia	61	24	36	0	0	1	1.6	1.6
Ib	282	0	235	17	2	28	9.9	16.7
IIa	102	0	4	68	5	25	24.5	33.3
IIb	67	0	0	14	29	24	35.8	56.7

Table XII. Meigs-Brunschwig's surgical-pathological classification of 158 cases from the material with *step-section microscopy* of the nodes.
The total error (including lymph nodes).

Clinical stage	No. of cases	A_0	A	B	C	D	% pos. nodes	Total errors
Ia	6	4	2	0	0	0	0	0
Ib	114	0	85	3	1	25	21.9	25.4
IIa	25	0	2	10	1	12	48.0	60.0
IIb	13	0	0	0	5	8	61.5	61.5

In our opinion, these values afford no measure of errors in the clinical assessment of tumour spread, as nodal metastases are never palpable in stages I and II, and since moreover the number varies enormously according to microscopic method, etc. (*vide supra*). Patients with positive lymph nodes are not included in the surgical-pathological assessment of tumour spread in the uterus, vagina, and parametria.

The error in the clinical staging according to our analysis of the *total material,* as outlined on p. 12 and presented graphically in the column diagram Table XIII and Table XIV, shows a shift of only 3–4 % within stages Ib and IIa and of only 1 % in IIb, stage Ib containing a number of patients with locally more extensive cancer, distributed on the surgical-pathological groups B + DB and C + DC.

Table XIII. The total material in clinical stages and surgical-pathological groups.

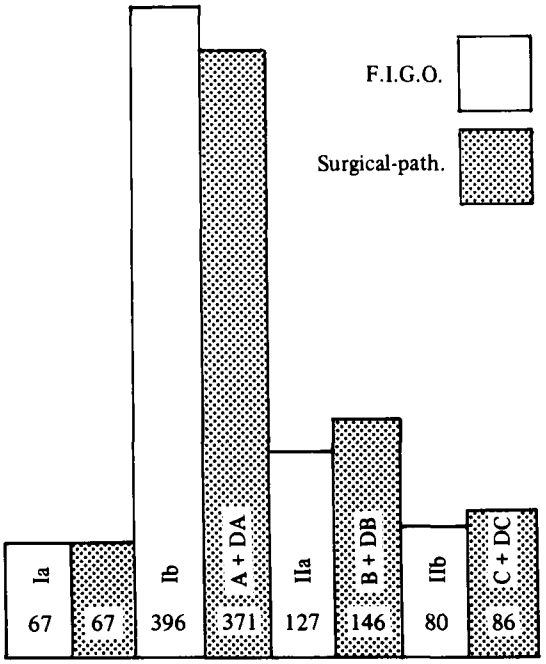


Table XIV. The total material in clinical stages and surgical-pathological groups.

Clinical stage		Surgical-pathological group	
670 patients		670 patients	
Ia	10.00 %		10.00 %
Ib	59.10 %	A + DA	55.37 %
IIa	18.96 %	B + DB	21.79 %
IIb	11.94 %	C + DC	12.84 %

The total error according to the Meigs-Brunschwig surgical-pathological system, classifying by positive lymph-node findings, affords – as demonstrated by our values after routine or step-section microscopy of the nodes – such a skew distribution that the method is inapplicable for comparing the survival results in the two surgical series. (Table XI and Table XII).

Results

Follow-up

The data concerning the results obtained in the 670 stage I and II patients, by primary surgical treatment using the two operative methods, were collected partly from our own files, partly from the Radium Centre, Copenhagen, and other hospitals where the patients have been admitted later.

Information about the time of death of non-admitted patients was supplied by the national registries.

The cause of death was confirmed by data from post-mortem reports, the Cancer Registry, and the Bureau of Medical Statistics.

Thereby, we have obtained satisfactory information about all the patients but 3 who have emigrated, address unknown.

Statistical Analysis

The collected data concerning time and cause of death (recurrence, intercurrent diseases, other types of cancer) were statistically analysed by the actuarial method with a view to corrected survival rate. The analysis was undertaken within each clinical stage and within each surgical-pathological group treated by the two surgical methods.

Methods of Calculating Survival Curves – Survival Curves After Operation

The calculations were carried out as follows, using the symbols:

d_t number dying between t–1 and t years after the operation,

a_t number alive at end of the follow-up period between t–1 and t years after the operation,

l_t number alive t years after the operation,

q_t estimate of the probability of dying between t–1 and t years after the operation,

L_t estimate of the probability of being alive at t years after the operation (plotted as dots on the survival curve).

d_t and a_t are the observations. l_t is calculated successively by means of the formula

$$l_t = l_{t-1} - (d_t + a_t).$$

This gives

$$q_t = \frac{d_t}{l_{t-1} - \frac{1}{2} a_t}$$

and so on successively.

$$L_t = L_{t-1} \cdot (1 - q_t),$$

as

$$L_0 = 100.0\ \%.$$

The above does not pay special regard to operative deaths, but in constructing the curves these patients are considered as having died at time zero, the calculation being made as if the period of operative deaths was a period prior to the first year after the operation. In the survival curves for the period 1961–69 the first year after the operation is divided into the first quarter, second quarter, and latter half. These periods are treated as if they were whole years, the calculations being made in the corresponding manner, regardless of the length of the period to which they apply.

Curves of Expected Survival in the Population

In calculating the curves for the expected survival in the population, use was made of the age distribution of the patients into 5-year age groups at operation. For each of these age groups calculation was made of the expected number of survivors at 5 years after the operation, at 10 years, and – for the period 1953–60 – at 15 years and at 20 years. By summing up the expected number in the age groups for a given number of years it is possible to ascertain how many are expected among all the patients. The percentage expected to survive may then be calculated by dividing this expected number by the total number of patients.

In analysing the period 1953–60 the population experience 1956–60 was applied to the first 5 years after the operation, for the second 5 years the experience from the period 1961–65, and for the third and fourth 5-year periods the experience from 1966–70 as apparent from the mortality tables in various editions of Statistisk Årbog (Danish Statistical

Yearbook). In the case of the period 1961–1969 the population experience from the period 1966–70 was applied to both 5-year periods.

The calculations were performed as follows:

In the mortality table there is listed for each 1-year age group a number of survivors – say L_x for age x – starting with L_0 = 100.000. Thus, if the expected number of survivors at 5 years is to be found for a group of n persons in the age group from x to x + 4 years, this is done by calculating

$$n \cdot \frac{L_{x+5} + L_{x+6} + L_{x+7} + L_{x+8} + L_{x+9}}{L_x + L_{x+1} + L_{x+2} + L_{x+3} + L_{x+4}}$$

(Arne Nielsen)

Therapeutic Results

For comparison of the therapeutic results, the material of both surgical series was classified partly by the international clinical method (FIGO) and partly by a *Modified Meigs-Brunschwig System* based upon the surgical-pathological findings. The statistical calculation of survival was carried out and the corresponding curves plotted on the basis of both principles of classification.

Calculation of Survival Based Upon the Clinical International Classification

Series 1: 320 cases treated during the period 1953–60 by primary radical hysterectomy with pelvic lymphadenectomy by the method of Meigs. The follow-up period is from 11 to 19 years, and the corrected survival rate was calculated for 5, 10, and 15 years.

Table XV gives a survey of the cases distributed by clinical stage: Ia, Ib, IIa, and IIb, and surgical-pathological groups: A, B, C, and D with sub-groups DA, DB, and DC. The table is supplemented by calculation of the erroneous assessment in the individual clinical stages found by a modified Meigs-Brunschwig system, since these values may be of importance in comparing the survival curves.

Table XVI lists data concerning deaths and loss to follow-up for the clinical stages in series 1.

Table XVI. Series 1. Clinical stage (FIGO), causes of death, and cases lost to follow-up.

Clinical stage	No. of cases	Dead					Cases lost to follow-up
		Total	Op. mortal.	Recurrence	Intercurr. dis.	New cancer	
Ia	9	3	0	1	2	0	0
Ib	234	63	2	49	9	3	0
IIa	54	21	0	16	3	2	1
IIb	23	13	0	13	0	0	0
Total	320	100	2	79	14	5	1

Comments:

Stage Ia: 9 patients.

None had lymph-node metastases.

One patient died of recurrence 5–6 years after the operation.

Two patients died of intercurrent diseases after 11 and 17 years' follow-up, whereas the remaining patients were alive at the end of 1972.

Table XV. 320 patients *(series 1)* classified by clinical stage and surgical-pathological group. Calculation of clinical error (error in heavy figures).

Clinical stage	No. of cases	Surgical-pathological classification							Clinical errors	
						D				
		A_0	A	B	C	DA	DB	DC	No.	%
Ia	9	6	3	0	0	0	0	0	0	0
Ib	234	0	188	**11**	**2**	21	**5**	**7**	25/234	10.7
IIa	54	0	**5**	30	**1**	**7**	4	**7**	20/54	37.1
IIb	23	0	0	**1**	11	**3**	**1**	7	5/23	21.8
Total	320	6	196	42	14	31	10	21	50/320	15.6

Stage Ib: 234 patients.

Two patients died in conjunction with the operation, one of profuse venous bleeding and the other one of pulmonary embolism 3 weeks after the operation.

Forty-nine patients died of recurrence, 38 of them within the first 5 years, the remaining 11 during the subsequent 5–11 years.

In 9 cases the cause of death was intercurrent disease, in 3 cases another type of cancer.

171 of the patients were alive at the end of 1972.

Five-year survival: 80.9 %, 10-year survival: 78.1 %, and 15-year survival: 78.7 %.

Stage IIa: 54 patients.

One patient was excluded because she was lost to follow-up. Sixteen died of recurrence, 14 of them within 5 years, the remainder before the end of the 7th year of follow-up.

Stage IIb: 23 patients.

Twelve patients died of recurrence within 5 years, one within 6–7 years. In this patient nodal metastases had been found in all 4 node groups. Deaths from intercurrent diseases or another type of cancer did not occur in this stage.

The 5-, 10-, and 15-year survival was 49.1 %, 46.0 %, and 48.4 %.

Series 2: 350 patients with cervical carcinoma treated during the period 1961–69 by primary radical hysterectomy with pelvic lymphadenectomy by the method of Okabayaschi. The maximum follow-up period in this series is 11 years, minimum 5 years. Calculation of the corrected survival was carried out for 5-year and 8-year follow-up.

A survey of the 350 cases, distributed by clinical stage and surgical-pahtological group, may be found in Table XVII which also includes the magnitude of the clinical errors.

Data concerning deaths and loss to follow-up for each clinical stage in series 2 are collected in Table XVIII.

Table XVIII. Series 2. Clinical stage (FIGO), causes of death, and cases lost to follow-up.

Clinical stage	No. of cases	Dead					Cases lost to follow-up
		Total	Op. mortal.	Recurrence	Intercurr. dis.	Other cancer	
Ia	58	4	1	2	1	0	0
Ib	162	32	0	26	2	4	1
IIa	73	28	1	25	0	2	1
IIb	57	28	0	25	3	0	0
Total	350	92	2	78	6	6	2

Stage Ia: 58 patients.

One patient died in conjunction with the operation of acute ulcerative colitis with septicaemia 18 days after the operation.

Two patients died of recurrence 2–3 years after the operation. One of them developed a vaginal recurrence one year after the hysterectomy. On pathological revision of the operative specimen it was discovered that the extent of the tumour had been misinterpreted at the primary examination. The other patient

Table XVII. Series 2. 350 patients classified by clinical stage and surgical-pathological group. Calculation of clinical error (error in heavy figures).

Clinical stage	No. of cases	Surgical-pathological classification							Clinical errors	
						D				
		A_0	A	B	C	DA	DB	DC	No.	%
Ia	58	22	35	0	0	1	0	0	0	0
Ib	162	0	132	**9**	**1**	8	**4**	**8**	22/162	13.6
IIa	73	0	**2**	51	**1**	**3**	14	**2**	8/73	11.0
IIb	57	0	0	**13**	23	**2**	**3**	16	18/57	31.6
Total	350	22	169	73	25	14	21	26	48/350	13.7

developed a recurrence on the pelvic wall 2 years after the primary operation. It was treated by irradiation, but the patient succumbed one year later.

Only one patient in this stage had positive nodes in just one group at routine microscopy. This patient is alive 7 years after the operation. One patient died of another disease – aplastic anaemia – after 18 months' follow-up.

5-year and 8-year survival: 93.5 % and 95.4 %.

Stage Ib: 162 patients.

One patient was lost to follow-up. Twenty-four patients died of recurrence within 5 years. Another two died of recurrence after 5–8 years.

Two patients died of intercurrent diseases 5–7 years after the operation, 4 of another type of cancer.

5-year and 8-year survival: 86.1 % and 82.2 %.

Stage IIa: 73 patients.

One patient was lost to follow-up.

One patient died of pulmonary embolism 10 days after the operation. Twenty-one died of recurrence within 5 years, 4 after 5–8 years. Two patients died of another type of cancer.

5-year and 8-year survival: 68.7 % and 60.9 %.

Stage IIb: 57 patients.

Twenty-five died of recurrence, including 23 within 5 years. Three died of intercurrent diseases.

5-year and 8-year survival: 58.2 % and 50.0 %.

The survival Table XIX and curves (Fig. 1–4) for the two surgical series show the same course in the clinical stages. However, there are small differences in stage Ia and stage IIb, but they are not comparable because of the small number of stage Ia patiens in series 1 and because of the clinical errors in stage IIb in series 2 in which 18 cases were overstaged, i.e. rate with a lower mortality (Table XVII).

Table XIX. Present material – Corrected survival for series 1 and 2, calculated for clinical stage and sub-stages.

Series 1.

Clinical stage	No. of cases	Corr.survival-rate 5-year	10-year	15-year
Ia	9	97.9	93.6	85.0
Ib	234	80.9	78.1	78.7
IIa	54	71.4	67.8	66.2
IIb	23	49.0	46.1	48.4
I	243	81.5		
II	77	64.7		

Series 2.

Clinical stage	No. of cases	Corr.survival-rate 5-year	8-year
Ia	58	93.5	95.4
Ib	162	86.1	82.2
IIa	73	68.7	60.9
IIb	57	58.2	50.0
I	220	88.1	
II	130	64.1	

If the two surgical series are compared in undivided stage I and II (Table XIX), there is no statistically significant difference between the two surgical methods for stage II, but at the 5 % significance limit for stage I, as series 2 (Okabayaschi) showed a 5-year corrected survival of 88.1 % against 81.5 % in series 1 (Meigs) for stage I.

Calculation of Survival on the Basis of the Surgical-Pathological Classification

In the calculation of survival according to clinical stage, an analysis was made according to surgical-pathological groups in surgical series 1 and 2, calculating the corrected survival rate and the corresponding curves for each group of patients.

As already mentioned, the present material was grouped according to the Modified Surgical-Pathological Classification described in the section on the clinical misinterpretation,

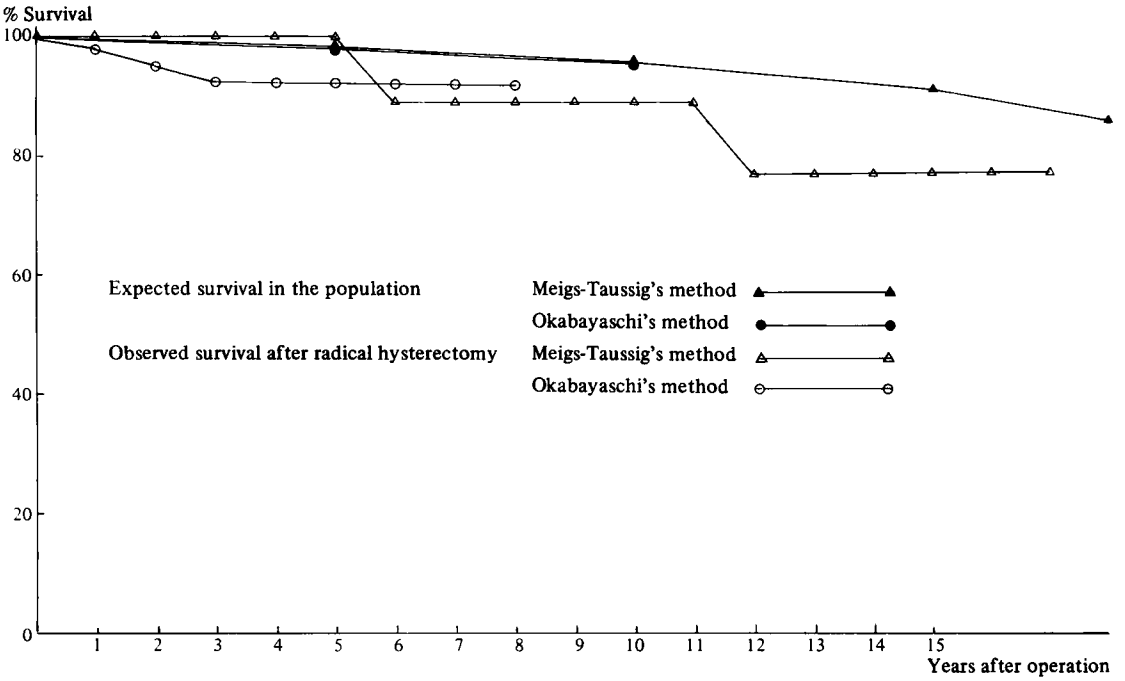


Fig. 1. Clinical Stage Ia.

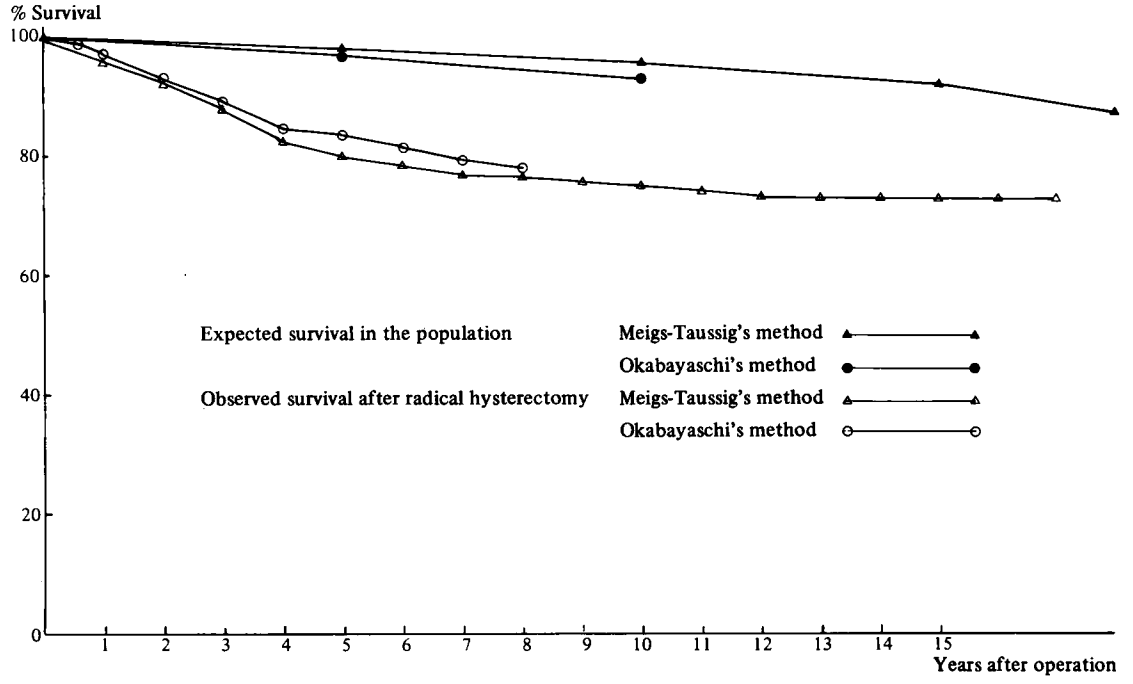


Fig. 2. Clinical stage Ib.

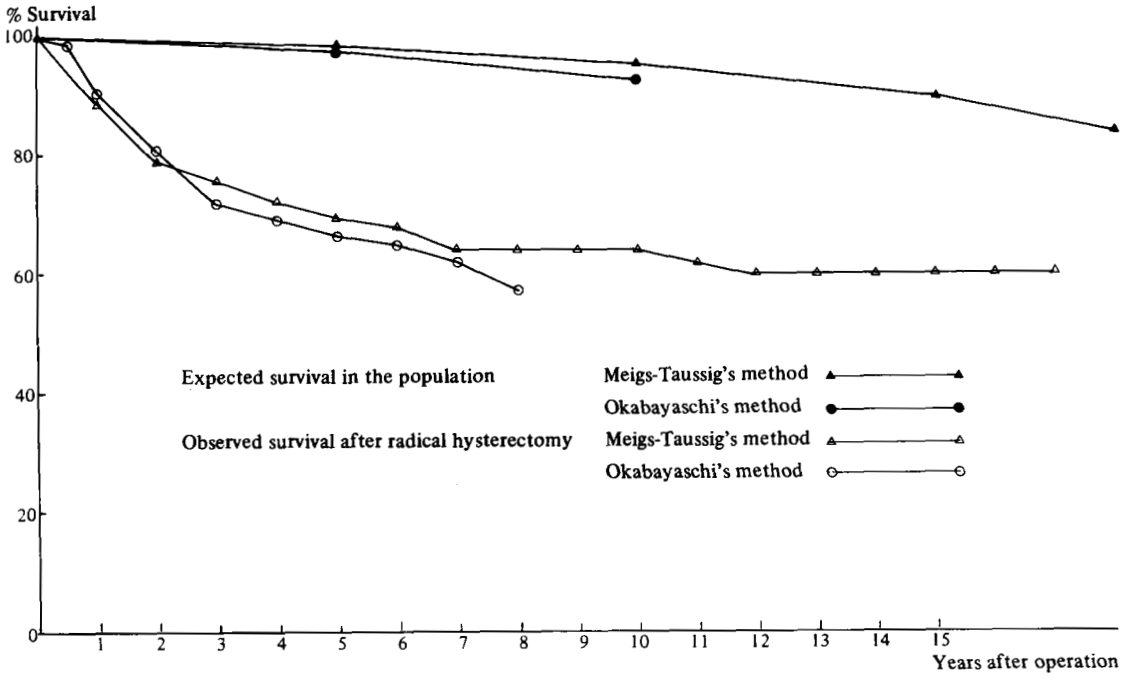


Fig. 3. Clinical stage IIa.

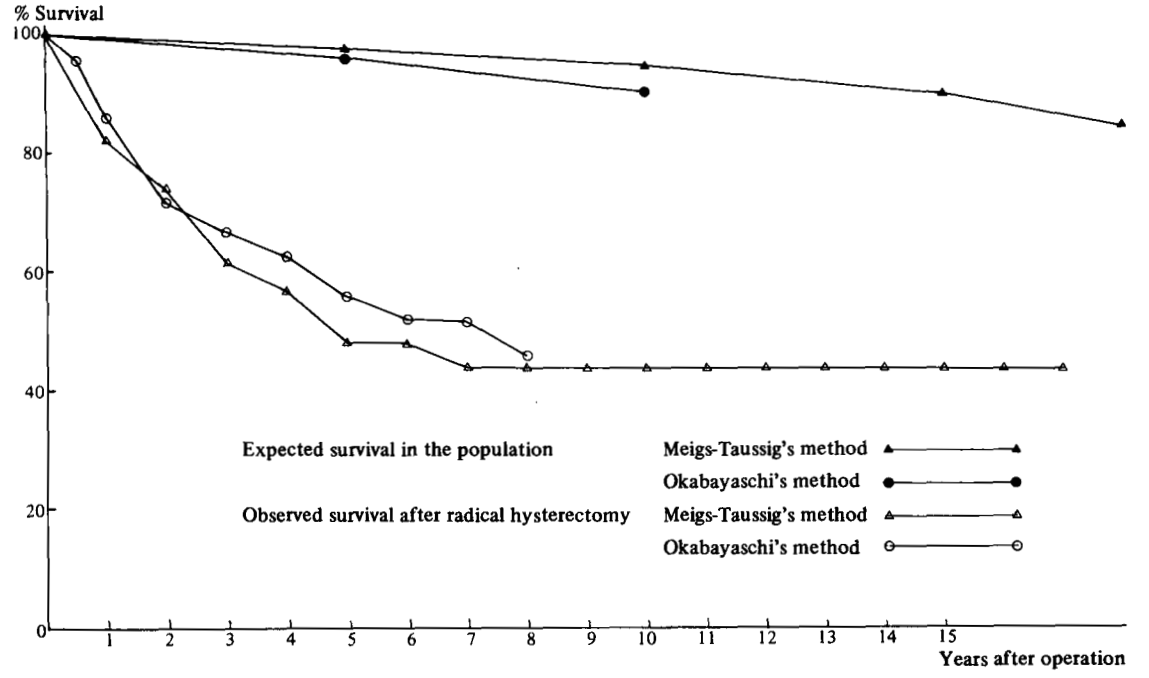


Fig. 4. Clinical stage IIb.

based exclusively upon the spread of the primary tumour in the uterus, vagina, and parametria, without paying regard to the demonstration of lymph-node metastases. Survival was calculated in both series for the groups: A + DA, B + DB, and C + DC, which are comparable with the clinical stages.

Series 1.

Data concerning the material and its distribution by clinical stage and surgical-pathological group are given in Table XV. Information concerning causes of death and loss to follow-up is supplied, for patients in the various surgical-pathological groups, in Table XX.

Table XX. Series 1. Surgical-pathological classification, causes of death, and cases lost to follow-up.

Surg.-path. group	No. of cases	Dead					Cases lost to follow-up
		Total	Op. mortal.	Recurrence	Intercurr. dis.	Other cancer	
A + DA	227	61	2	45	10	4	1
B + DB	52	16	0	12	4	0	0
C + DC	35	23	0	22	0	1	0
Total	314	100	2	79	14	5	1

6 A_0 patients are not included. All are alive.

Comments:

Group A + DA: 227 patients.

This group includes 3 patients from clinical stage Ia. Six patients were excluded, as all were alive at the end of the follow-up period and as they belonged to surgical-pathological group A_0.

Two patients died in conjunction with the operation (identical with those mentioned under Ib). Forty-five died of recurrence, 35 of them within 5 years, 10 patients died of intercurrent diseases, and 4 of another type of cancer. One was lost to follow-up.

5-year, 10-year, and 15-year survival: 82.7 %, 79.3 %, and 79.6 %.

Group B + DB: 52 patients.

Twelve patients died of recurrence, 10 within 5 years. Four patients died of intercurrent diseases.

5-year, 10-year, and 15-year survival: 78.6 %, 75.2 %, and 76.5 %.

Group C + DC: 35 patients.

Twenty-two patients died of recurrence, 19 of them within 5 years.

5-year, 10-year, and 15-year survival: 43.8 %, 42.2 %, and 36.9 %.

Series 2.

Table XVII presents the distribution of the patients by stage and group. Data concerning deaths and loss to follow-up may be seen from Table XXI.

Table XXI. Series 2. Surgical-pathological classification, causes of death, and cases lost to follow-up.

Surg.-path. group	No. of cases	Dead					Cases lost to follow-up
		Total	Op. mortal.	Recurrence	Intercurr. dis.	Other cancer	
A + DA	183	28	1	21	2	4	1
B + DB	94	33	0	28	3	2	1
C + DC	51	31	1	29	1	0	0
Total	328	92	2	78	6	6	2

22 A_0 patients are not included. All were alive at end of follow-up period.

Group A + DA: 183 patients.

The group includes 36 patients from clinical stage Ia, while 22 patients of group A_0 were excluded from the calculation, as all are alive without recurrence.

Of the 183 patients 1 was lost to follow-up, 21 died of recurrence, 16 of them within 5 years. Two died of intercurrent diseases and four of another type of cancer.

5-year and 8-year survival: 90.1 % and 86.8 %.

Group B + DB: 94 patients.

One patient was lost to follow-up. Twenty-eight died of recurrence, 23 of them within 5 years. In 3 patients the cause of death was

intercurrent disease, in 2 another type of cancer.

5-year and 8-year survival: 73.4 % and 64.8 %.

Group C + DC: 51 patients.

Twenty-nine patients died of recurrence, 28 of them within 5 years. One patient died of an intercurrent disease.

5-year and 8-year survival: 44.3 % and 35 %.

In accordance with the survival calculation for the international clinical stages I and II (Table XXII) in the two surgical series, uniform survival results were found in the two series by surgical-pathological groups within: B + DB and C + DC (corresponding in extent to clinical stage II).

In A + DA (corresponding in extent to clinical stage I) the Okabayaschi-operated patients showed a significantly better survival (90.1 % against 82.7 %).

In B + DB (corresponding to stage IIa) the Meigs-operated patients (a total of 52) showed a higher corrected survival, presumably because of a lower frequency of nodal involvement despite the fact that in series 1, 20 of these patients the nodes were step sectioned (Table XXIV).

The survival curve for groups C + DC of both series coincides.

Table XXII. Present material. Corrected survival calculated for surgical-pathological groups.

Series 1.

Surg.-pathol. group.	No. of cases	Corr.survival rate		
		5-year	10-year	15-year
A + DA	227	82.7	79.3	79.6
B + DB	52	78.6	75.2	76.5
C + DC	35	43.8	42.2	36.9

Series 2.

Surg.-pathol. group.	No. of cases	Corr.survival rate	
		5-year	8-year
A + DA	183	90.1	86.8
B + DB	94	73.4	64.8
C + DC	51	44.3	35.0

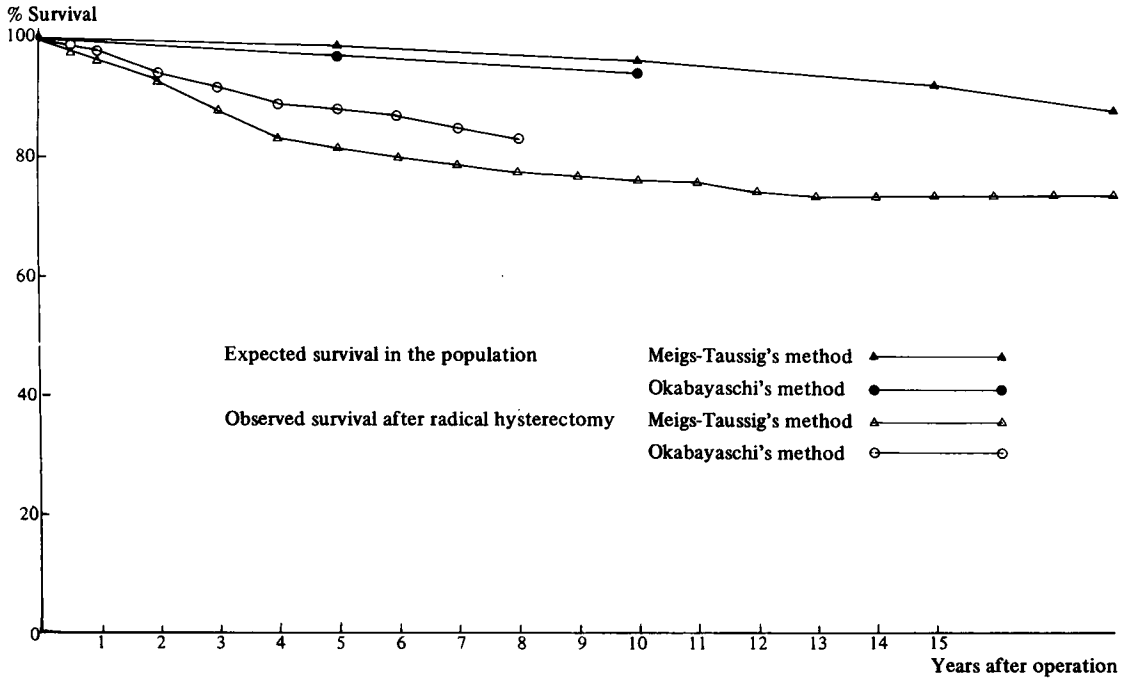


Fig. 5. Surgical-pathological group A + DA.

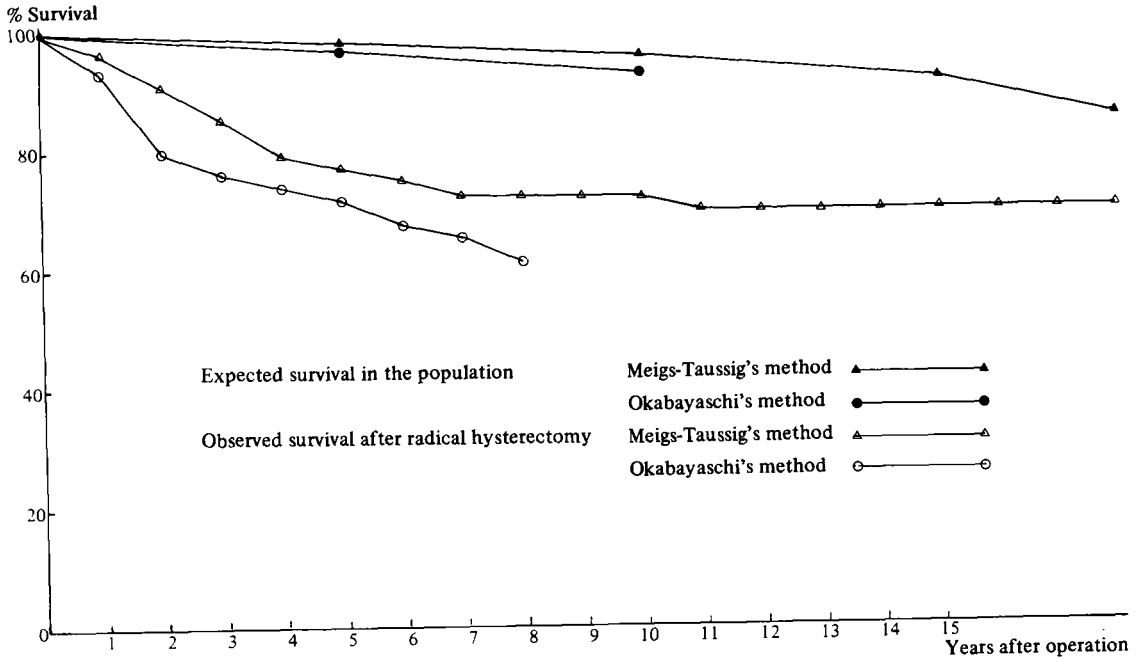


Fig. 6. Surgical-pathological group B + DB.

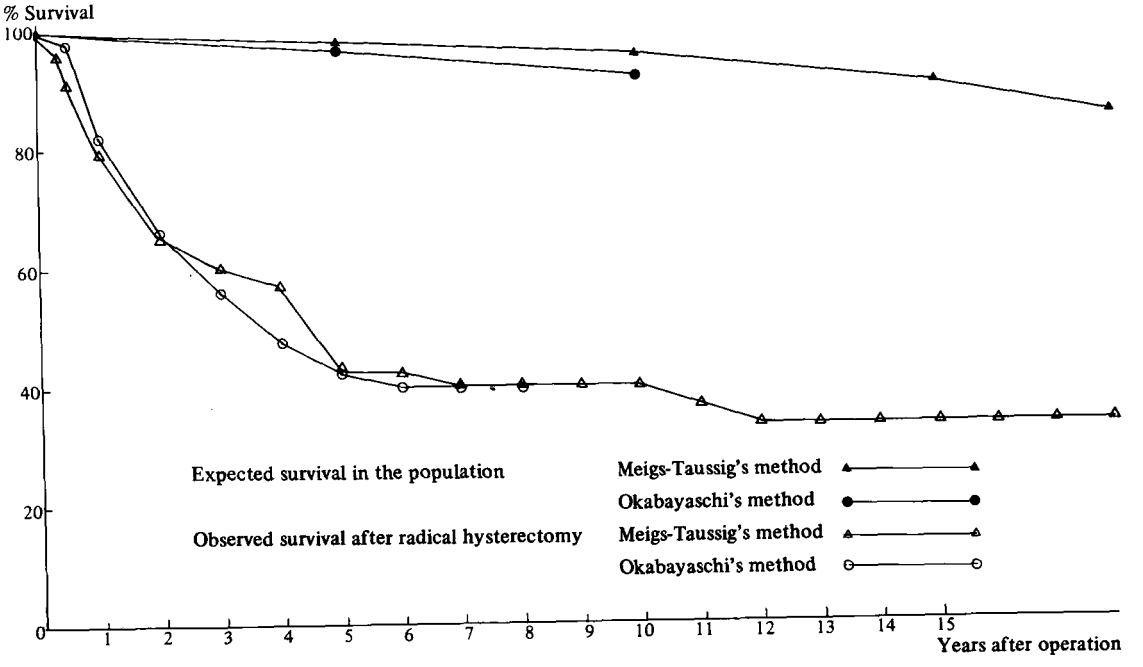


Fig. 7. Surgical-pathological group C + DC.

Table XXIII. 5-year corrected survival clinical stage I and corresponding surgical-pathological group A + DA.

Classification	*Series 1*		*Series 2*	
	No.	Survival-rate	No.	Survival-rate
Clinical stage I	243	81.5	220	88.1
Surg.-path.gr. A + DA	227	82.7	183	90.1

5-year corrected survival clinical stage II and corresponding surgical-pathological group { B + DB / C + DC

Classification	*Series 1*		*Series 2*	
	No.	Survival-rate	No.	Survival-rate
Clinical stage II	77	64.7	130	64.1
Surg.-path.gr. B + DB and C + DC	87	64.6	145	63.1

Critical Survival Calculation

The conventional calculation of survival, based upon the clinical international staging has often been supplemented with survival results within the same groups of patients, classified according to positive or negative nodes after histo-pathological study of the operative specimen. However, the survival results according to this classification depend so much upon (a) the microscopic technique used for detecting involved nodes and upon (b) the staging, that it affords no definite impression of the severity of the material or the therapeutic standard (Table XXIX).

These factors may be elucidated by comparing tables and figures representing the survival calculations in groups of patients whose nodes have been studied by routine histological methods and groups whose nodes have been step-sectioned, as e.g. in part of the present material.

We have 154 cases whose nodes had been step-sectioned from surgical series 1, listed by surgical-pathological classification in Table XXIV. For comparison we have 328 cases from surgical series 2 studied by routine histology (Table XXV).

Table XXIV. Classification of 154 cases from *series 1*, by clinical international staging and surgical-pathological classification (Meigs-Brunschwig). *All nodes examined by step-section microscopy.*

Clinical stage	No. of cases	Surgical-pathological classification					
		A	B	C	DA	DB	DC
Ia	2	2	0	0	0	0	0
Ib	114	85	3	1	15	4	6
IIa	25	2	10	1	5	2	5
IIb	13	0	0	5	1	1	6
Total	154	89	13	7	21	7	17

4 A_0 cases excluded.

Table XXV. Classification of 328 cases from *series 2*, by clinical international staging and surgical-pathological classification (Meigs-Brunschwig). *All nodes examined by routine microscopy.*

Clinical stage	No. of cases	Surgical-pathological classification					
		A	B	C	DA	DB	DC
Ia	36	35	0	0	1	0	0
Ib	162	132	9	1	8	4	8
IIa	73	2	51	1	3	14	2
IIb	57	0	13	23	2	3	16
Total	328	169	73	25	14	21	26

22 A_0 cases excluded.

The severity of the two materials was assessed on the basis of the percentage distribution and calculation of 5-year survival of the surgical-pathological groups: A + DA, B + DB, and C + DC in the two materials (Table XXVI and Figs. 8–9–10, Modified Meigs-Brunschwig Classification, p. 12).

The poorest prognostic group C + DC makes up the same percentage of both materials, viz. 16 %. A + DA, corresponding in clinical extent to stage Ib, and prognostically the most favourable, made up 71 % of the step-sectioned material and 56 % of the routinely studied material. B + DB, corres-

ponding in clinical extent to stage IIa, makes up 13 % of the step-sectioned material and 28 % of the routinely studied material.

As in Meigs-Brunschwig's surgical-pathological system all cases with involved nodes were collected in group D (sub-groups DA, DB, and DC), whereas cases with negative nodes were classified in groups A, B, and C according to the extent of the tumour in the uterus,

Table XXVI. Percental distribution of surgical-pathological groups: A + DA, B + DB and C + DC for *assessing severity of the series from* table XXIV with step sectioning and from table XXV with routine microscopy of the nodes.

Surg.-pathol. group	Step section microscopy		Routine microscopy	
	No.	%	No.	%
A + DA	110	71	183	56
B + DB	20	13	94	28
C + DC	24	16	51	16
Total	154	100	328	100

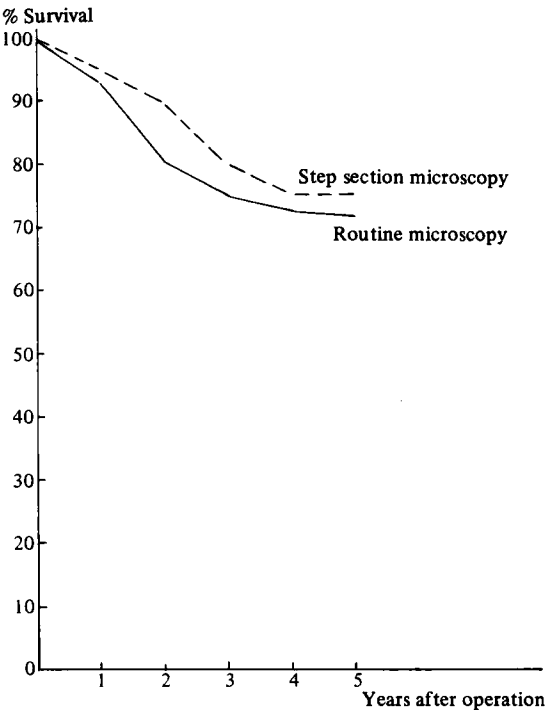


Fig. 9.
5-year survival for surgical-pathological group B+DB.

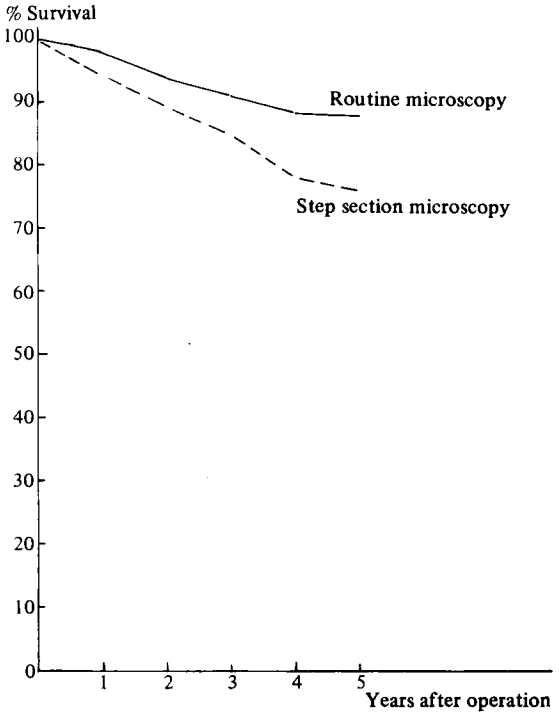


Fig. 8.
5-year survival for surgical-pathological group A + DA.

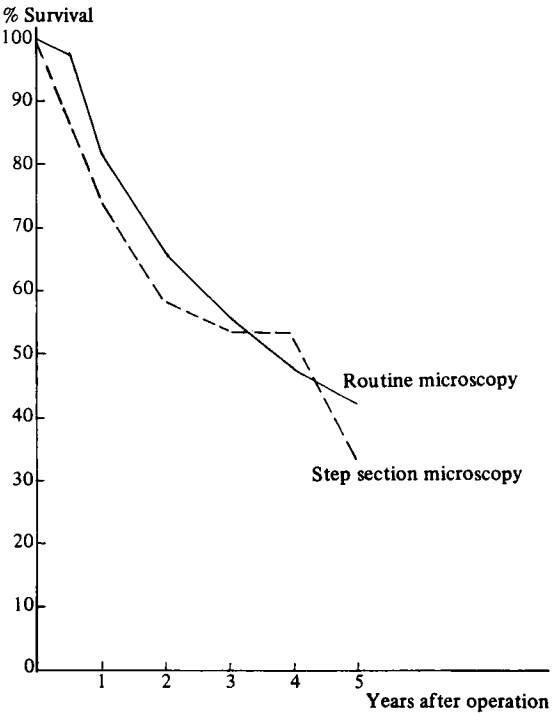


Fig. 10.
5-year survial for surgical-pathological group C+DC.

vagina, and parametria, corresponding to clinical stages Ib, IIa, and IIb.

The 5-year survival was calculated for patients with involved nodes (groups DA, DB, and DC) and for patients with negative nodes (groups A, B, and C), partly for the step-sectioned and partly for the routinely studied cases. Results for comparison are presented in Tables XXVII and XXVIII, and the survival curves are plotted on Figs. 11–16.

In Table XXVII the 5-year survival for cases with step-sectioned positive nodes in group D was 16.7 % lower than in group D with routinely studied involved nodes.

As a number of the nodal metastases demonstrated by step sectioning were insignificant, and had a favourable prognosis, it must be assumed that the reduction in the survival rate for the group D patients is not due solely to nodal involvement, but also to a marked degree to the primary tumour. Patients having

Table XXVII. 5-year survival for *groups with positive nodes* by Meigs-Brunschwig's surgical-pathological classification of the materials having step sectioning and routine microscopy of the nodes.

Surg.-path. group	Step section microsc. No.	Step section microsc. 5-year survival-rate	Routine microscopy No.	Routine microscopy 5-year survival-rate
DA	21	19.4	14	43.3
DB	7	29.2	21	53.9
DC	17	18.3	26	20.3
Total	45	20.4	61	37.1

Table XXVIII. 5-year survival for *groups with negative nodes* by Meigs-Brunschwig's surgical-pathological classification of the materials having step sectioning and routine microscopy of the nodes.

Surg.-path. group	Step section microsc. No.	Step section microsc. 5-year survival-rate	Routine microscopy No.	Routine microscopy 5-year survival-rate
A	89	89.9	169	92.6
B	13	100	73	79.3
C	7	71.4	25	71.3
Total	109	89.9	267	86.8

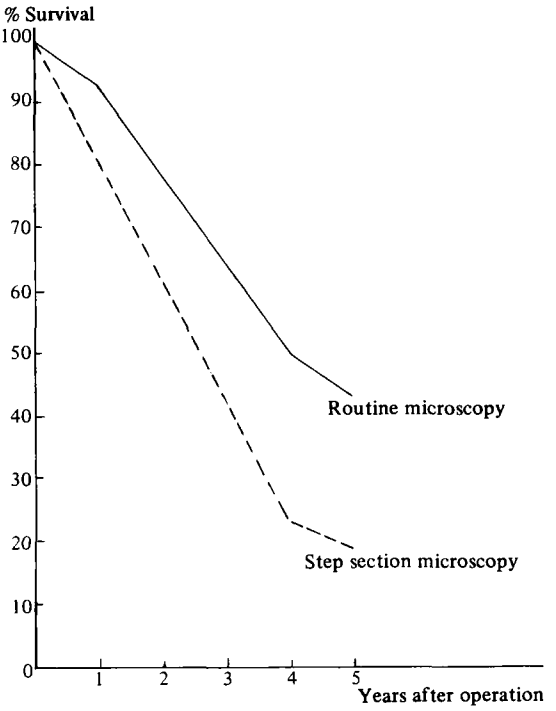


Fig. 11.
5-year survival for surgical-pathological group DA.

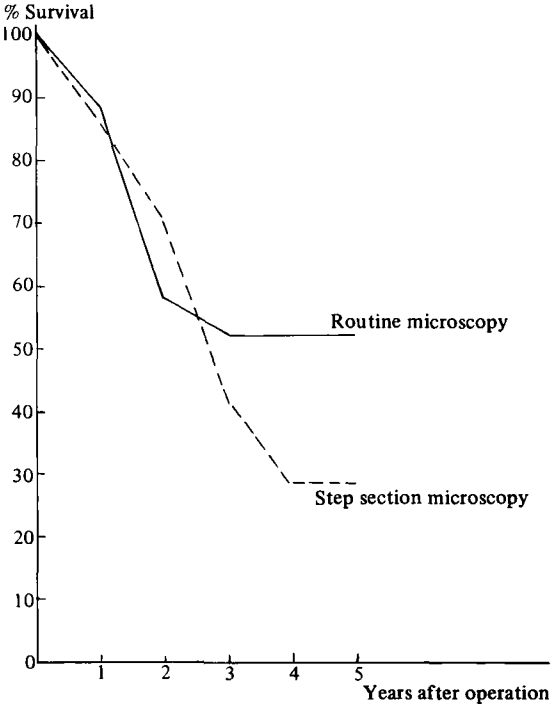


Fig. 12.
5-year survival for surgical-pathological group DB.

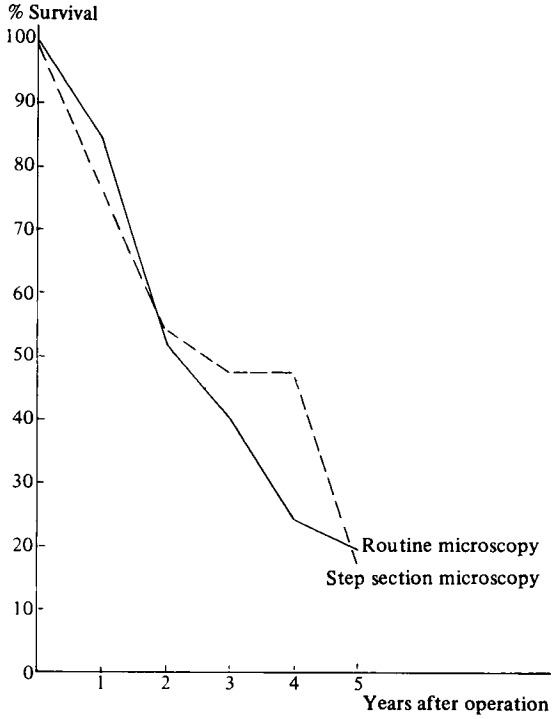


Fig. 13.
5-year survival for surgical-pathological group DC.

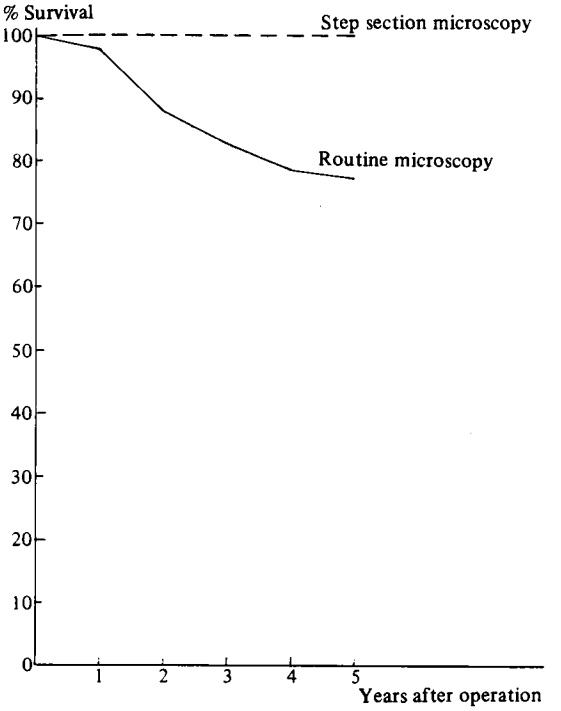


Fig. 15.
5-year survival for surgical-pathological group B.

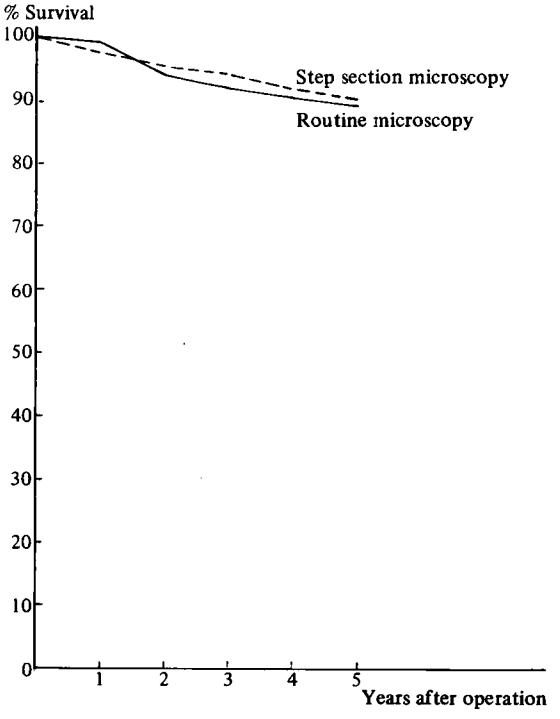


Fig. 14.
5-year survival for surgical-pathological group A.

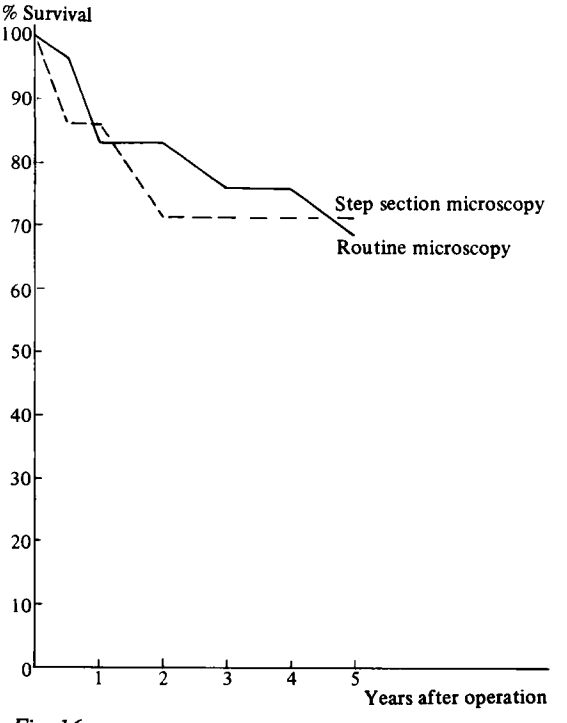


Fig. 16.
5-year survival for surgical-pathological group C.

Table XXIX. Therapeutic results after primary radical hysterectomy with lymph node dissection for stage I and II cervical carcinoma from the literature and the present material.

Literature	Clinical stage	No. of cases	5-year survival-rate			% positive nodes
			Total	With negative nodes	With positive nodes	
Brunschwig, A	I	222	79.8	83.0	39.0	8.8
1968	II	220	53.2	60.0	28.0	24.3
Bruntsch, K. H.	I	234			37.5	12.8
1957	II	249			21.8	24.5
Froewis, I. & Ulm, R.	I	95	87.4	85.3	46.7	11.6
1959	II	62	58.0	75.0		30.6
Kelso, J. W. & Funnell, J. D.	I	132	84.8		57.1	10.6
1973	II	92	78.3		53.6	30.4
Ketcham, A. S.	I	28	86.0			25.0
et al.	IIa	14	88.0	91.0	66.0	
1971	IIb	26	78.0			31.0
Masterson, J. G.	I	120	87.0	92.0	42.0	10.0
1967	II	30	63.0	71.0	33.0	20.0
Masubuchi, K. et al.	I	296	90.5	92.2	57.1	4.7
1969	II	266	74.4	81.2	50.8	22.2
Meigs, J. V. et al,	I	315	83.0	89.0	44.0	13.7
1962	II	171	55.0	71.0	27.0	36.7
Navratil, E.	Ib	18	72.2	86.6	–	16.5
1965	II		56.8	62.5	37.9	23.2
Spurny, J.	I	66	81.8	83.3	45.8	15.6
1958	II	52	63.5	76.5		35.0
Yagi, H.	I	279	88.5	94.4	50.0	12.0
1961	II	1028	64.0	71.1	29.6	23.7
Masubuchi, K. et al. 1969. (Ref.). The seventh annual Report of japanese Committee on uterine Cancer, 1965.	I	3869	80.6			
	II	5822	64.1			
Annual Report Vol. 15, 1973 Stockholm.	I	4464	83.4			
	II	2815	67.4			

Present material	Clinical stage	No. of cases	5-year survival-rate						% positive nodes
			Total	With negative nodes			With positive nodes		
Surgical Series 1 Meigs-Taussig	I	243	81.5	[1])			[2])		[3])
	IIa	54	71.4						
	IIb	23	49.0						
	II	77	64.7						
Surgical Series 2 Okabayaschi cf. table XIX	I	220	88.1	Surg. group		(No)	Surg. group		(No)	Routine microscopy
	IIa	73	68.7	A	92.6	(169)	DA	43.3	(14)	7.7
	IIb	57	58.2	B	79.3	(73)	DB	53.9	(21)	22.3
	II	130	64.1	C	71.3	(25)	DC	20.3	(26)	51.0
				B+C	77.3	(98)	DB+DC	35.3	(47)	32.4
				cf. table XXVIII			cf. table XXVII			

[1]), [2]) and [3]): Series 1 excluded because of the partly used step section microscopy.

a poor prognosis because of the spread of the primary tumour were transferred, by reason of the involved nodes, from groups A, B, and C to group D. Thereby the survival rate in group D decreases "proportionally" to the increasing number of positive nodes. This will increase with step or serial sectioning and with increasing extent of the tumour. The survival rate increases for groups A, B, and C the more cases with involved nodes are sorted off (Table XXVIII).

In Table XXVII the survival of the step section-studied sub-groups DA and DB is about 20 % lower than for the routinely studied ones, whereas group DC differs by only 2 %. The explanation is presumably that the poor prognosis of this group is determined mainly by the parametrial infiltrates, the extra nodal metastases added by step-section microscopy being small and having little influence upon survival.

The exact fall in the survival rate for patients in whom an increased number of involved nodes was found by step or serial sectioning depends – *ceteris paribus* – upon the severity of the material.

These factors must be taken into consideration in assessing therapeutic results in groups of patients with positive and negative nodal findings. When stating the survival rate for these histologically defined groups, the microscopic technique should be described, and the metastatic rate for the individual clinical stages should be stated.

Adenocarcinoma of the Cervix Uteri

Out of the 670 cases of stage I and II cervical carcinoma in the present material 37 (5.5 %) were histologically adenocarcinoma, 31 being pure adenocarcinoma and 6 mixed, i.e. squamous-cell carcinomas with distinct adenomatous components.

Table XXX lists the staging.

Table XXX. Distribution of Adenocarcinoma in clinical stage.

Total No.	Stage I		Stage II	
	24		13	
	Ia	Ib	IIa	IIb
37	4	20	9	4

Ten of the patients had nodal metastases, pure adenocarcinomas in 9 and a mixed tumour in one case.

Table XXXI sets out the distribution of metastases in the 10 patients with cervical adenocarcinoma. Three of these cases were

among 10 in which the nodes were step sectioned (Nos. 1, 2, and 5), 7 among 27 in whom the nodes were routinely studied. There is a distinct left-sided preponderance.

Table XXXI. Distribution of metastases in the different groups of lymph nodes in 10 patients with cervical Adenocarcinoma.

Patient	Group of Pelvic lymph. nodes			
	1.	2.	3.	4.
1.		+	+	+
2.	+	+	+	+
3.	+			
4.			+	
5.			+	
6.		+		+
7.			+	
8.	+		+	
9.			+	+
10.		+		

Table XXXII shows the recurrences in relation to node findings and clinical stage.

Table XXXII. Recurrences of Adenocarcinoma in relation to node findings and clinical stage.

Stage	No.	Neg. nodes	Pos. nodes	Deaths with recurr.	
				Neg. nod.	Pos. nod.
I	24	19	5	3	3
II	13	8	5	5	3
Total	37	27	10	8	6

Among 37 patients with stage I and II cervical adenocarcinoma the 5-year survival, non-corrected, is 70 % as compared with 78.5 % corrected survival in the total material. However, the material of adenocarcinomas is heavier, and there is a more erroneous staging, 29.7 % against 14.6 % in the total material (Modified Meigs-Brunschwig Surgical-Pathological Classification, p. 12). Positive nodes were found by routine histology in 25.9 % of the patients with adenocarcinoma as compared with 15.2 % of the entire routinely studied material, but 2 patients who had bilateral metastases from adenocarcinoma at operation are still without recurrence after 10 and 11 years (cf. J. Botella Llucia 1972 (6)).

Stump Carcinoma

The material includes 17 cases of cervical carcinoma in patients who had undergone supravaginal hysterectomy for benign diseases. Sixteen of these tumours were histologically classified as squamous-cell carcinoma and one as cervical adenocarcinoma.

The therapeutic results are listed in Tables XXXIII and XXXIV (7 cases occurred in series 1 and 10 in series 2).

Table XXXIII. Therapeutic results for cases of stump carcinoma.

Series 1.

Stage	No.	Neg. nod.	Recurr.	Pos. nod.	Recurr.
I	6	5	0	1	0
IIa	1	1	0	0	0

Table XXXIV. Therapeutic results for cases of stump carcinoma.

Series 2.

Stage	No.	Neg. nod.	Recurr.	Pos. nod.	Recurr.
I	6	5	0	1	1
IIa	1	0	0	1	0
IIb	3	3	2	0	0

Seven patients had the Meigs operation. In one it revealed positive nodes in one group. All 7 patients were alive after 13–18 years.

Ten patients were treated by the Okabayaschi operation. Within this group 3 patients were in stage IIb. Two have died of recurrence. One of them had an adenocarcinoma without nodal metastases. The recurrence appeared after 5–6 years' follow-up. One patient (aged 72) died of an intercurrent disease – cerebral haemorrhage causing dementia 4–5 years after the operation.

The two groups are too small and heterogeneous to be used for comparing the effect of the two operations.

Therapeutic Results in Stage I and II Cervical Carcinoma Combined with Pregnancy

Of the 670 patients with stage I and II cervical carcinoma 13 were pregnant, 6 in series 1 and 7 in series 2.

In 4 of these cases invasive cancer was found in the course of routine investigations prior to induced abortion in the 2nd month of pregnancy.

In another 4 cases the tumour was demonstrated in connection with pregnancy examination in a gynaecological out-patient department.

Five patients were referred by their own doctors because of metrorrhagia during pregnancy.

The patients are included in the total material, but the therapeutic results will be briefly reported here.

Table XXXV. Therapeutic results for cervical carcinoma combined with pregnancy.

Series 1.

Stage	No.	Neg. nod.	Recurr.	Pos. nod.	Recurr.
I	5	5	0	0	0
IIa	1	0	0	1	1

Table XXXVI. Therapeutic results for cervical carcinoma combined with pregnancy.

Series 2.

Stage	No.	Neg. nod.	Recurr.	Pos. nod.	Recurr.
Ia	2	2	0	0	0
Ib	5	4	1	1	0

Six had a Meigs operation. One, who had nodal metastases in two groups, died with recurrence within one year of the operation. The others are alive after 13–18 years' follow-up.

Seven had an Okabayaschi operation. One, without nodal metastases, died with recurrence 3–4 years after the treatment. One, with positive nodes in one group, is alive after 5–6 years' follow-up.

None has died of intercurrent diseases.

Management of Recurrences After Radical Hysterectomy

Series 1.

85 patients treated by the Meigs operation developed recurrence of the tumour, and of them 79 died. Six are alive 9–12 years after the recurrences were treated.

22 patients had localized recurrence in the vaginal vault, one had a metastatic deposit in the lower part of the vagina, observed 3 years after the primary operation, while in the remaining cases the recurrences were diffuse.

Secondary Surgical Treatment

In 7 cases the recurrence could be treated surgically. Extirpation of the tumour tissue was performed in 3 cases, vaginectomy in 2 cases, and cystectomy + vaginectomy in one. All six have died.

Total exenteration was done on one patient who is *alive 18 years later.*

Secondary Radiotherapy

Radiotherapy was used in a total of 52 cases of recurrences from series 1, including 22 with localized recurrence in the vaginal vault. Five of these patients are alive 9–12 years after the irradiation (3 stage Ib and 2 stage IIa patients. All 5 had been correctly classified and had shown no involved nodes at the primary operation).

Series 2.

85 patients treated by the Okabayaschi operation developed recurrence, and of them 78 died. 7 are alive 5–10 years after the primary operation.

35 patients had localized recurrence.

Secondary Surgical Treatment

Four patiens had reoperation for their recurrent tumours. All have died.

Secondary Radiotherapy

Irradiation was administered to 29 patients with recurrences in the vagina. *Five were alive* at the end of the follow-up period (2 stage Ib, 1 stage IIa, and 2 stage IIb patients. One of the latter, having involved nodes at primary operation, has later died).

Two patients with recurrence of the pelvic wall are *still alive* 3–5 years after the secondary irradiation (1 stage Ib and 1 stage IIb patient, the latter with involved nodes at primary operation).

Two patients with residual tumour in the vaginal resection border were irradiated in connection with the operation. Both were alive at the end of the follow-up period.

Within both surgical series 78–92 % of patients with recurrences died within the first 5 years after the operation.

Table XXXVII gives the mortality from recurrences during the first 5 years after the primary operation, calculated in per cent of all deaths from observed recurrences (Series 1). The percentage is increasing with the increasing surgical-pathological spread of the tumours (cf. Sørensen 1958 (60)).

Table XXXVII. Mortality from recurrences during the first 5 years after the primary operation, calculated in per cent of all deaths from observed recurrences (Series 1).

Clinical classification		Surgical-path. classific.	
Clinic. stage	Series 1 %	Surg.-path. gr.	Series 1 %
Ib	78	A + DA	78
IIa	87	B + DB	83
IIb	92	C + DC	86

Deaths from New Cancer

In 11 cases the cause of death was a new cancer.

Surgical series 1:

1. Aged 60. Stage Ib cerv. carc., involved nodes in one group.
   Type: Squamous-cell carc. Operation in 1953.
   Died in 1959 of lung cancer. Autopsy: Solid, anaplastic cancer of the lung. No signs of a recurrence of the original cerv. carc.

2. Aged 50. Stage IIa cerv. carc., involved nodes in one group.
   Type: Squamous-cell carcinoma. Operation in 1956.
   Died in 1960 of hypernephroma. Autopsy: No signs of a recurrence of the cerv. carc.

3. Aged 56. Stage Ib cerv. carc., no nodal metastases.
   Type: Squamous-cell carc. Operation in 1956.
   Died in 1962 of an adenomatous carcinoma of the gallbladder. At the operation the pelvis was inspected, but showed no signs of a recurrence of the cerv. carc. The patient died in her home, and no autopsy was done.

4. Aged 65. Stage IIa cerv. carc., no nodal metastases.
   Type: Anaplastic squamous-cell carc. Operation in 1957.
   Died in 1969 of a pancreatic carc. Gynaecological examination showed no signs of a recurrence of the primary cerv. carc. This patient too died in her home, and no autopsy was performed.

5. Aged 55. Stage Ib cerv. carc., no involved nodes.
   Type: Squamous-cell carc. Operation in 1958.
   Died in 1965 of an adenocarcinomatous pleural tumour. No autopsy, but gynaecological examination had shown no signs of a recurrence of the cerv. carc.

Surgical series 2:

6. Aged 55. In 1962 a solid carc. of the breast. Treated with simple mastectomy and irradiation. During the stay in the Radium Centre a squamous-cell carcinoma of the cervix uteri was diagnosed, and the patient was transferred to our department.
   Operation in Jan. 1963 for a stage IIa cerv. carc., no involved nodes.
   In Aug. 1963 a cutaneous recurrence of the mammary tumour was excised and treated by X-radiation.
   Died in her home a few months later. No

autopsy, but there had been no signs of a recurrence of the cerv. carc.

7. Aged 50. Operation in 1963 for a stage Ib cerv. carc., no involved nodes.
   Type: Squamous-cell carc.
   Died in 1970 of a hypernephroma with multiple metastases. Autopsy did not show any recurrence of the primary cerv. carc.
8. Aged 71. Operation in 1966 for stage Ib cerv. carc. without nodal metastases.
   Type: Solid squamous-cell carc.
   Died in 1971 of a bronchogenic cancer. Autopsy showed no recurrence of the cerv. carc.
9. Aged 67. Operation in 1968 for stage Ib cerv. carc. without any involved nodes.
   Type: Squamous-cell carc.
   In 1971 multiple lymphomas were diagnosed. Micr.: Reticulosarcoma. Radiotherapy without any effect.
   Died a few months later. Autopsy: Generalized reticulomatosis. No signs of a recurrence of the cerv. carc.
10. Aged 64. Operation in 1968 for stage IIa cerv. carc. with no involved nodes.
    Type: Squamous-cell carc.
    Died in 1973 of a bronchogenic cancer of the lung. Autopsy showed no signs of a recurrence of the cerv. carc.
11. Aged 63. Operation in 1968 for stage Ib cerv. carc. No involved nodes.
    Type: Squamous-cell carc.
    In 1970 a cancer of the mammary ducts was diagnosed. Treated with mastectomy. Died in 1971 of a recurrent tumour of the breast. Autopsy showed no recurrence of the cerv. carc.

Complications

Complications in connection with radical hysterectomy for carcinoma of the cervix uteri may be divided as follows:

1. Primary operative mortality.
2. Blood loss.
3. Primary operative injury to the great pelvic vessels, urinary organs, rectum, peripheral nerves, and nervous plexuses.
4. General surgical complications.
5. Drainage type and complications.
6. Complications due to vegetative disturbances in the lower part of the ureters and adjacent part of the bladder owing to tissue necrosis with subsequent development of fistulae and strictures.

1. Primary Operative Mortality

The primary operative mortality (death within 30 days after the operation) is 0.6 % in the total material, viz. 4 patients out of 670.

Two patients among the 320 in series 1 = *0.63 %.*

1. A 45-year-old stage I patient with nodal metastases, uncomplicated operation. Died in 3 weeks of an *embolus in the pulmonary artery.*
2. A 39-year-old stage II patient who *died on the operating table* because of profuse venous bleeding from the hypogastric area. Ligation of the hypogastric artery proved ineffective.

Two patients among the 350 in series 2 = *0.57 %.*

1. A 61-year-old stage I patient who underwent conization, followed 2 weeks later by radical hysterectomy. The operation was uncomplicated, but a few days later the patient developed a state suggesting septicaemia, with anuria. The anuria could be controlled, but the patient deteriorated and died 18 days after the operation. Postmortem findings: *Severe, acute ulcerative colitis, septicaemia.*
2. A 55-year-old stage II patient with bilateral lymph node involvement, very obese (82 kg, 154 cm). Died 16 days after the operation of *an embolus in the pulmonary artery.*

2. Blood Loss

Radical hysterectomy always entails a considerable loss of blood (according to the literature more than 1000 ml during an uncomplicated operation). The bleeding is most often in the form of oozing from plexuses drained through the hypogastric vein. During resection of the deep parts of the

sacrouterine ligament there is a great risk of injuring the named venous plexuses, and this will give rise to very profuse bleeding which is difficult to control. At times ligation of the hypogastric artery will help. Dissection of the nodes in the obturator fossa does not uncommonly cause profuse venous bleeding, and since the veins in this region often retract, ligation may even be rendered impossible.

3. Primary Operative Injury to the Great Pelvic Vessels, Urinary Organs, Rectum, Peripheral Nerves, and Nervous Plexuses

Table XXXVIII lists the primary operative injuries occurring within the two types of operation and the treatment applied.

Primary injuries to the bladder and rectum were immediately sutured, and generally they healed without complications.

Ureteral injuries close to the bladder were treated by ureterovesicostomy, primarily or secondarily.

In one case, when the ureter was cut on a level with the linea terminalis, end-to-end suturing was done over an inserted soft catheter passed down into the bladder. The catheter was removed at the end of 3 weeks. Uncomplicated course and normal postoperative pyelogram.

4. General Surgical Complications

Table XXXIX. General surgical complications.

Complications	Series 1 (Meigs) No.	Series 2 (Okabayaschi) No.
Postoperative haemorrhage	3	3
Vaginal haematoma	8	9
Vaginal abscess	5	0
Wound rupture	1	4
Paralytic ileus	8	12
Mechanical ileus	1	1
Phlebitis of lower limb	6	7
Pneumonia and pulm. infarction	17	10
Embolus of pulm. artery	1	1
Coronary occlusion	0	1
Total	50	48

Table XXXVIII. Primary operative injuries.

Injury	Series 1 (Meigs) No.	%	Series 2 (Okabayaschi) No.	%	Treatment – Comments
Bladder	4	1.3	7		Primary suture, uncomplicated course.
			1	2.3	Primary suture, complicated with ureteral fistula. Treatm.: Secondary ureterovesicostomy.
Ureter	2	0.6	3		Ureterovesicostomy, uncomplicated.
			1		Ureterovesicostomy, complicated with stenosis. 2 years later nephrectomy.
			1		High injury, end-to-end suture, uncompl.
			1	1.7	Abnormal course of ureter. Treatm.: Ureterosigmoideostomy, uncompl.
Rectum	0		5	1.4	Primary suture, uncompl.
Iliac artery	0		0		
Ext. and int. iliac veins	9		2	0.6	Suturing, uncompl.
	1	3.1			Died on the operating table.
Sacral plexus	1	0.3	2	0.6	No permanent sequelae.
Obturator nerve			1	0.3	No treatment.
Total	17	5.3	24	6.9	

5. Drainage Type and Complications

Vaginal drainage was used in a total of 375 patients, the vagina being left open extraperitoneally. 320 of these patients had the Meigs and 55 the Okabayaschi operation. In a few cases a short gauze drain was inserted into the vagina to drain the discharge from the wound during the first 24 hours. The gauze was removed on the following day.

Among these 375 patients there were 49 complications that could be ascribed to afterbleeding, retention, or infection in the wound cavity, and occasionally vaginal haematomas, a total of 13 %.

In *295 patients,* all having the Okabayaschi operation, suction drainage was set up by way of two Foley balloon catheters placed into the pararectal cavities and passed extraperitoneally to the abdominal wall and out through the lower angle of the wound. The suction drainage was continued until the amount of secretion was 10–20 ml/24 hours.

126 patients had drainage for up to 3 days, 163 patients for 3–5 days, and 6 patients for more than 5 days.

The total number of complications in this group was 30, viz. 10 %.

In other words, there was no decisive difference in the complication rate according to type of drainage.

6. Postoperative Urological Complications

The main complications of radical Wertheim hysterectomy, which give rise to most difficulty later, are the urological ones.

Most patients develop dysfunction due to inevitable injury to the vegetative nerve supply to the bladder, resulting in disturbances of emptying. However, this may be remedied by training and manual pressure on the abdomen.

The most serious postoperative complications are *ureteral fistulae and strictures,* both of which may require secondary operation and occasionally loss of renal function. The incidence of these complications ranges from 5–15 % in the various analyses. With purely surgical treatment, they can hardly be reduced much below 5 % in stages I and II, without compromising the radicality of the operation.

Postoperatively ureteral injuries affect the prevesical segment because of ischaemia, inflammatory changes, necrosis, and denervation of the ureteral wall. This is primarily caused by the mobilization of the ureter between the cardinal and vesicouterine ligaments, as the thin vascular adventitia around the ureter is easily damaged, so that the small branches of the internal iliac and superior vesical arteries will be damaged. The ischaemic necrosis may secondarily be increased by the formation of haematoma and inflammatory processes in the surrounding tissue.

At a later stage of healing the ureter will not uncommonly adhere to the pelvic wall, with formation of fibrous connective tissue which may thus cause angulation and strictures. In mild cases a temporary stricture will occur as a consequence of mucosal oedema in the lower segment of the ureter and in the bladder. When combined with an inhibited peristalsis, this gives rise to moderate hydronephrosis which is usually silent and subsides spontaneously in a few months.

If the necrotic process in the ureteral wall is more extensive, no stricture will arise, but the ureteral fistula appears primarily and only a few days after the operation.

In most cases the fistula takes 1–4 weeks to form, during which there will be attacks of fever and pain in the region of the kidneys; a pyelogram shows hydronephrosis. In 60 % of our cases with ureteral fistula it developed in this way.

An attempt may be made to reduce the risk of the named ureteral complications by various precautions, aiming partly at preserving the blood supply to the ureteral wall, partly at avoiding infection in the surrounding tissue. Mobilization of the ureter must be performed as gently as possible, preserving the vascular sheath and the above-mentioned small arterial branches. The prevesical part of the ureter should be left in connection with the vesical part of the vesicouterine ligament,

whenever this is possible without compromising radicality. It is important to secure sufficient haemostasis and drainage and to combat infection by antibiotic after-treatment. The bladder should be kept empty until the residual urine is below 50 ml. The urine should be checked by repeated microbiological tests.

Below we shall give a survey of the vesicovaginal and ureterovaginal fistulae as well as ureteral strictures which occurred in the material and report their treatment.

Vesicovaginal Fistulae

Three cases (0.9 %) occurred in series 1, none in series 2.

1. In one case a fistula developed 3 weeks after the operation and healed spontaneously after treatment with indwelling catheter.
2. In another case a fistula developed 3 months after the hysterectomy. Occlusion of the fistula was performed by the vaginal route, without any complications.
3. In the third case the fistula formed shortly after the operation which had been difficult because of profuse venous haemorrhage. It was attempted to close the fistula, first by the vaginal and later by the abdominal route, but both attempts failed. The patients was then offered bladder substitution, but she refused. However, this operation was carried out 3 years later in another department. After another 5 years the patient died in uraemia. Autopsy showed no signs of recurrence.

Ureterovaginal Fistulae

Within the present material 20 cases of ureterovaginal fistula occurred in series 1 and 18 in series 2, bilateral in two cases of each. All developed within the first 4 weeks after the Wertheim operation.

Three patients with late ureteral fistulae are not included. In 2 of them the fistulae were due to recurrence of the tumour, and in one it arose after the appearance of another type of tumour (hypernephroma).

1. A stage IIa patient with involved nodes in 2 groups. The fistula arose 2 ½ months after the operation, and 2 months later a recurrence was demonstrated. It was treated by irradiation, but without effect, and the patient died one year after the operation.
2. A stage IIa patient without nodal metastases. The fistula arose in direct connection with a recurrence 6 months after the hysterectomy. Death 2 months later, and autopsy showed invasion of the bladder and both ureters.
3. A stage IIa patient with involved nodes in one group. The fistula arose 2 years later, but further examination disclosed a hypernephroma of the homolateral kidney. Died 4 years after the primary treatment. Autopsy: No sign of a recurrence of the cervical carcinoma.

Tables XL and XLI set out the ureterovaginal fistulae within the two surgical series, their treatment and its results.

Ureterovaginal fistulae were treated by us as a rule 6–8 weeks after the hysterectomy. It is important that the ureter be well mobilized before, and without any stretching after, the implantation. An indwelling Pflaumer catheter has been left for 3 weeks after the implantation.

Analysis of the distribution of ureterovaginal fistulae in relation to the clinical stages in the two surgical series revealed in:

Series 1:

Stage I: 13 ureterovaginal fistulae among 243 patients = 5.4 %.
Stage II: 7 ureterovaginal fistulae among 77 patients = 9.1 %.

Series 2:

Stage I: 9 ureterovaginal fistulae among 220 patients = 4.1 %.
Stage II: 9 ureterovaginal fistulae among 130 patients = 6.9 %.

Table XL. Ureterovaginal fistulae in series 1, treatment and results.

	No.	Stage I	Stage II	Treatment	Renal function preserved
Unilateral fistula	3	2	1	Spontaneous healing	2 bilat. 1 unilat.
	2	1	1	Nephrectomy	2 unilat.
	12	8	4	Ureterovesicostomy	12 bilat.
	1	1		Ureterovesicostomy Nephrectomy	1 unilat.
Bilateral fistula	2	1	1	Bilateral ureterovesicostomy[1])	2 bilat.
Total No.	20	13	7	Renal function preserved on both sides: 16.	
Total %		5.4	9.1	» » » on one side: 4.	

1) In one of these patients unilateral ureterovesical neostomy and ureterosigmoideostomy were carried out primarily, as one ureter could not reach far enough to be implanted into the bladder. After recurrent urinary tract infections, the ureterosigmoideostomy was closed in another hospital and substituted by a uretero-ureteroanastomosis which functioned satisfactorily. The patient died 12 years after the primary operation of pancreatic cancer, without signs of recurrence of the cervical carcinoma.

Table XLI. Ureterovaginal fistulae in series 2, treatment and results.

	No.	Stage I	Stage II	Treatment	Renal function preserved
Unilateral fistula	12	7	5	Ureterovesicostomy	12 bilat.
	1		1	» [1])	1 unilat.
	1	1		»	
				Nephrectomy[2])	1 unilat.
	1	1		Ureterosigmoideostomy	1 bilat.
	1		1	No treatment[3])	1 unilat.
Bilateral fistula	2		2	Bilateral ureterovesicostomy	2 bilat.
Total No.	18	9	9	15 patients retained renal function on both sides,	
Total %		4.1	6.9	including 2 with bilat. fistula, 3 only on one side.	

1) In this patient renal function was lost on the operated side, but the patient is symptom-free, and the healthy kidney is functioning normally. Follow-up period 7 years.

2) In this case oozing of urine occurred after the implantation. It stopped spontaneously, but 1 year later she was found to have a ureteral stricture and a fistula from the ureter to the colon. Nephrectomy was performed, and the patient is now symptom-free. Follow-up period 7 years.

3) Patient aged 70 in a poor general condition.

Analysis of the individual cases shows, moreover, that 3 patients of series 1 with fistula developed a recurrence, one within the first year after the operation. In series 2 recurrences appeared in 4 patients with fistula, in 2 of them less than one year after the operation.

Ureterovaginal fistulae are not caused exclusively by damage to the tissue during the operation. In the present material they occur-

red mainly in patients with extensive tumours having a marked tendency to recur – patients who are also apt to have parametrial inflammatory processes (Bruntsch 1957 (10), Kratochwil 1962 (28)).

Ureteral Strictures

Postoperative pyelography done on approx. the 14th day disclosed about 10 % mild cases of ureteral strictures which were silent and which subsided spontaneously in 2–3 months.

Within surgical series 1 there were 31 cases of this nature, within series 2 there were 39.

Besides, 8 patients had more serious strictures, arising in consequence of the operation. Comments on these 8 cases will be given in Table XLII.

This table does not include ureteral stenosis due to recurrence of the tumour.

Thus in *series 1* a serious type of ureteral stricture occurred postoperatively in a total of 4 patients. Renal function was abolished on one side in 3, otherwise symptom-free patients.

In *series 2* serious ureteral stricture occurred in 4 patients, in 3 of whom renal function was abolished. Two were treated by nephrectomy after which they have been symptom-free. One patient died of another disease one year after the operation.

The total number of ureteral fistulae and ureteral strictures was in

series 1: (320 pts.) 7.5 % + 3 vesicovaginal fistulae,

series 2: (350 pts.) 6.3 %, no vesicovaginal fistulae.

In 60 % of all patients having ureterovaginal fistulae the fistula formation was preceded by ureteral stenosis.

Retention of Urine

Postoperatively the indwelling bladder catheter was left for two weeks and was removed if the residual urine, at repeated measurements, was below 50 ml. In the event of signs indicating urinary retention, it was re-inserted for a few days, whereupon determination of residual urine and microbiological examination of the urine were repeated. Antibiotics were administered prophylactically during the postoperative period.

Table XLII. Postoperative ureteral strictures in series 1 and 2.

Ureteral stricture	Series 1 No.	Series 2 No.	Treatment – Comments
Unilat.	1		Moderate obstruction with preserved renal function. Treatment deferred.
	1		Stenosis with abolished renal function. Symptom-free. No treatment.
		3	Late strictures (8 months – 7 years). Abolished renal function. 2 treated by nephrectomy.
Bilat.	1		Abolished renal function on one side, hydronephrosis on the other. Treated by ureterovesicostomy.
	1		6 months after operation strictures on both sides, abolished renal function on one side, mild obstruction on the other. No symptoms. No treatment.
		1	Moderat obstruction. The pt. was suffering from anaplastic anaemia to which she died one year later. No treatment of the stricture.
Total No.	4	4	
Total %	1.3	1.1	

With increasing radicality of the hysterectomy the vegetative nerve supply to the bladder is increasingly disturbed, and this gives rise to bladder paresis and injury.

In the great majority of cases the retention of urine is abolished after 1–3 weeks' treatment by permanent drainage of the bladder. Both surgical series included 70 patients in whom the retention persisted beyond 2 weeks.

Table XLIII shows how the retention subsided in both surgical series from the 3rd to the 8th week:

After 8 weeks 8.4 % of the patients in *series 1* still had a residual urine of more than 50 ml, whereas in *series 2* only 5.4 % patients had difficulties of emptying at that time.

Table XLIII. Retention of urine in the postoperative period.

Retention > 50 ml.	Series 1 320 pt.		Series 2 350 pt.	
Weeks after operation	No.	%	No.	%
3	70	21.9	70	20.0
4–6	48	15.0	46	13.1
6–8	30	9.4	26	7.4
8	27	8.4	19	5.4

During the treatment the bladder is kept empty by an indwelling Foley catheter changed weekly because of the risk of infection. Besides, antibiotics are administered according to the result of the microbiological analysis of the urine.

After the final removal of the catheter a sensitivity test of the urine is performed yet again, and the amount of residual urine is checked on an out-patient basis.

After training of the bladder recurrent cystitis is uncommon.

Urinary Incontinence

Urinary incontinence was observed postoperatively in 10 % because of injury to muscles in the bladder and pelvic floor, partly due, as already mentioned, to interrupted innervation – in both surgical series.

The incontinence is most marked immediately after the postoperative removal of the catheter. After training of the bladder and pelvic floor and systematic micturition, the incontinence subsided in half the cases within the first few years.

In a total of 13 patients incontinence operations were performed after the Wertheim hysterectomy. Twenty patients still have stress incontinence and overflow without this being disabling, as it occurs only when they are inattentive, but of course this is a nuisance.

Table XLIV. Incontinence operations.

	No.	Kelly operation	Marshall-Marchetti op. prim.	Marshall-Marchetti op. secund.
Series 1	8	6	2	1
Series 2	5	5	0	2
Total	13	11	2	3

Summary and Results

The present paper reports the therapeutic results obtained by *primary radical hysterectomy with pelvic lymph-node dissection* on 670 patients with stage I and II invasive cervical carcinoma.

In the first 320 patients the operation was by the method of Meigs-Taussig, but from 1961 the procedure was changed to Okabayaschi's. The latter procedure was found to afford a more perspicuous operative field and thus a more radical operation with fewer complications. 350 of the patients underwent operation by this technique.

Like other surgical materials the present one is *selected. All patients admitted with cervical carcinoma in clinical stages I and II during the period 1953–1969, and in whom the operation was considered definitive, are included in the analysis.*

No stage 0 case is included.

Radiotherapy was used only *secondarily* of recurrences, and in 2 patients in whom

tumour tissue had been left in the vaginal resection border.

Survival results were analysed statistically by the actuarial method. In both surgical series the calculation was based partly upon the *international clinical staging* and partly upon a *Modified Meigs-Brunschwig Surgical-Pathological Classification.*

The follow-up period extends from early 1953 to early 1973, that for the Meigs series being 12–19 years and for the Okabayaschi series 5–11 years.

Only 3 patients out of 670 have been lost to follow-up, as they have emigrated, address unknown.

The object of the present analysis is to submit a *purely surgical material* which is comparable with other surgical materials. At the same time, survival results and complications of the Meigs and Okabayaschi modifications of radical hysterectomy are compared.

With regard to preoperative investigations there is reason to emphasize the importance of *pyelography* which disclosed *congenital anomalies* in 4.3 % of the patients. In addition, *a mild degree of hydronephrosis, without demonstrable cause, was found in 2.1 %.* In these cases, the stasis may presumably be attributed with a prognostic role, as the 5-year survival was only about half the average in the total material.

The two operative methods were according to the original procedures, except for the draining in the Okabayaschi operation which was in the form of suction drainage, passed extraperitoneally out through the abdominal wound. In both surgical series particular emphasis was laid on *careful extirpation of the primary tumour* as the most important part of the operation, and gentle mobilization of the ureters.

Lymphadenectomy was *obligate* in both operations and also done with the utmost care. In the Meigs operation it was done primarily, in the Okabayaschi operation after the hysterectomy. The latter method definitely affords a better view of the pelvic cavity.

Node dissection comprised: Common and external iliac nodes, hypogastric nodes, and obturator nodes.

Histological examination of the operative specimen was according to the general hospital routine, without step or serial sectioning. The extirpated nodes were studied by *routine microscopy* in 512 cases, whereas 158 cases (half the Meigs series) were studied by *step sectioning* of the individual isolated nodes (Lange).

The *metastatic rate* found by routine microscopy of the nodes was 8.5 % in stage I and 29 % in stage II.

The rate found by step section microscopy of the nodes was 20.8 % in stage I and 52.6 % in stage II.

Both methods revealed a slight predominance of left-sided nodal metastases.

Apart from the histological technique, clinical staging and the radicalness of the lymphadenectomy determine the metastatic rate. If a case has been under-staged, the frequency of nodal involvement in that stage will be increased.

Errors in Clinical Staging

With a view to analysing errors in clinical staging, we chose classification into surgical-pathological groups based only upon the *localization of the primary tumour in the uterus, vagina, and parametria* in the operative specimen, paying no regard to possible positive nodes.

Histopathologically the operative specimens were studied by the ordinary routine method, without using serial or step section microscopy.

This affords a uniform basis for correcting the clinical staging according to the operative findings, in a *Modified Meigs-Brunschwig System.*

The *node error* according to the Meigs-Brunschwig surgical-pathological classification in the event of positive findings in clinical stages I and II, may be *doubled,* if the histo-pathological examination is altered from routine to step section microscopy of the nodes.

In a *Modified Surgical-Pathological Classification,* as described above, the clinical errors ranged from 11.8–28.8 %, increasing with increasing clinical stage.

5-year corrected survival based upon the international clinical staging was in
series 1 (Meigs):

Stage I: 81.5 %
Stage II: 64.7 %

series 2 (Okabayaschi):

Stage I: 88.1 %
Stage II: 64.1 %

If the 5-year corrected survival was based upon the Modified Surgical-Pathological Classification, i.e. the actual spread of the tumour, the finding was for
series 1 (Meigs):

Group A + DA: 82.7 %
» B + DB: } 64.6 %
» C + DC: }

series 2 (Okabayaschi):

Group A + DA: 90.1 %
» B + DB: } 63.1 %
» C + DC: }

The results of the Okabayaschi operation were significantly better than those of the Meigs operation in clinical stage I and in surgical-pathological group A + DA.

If a survival calculation based upon the clinical staging is supplemented with results for cases with *positive* and *negative* nodes, the survival has unknowingly been calculated in a *surgical-pathological system,* the group with positive nodes being identical with Meigs-Brunschwig's group D and that with negative nodes with groups A + B + C. These survival results are comparable with those of other materials *only if the histo-pathological technique of studying the nodes is stated,* as the number of positive nodes within an isolated clinical stage does not express the severity of the material or the standard of the operation.

Operative Complications

The *primary operative mortality* in the total material is 0.6 %.

The *primary operative injuries* made up 5.3 % in series 1 (Meigs) and 6.9 % in series 2 (Okabayaschi). Injuries to the bladder and rectum were more common in series 2; venous injuries occurred in 3.1 % of series 1, but in only 0.6 % of series 2.

General surgical complications were of the same frequency in both series.

Most importance attaches to the postoperative urological complications. Those which occur in connection with recurrences are not included as operative complications.

Ureteral fistulae and strictures occurred in 7.5 % of series 1 (including 3 vesicovaginal fistulae: 8.4 %). Ureteral fistulae and strictures were found in 6.3 % of series 2.

Retention of urine beyond the 8th week after the operation was found in 8.5 % of series 1 and in 5.4 % of series 2.

Thus, the postoperative urological complications were 2–3 % lower with the Okabayaschi method. Operative vascular injuries were also less common in this operation. Both can presumably be ascribed to the far better view in the Okabayaschi operation, during the mobilization of the ureters as well as in the node dissection.

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