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Results of surgical treatment of carcinoma of the cervix

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RESULTS OF SURGICAL TREATMENT OF CARCINOMA OF THE CERVIX

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INTRODUCTION

Squamous cell carcinoma of the cervix is a significant
cause of death in our female population. The contributions of
George N. Papanicolaou have resulted in massive reduction in the
number of deaths from this disease by increasing the number of
cases discovered in a completely curable stage.[20] It must be
remembered that invasive carcinoma of the cervix still exists
and that being a killer it demands adequate treatment however
radical this may be. This disease ranks second in frequency
only to carcinoma of the breast among malignant neoplasms of
American women. It is far and away the greatest killer among
gynecologic patients; for this reason the gynecologist is
obligated to be aware of all methods of diagnosis, and the most
efficacious methods of treatment.[14]

Over the years, large numbers of patients have been treated
for this disease by a variety of methods. The results obtained
are valuable, not only from the points of view of the individual
patients, but also as sources of data for statistical analysis.
The compiled statistics are valuable in that they will offer a
guide to the most successful methods of attack.

The purpose of this report is to gain an impression of what

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modern surgery alone can do in treating carcinoma of the cervix.
There is a definite paucity of papers dealing with this subject
at the present time. On the other hand, the results of radiation
therapy alone are fairly well known. One result of the lack of
reports dealing with purely surgical methods of attack is that
in the teaching of medical students over the last three decades,
it has been stated that radiation is the primary method of choice.
This categorical statement seems justified only by tradition
since surgical results have been published so infrequently.
One thing that must be remembered is that modern surgery is not
to be disregarded in the attack upon carcinoma of the cervix. It
is a highly effective method of treatment and its possibilities
have not yet been extensively explored. It is important that a
"baseline" be established to show what modern surgical treatment
alone can do. This report is an attempt to establish such a
baseline.

HISTORY

During the early 1800's, a number of investigators attempted
to treat cancer of the cervix with various methods of local
excision but their obvious lack of understanding of the metastatic
features of malignant disease resulted in the overall failure of
their efforts.

In the 1870's, a somewhat more realistic approach to the
problem was taken by Freund of Strassburg who advocated total
abdominal hysterectomy, but his immediate mortality was somewhere
in the range of 72%. Other surgeons tried to amputate the cervix
vaginally and then remove the rest of the uterus abdominally, or
to do the entire hysterectomy by the vaginal route. All these
methods, of course, were doomed to failure since none of these
physicians were aware of the lymphatic extension of the disease.

In 1890, Pawlik introduced the concept of dissection of
parametrial tissues and in 1908, Schauta modified Schuschardt's
radical vaginal operation. In 1900, Wertheim advocated a radical
abdominal hysterectomy with removal of parametrial tissues,
regional lymph nodes, and the upper half of the vagina. His
method found wide acceptance and modifications of it are the
mainstay of surgical treatment today.

After the discovery of x-rays by Roentgen in 1895, a number of investigators began to irradiate patients with carcinoma of the cervix in an attempt to effect a cure. With the primitive means of generating, controlling, and measuring the radiation, very few cures were accomplished and many complications occurred.

The Curies discovered radium in 1898 and this new agent began to be explored as regards its anti-neoplastic properties. This application for radium was suggested, strangely enough, by Alexander Graham Bell. Between 1910 and 1920, radium was widely and success--fully employed to the virtual exclusion of x-ray, but around 1930, combinations of x-ray and radium began to be used with some degree of success.

During the time of this widespread usage of irradiation therapy in carcinoma of the cervix, the radical surgical attack, with its 15-30% operative mortality, had largely fallen into disrepute.[7] By 1937, even the strongest advocates of surgery had come to the conclusion that radium offered the best chance of cure with the least chance of unpleasant sequellae.

It was the almost universal belief at that time that if the disease had spread to the lymph nodes of the lateral pelvic wall, these metastases could not be eradicated by the currently existing methods of irradiation, and those thoughts seemed to be substantiated

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by statistics. With this in mind a few daring investigators began
to suggest that surgical lymphadenectomy after irradiation of the
primary tumor might be in order. The most prominent of these
pioneers were Leveuf in France and Taussig in St. Louis. The
real stimulus for the return of surgical treatment of carcinoma
of the cervix, however, was J. V. Meigs' report in 1944 of a
series of cases in stages I and II treated by radical hysterectomy
and pelvic node dissection. Further interest was aroused in 1947
by Brunschwig's report of his experience with pelvic exenteration
in women with far advanced disease.[27] The surgical attack was
coming back, but the surgical gynecologists and the radiotherapists
still stood largely in their separate camps.[14]

MATERIALS

In this report, we are primarily interested in results of treatment of carcinoma of the cervix at the University of Nebraska Hospital, although we will compare these results with those obtained at other centers.

Between January 1, 1958, and October 1, 1963, there was a total of 99 patients treated for carcinoma of the cervix at the University of Nebraska Hospital. Table I shows the number and per-centage of patients presenting with each stage of the disease.

Stage	# of Patients	% of Total
0	38	38.4
I	25	25.2
II	17	17.2
III	14	14.1
IV	5	5.1

Table I-Distribution by Clinical Stage of Patients with Squamous Cell Carcinoma of the Cervix. 1958-1963

There was a total of 88 white patients and 11 Negroes. They were taken from the whole state of Nebraska, although the largest per-centage was from the Omaha area.

The average age of the patients was 46.4. Table 2 shows the distribution of patient ages by clinical stage of the disease.

Stage	20-29	30-39	40-49	50-59	60-69	70-79	80---	Average Age at Treatment
0	11	15	8	0	4	0	0	35.8
I	2	10	5	2	3	3	0	45.4
II	0	4	4	4	2	1	2	54.1
III	0	0	3	3	3	5	0	62.4
IV	0	0	1	2	1	0	1	61.8
Total	13	29	21	11	13	9	3	46.4

Table 2-Distribution of Ages at Time of Diagnosis of Patients with Carcinoma of the Cervix. By Stage of Disease. 1958-1963.

These figures compare nicely with the average age of 47 found in a group of patients studied by Campos.[8] They also fit the observation of Dodds that the older patients tend to have the more advanced stages of the disease.[12]

It is interesting to note that the vast majority of the patients in the study group are parous. Taking the whole group into consideration, there was a total of 406 full-term pregnancies in 98 mothers, or an average of 4.1 full-term pregnancies per patient. The parity of one patient is unknown. Many of the patients had premature deliveries. Considering the group as a

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whole, there were 28 premature deliveries in 98 women. This is
an average of 0.28 prematures per patient. In the entire group
of patients, there were a number of miscarages. In the 98 patients
whose parity is known, there were 76 miscarriages, or an average
of 0.78 miscarriages per patient.

These figures are broken down for each stage of the disease
and are presented in Table 3.

Stage	Mean # Full Term Pregnancies per Patient	Mean # Prematures per Patient	Mean # Miscarriages per Patient
0	4.1	0.50	1.02
I	3.8	0.20	0.52
II	4.6	0.19	0.93
III	3.6	0.07	0.43
IV	2.8	0.28	0.78
All Stages	4.1	0.28	0.78

Table 3-Mean Number of Full Term Pregnancies, Prematures, and
    Miscarriages per Patient.

These data do not seem to fit any logical pattern and tend
only to substantiate the observation of Rotkin[29] that the majority
of cervix cancer patients are parous.

Seventy-two of the 99 patients had their blood typed. The

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results of this blood typing can be seen in Table 4.

Stage	Group A	Group B	Group AB	Group O
0	20	1	0	16
I	11	0	0	7
II	3	0	1	3
III	1	0	0	6
IV	1	0	0	2
Total	36	1	1	34
Percent	50%	1.4%	1.4%	47.2%

Table 4-Distribution of Blood Types in Patients.

It is interesting to note the variability in initial symptomatology observed by the patients. We can see by examining this factor in the various clinical stages of the disease that there is a marked difference in initial symptoms between the stages.

Stage 0. In the 38 patients in Stage 0, it is noted that 33 carcinomas-in-situ were discovered by way of routine Papanicolaou smears followed by cervical conization. These 33 patients (86.9% of Stage 0) had absolutely no signs or symptoms of their cancers and the disease was discovered by routine smear.

These asymptomatic patients waited varying lengths of time

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after they knew they had suspicious Pap smears before submitting themselves to therapeutic measures. Time from suspicious Pap smear to definitive treatment ranged from one week to four years, with a mean waiting period of six months.

Four patients (10.5%) were directed to the Gynecology Clinic because of vaginal bleeding of varying degrees. One of these patients was bleeding from uterine fibroids and the cancer was discovered by routine Pap smear. Another patient complained of excessive bleeding and her cancer was likewise discovered by routine Pap smear. The other two patients complained of occasional foul bloody discharge and inter-menstrual spotting respectively, and their neoplasms were also discovered by routine Papanicolaou smear. These patients had been bleeding from three to twelve weeks before they came to the clinic. These patients all submitted to treatment within a week after they were found to have suspicious Pap smears.

One patient (2.6%) was found to have an unsuspected Stage 0 cancer at routine pathological examination of a cervical polyp which she had removed. She submitted to treatment while still in the hospital recovering from her polypectomy.

Stage I. Thirteen of the 25 Stage I patients (52%) were asymptomatic and were found to have carcinoma of the cervix by way

of routine Papanicolaou smears followed by cervical conization
and definitive treatment.

Ten Stage I patients (40%) had some form of vaginal bleeding
as initial symptomatology. The time span from initial symptoms
to treatment ranged from 2 weeks to 13 months. One patient had
post-coital bleeding for 6-7 years before consulting her physician.

One patient (4%) complained only of a foul discharge (associated
with pelvic inflammatory disease) of long standing. Her neoplasm
was detected by way of a Papanicolaou smear followed by a cervical
conization 2 months later.

One patient (4%) was found to have Stage I carcinoma of the
cervix on pathological examination of her uterus following a
hysterectomy. This elderly lady had worn a Gellhorn pessary for
uterine prolapse for 15 years, and had never once removed it.

Stage II. Twelve of the 17 patients with Stage II cancer
(70.6%) had vaginal bleeding as their initial symptom. The time
interval from the onset of symptoms to treatment in these patients
ranged from 2 weeks to 13 months, with a mean time interval of
3.6 months.

The initial symptoms of three of the Stage II (17.6%) patients
are unknown.

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Two of the Stage II patients (11.8%) were found to have cervical neoplasms by way of routine Papanicolaou smear followed by cervical conization. One patient was treated 10 months after the first suspicious smear. The other Pap-to-treatment time interval is not known.

Stage III. Bleeding vaginally was the initial symptom in 6 of the 14 patients in Stage III (42.9%). The time from first symptom to treatment ranged from 3 months to 12 years. Excluding the patient with the 12 year bleeding history, average time from symptom to treatment was 7.4 months.

Vaginal discharge was the initial symptom in 3 patients (21.4%). Two of these patients later developed vaginal bleeding. The symptom-to=treatment time ranged from 2 weeks to 19 months, averaging 10.3 months.

One patient of the Stage III group (7.1%) had right lower quadrant pain as her first symptom. It lasted three months, and later progressed to vaginal bleeding.

One patient (7.1%) had her disease diagnosed two years previously at another institution, and the initial symptoms of three Stage III patients (21.4%) are not known.

Stage IV. Four of the five Stage IV patients (80%) had

vaginal bleeding of some type as initial symptoms. Time from
symptoms to treatment ranged from 4 months to 16 years. The
initial symptoms of one patient are unknown.

Data regarding the initial symptoms are summarized in
Table 5.

Stage	Routine Pap & Cone	Vaginal Bleeding	Incidental Findings after Unrelated Surgery	Vaginal Discharge	Not Known	Pain
0	86.9%	10.5%	2.6%	–	–	–
I	52.0%	40.0%	4.0%	4.0%	–	–
II	11.8%	70.6%	–	–	17.6%	–
III	–	42.9%	–	21.4%	28.5%	7.1%
IV	–	80.0%	–	–	20.0%	–

Table 5-Initial Symptoms of Patients, by Stage of Disease.

GENERAL ASPECTS OF SURGERY OF CERVIX NEOPLASMS

Carcinoma in situ-(Stage 0)

After it has been proven by cervical conization or other

biopsy procedure that a carcinoma is present and that there is

no invasion of the neoplasm beneath the basement membrane, then

Stage 0 carcinoma is said to exist. There is little necessity to

do radical surgery on patients with carcinoma in situ because,

by definition, there has been no invasion and the lymphatics are

not involved. It is currently felt that once the presence of

Stage 0 cancer is proven, the physician must be guided by the age,

parity, and wishes of the patient.[19] For example, a patient in

her 20's with three children should probably have a hysterectomy,

but if the patient is under 30 and desires more children, definitive

therapy can be delayed if the patient is followed closely by

cervical smears. If at any time, however, a positive smear is

seen and the presence of carcinoma is confirmed by repeat

conization, this conservative management must end, and hysterectomy

be carried out at once.[1, 36,13]

It is now agreed by most authorities that definitive treat-

-ment for carcinoma in situ of the cervix is total abdominal

hysterectomy with removal of at least a 3 cm vaginal cuff. It

is not necessary to remove the ovaries since there has been no

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trouble with recurrence in these organs.[1, 19, 36]

Some investigators feel that a more conservative treatment
for Stage 0 carcinoma is in order. According to Bret, et al,
Stage 0 carcinoma is, "only a pattern in the definition of
irregular dysplasias," and some 15-20% of these cannot later be
traced after biopsies, cautery, topical antibiotics, and trauma
of childbirth.[5] Boyd and his group reviewed the records of 71
patients with Stage 0 carcinoma of the cervix who did not have
hysterectomy. All these patients had only cervical conization
as primary treatment. Of these, 80.2% are alive with negative
cytology and 8.3% are alive with abnormal cytology. Hysterectomy
was performed after conization in 3.2%, and 8.3% died of unrelated
causes.[4] Bickenbach feels that conization is adequate temporary
management of Stage 0 cancer in patients who want children.
Conization was the only means of therapy in 74 of his patients,
and there have been no recurrences in 1-5 years. He stresses
that follow-up smears must be taken regularly.[2] Hillemans and
Kottmeier feel that conization will not increase the incidence
of later invasions because bleeding carries cells out of the
wound and because forming granulation tissue is hostile to
neoplastic cells.[18]

If the patient is in such poor general physical condition

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that surgery is contraindicated, it is perfectly acceptable to use radiation therapy as definitive treatment. Radiation is felt to be almost 100% effective.[1,19,21,36]

Invasive carcinoma

When the neoplastic growth has invaded beneath the cervical basement membrane, invasive carcinoma is said to be present. This condition requires more radical treatment than non-invasive carcinoma, since the lymph nodes are potentially involved.

The surgical approach to invasive cancer has many advantages. First of all, surgery permits exploration of the pelvis under direct vision, thereby enabling the physician to more accurately evaluate the extent of the disease. In addition to this, the surgical attack removes the cervix, uterus, and node bearing areas and it is well known that a recurrence cannot take place in extirpated areas.[30,35]

It is now felt by many that surgery can be used as adequate primary treatment in Stage I.[26,30,35] It may also be used in combination with radiation in Stages I through IV. There are, however, many radiotherapists who feel that surgery is not indicated except in situations where radiation has been shown to fail, or in cases where infection or pelvic abnormalities preclude the use of radiation.[3,19]

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Cervical Lymphatic System. In order to understand the various surgical procedures used in treating invasive carcinoma of the uterine cervix, and the degree of success of each of these procedures, it is necessary to be familiar with the lymphatics that drain the cervix since it is by way of the lymphatics that metastases occur. It is on a firm knowledge of the anatomy of the lymphatic drainage that modern cancer surgery is based.

The lymphatics which drain the cervix converge in the same area of the isthmus to form the so-called paracervical plexus, and from here individual lymph channels follow the course of the uterine vessels. There are three main channels. The major drainage is the anterior, preureteric, or external iliac route. As the name implies, this drainage follows the uterine artery and extends laterally, anterior to the ureter, to the hypogastric, obturator, external iliac and sacral nodes. The posterior, retroureteric, or internal iliac drainage follows the uterine vein posteriorly to terminate in the hypogastric nodes. The sacral drainage passes within the uterosacral folds to terminate in nodes near the sacral promontory or in the lateral sacral nodes.

As regards the lymph nodes themselves, they are variable in size from 4 mm to 1.5 cm and are embedded in fat and areolar tissue. Even though they vary in size and number, they tend to appear in

distinct groups which can be classified.

I. THE PRIMARY GROUP

    A. Parametrial Nodes. This is a constant group of small
nodes which occur along the lymphatic channels as they
cross the parametrium.

    B. Paracervical or Ureteral Node. This node is found at
the junction of the uterine artery and ureter. It may
be absent or may be found with other nodes.

    C. Obturator Nodes. These nodes are found in the obturator
fossa near the obturator vessels and nerve. There may
be a few nodes or one large node, the so-called Leveuf's
node.

    D. Hypogastric Nodes. These nodes are found along the
hypogastric vein near its junction with the external iliac.
This group usually consists of a few small nodes.

    E. External Iliac Nodes. These nodes which consist of six
to eight large nodes, are found in the sulcus between the
external iliac vessels but may occasionally be found
medial to the vein.

II. THE SECONDARY GROUP

    A. Sacral Nodes. These are found along the concavity and
promontory of the sacrum.

B. <u>Common Iliac Group.</u> This group of four to six nodes lies
along the course of the common iliac vessels just below
the bifurcation of the aorta.

C. <u>Inguinal Group.</u> This group, including the deep and super-
ficial femoral lymph nodes, is made up of large nodes.

D. <u>Periaortic or Aortic Nodes.</u> These run along the aorta
and vena cava from the bifurcation to the diaphragm.[14]

<u>Wertheim Hysterectomy.</u> This operation, more properly called
a radical hysterectomy with bilateral pelvic lymph node dissection,
is the most widely used surgical procedure against invasive
carcinoma of the cervix. According to Meigs,

"This type of surgical approach should be confined to Stage

I, most Stage II, and especially early Stage III cases...

The more advanced the disease, the more likelihood of

extension and of positive nodes, and the less likelihood

of cure." [26]

The technique is based on a surgical concept for treating
malignant disease that is entirely different from the approach to
benign conditions. That concept is that the operation must
begin at the most lateral point of potential spread and work
toward the primary; whereas, operations for benign disease begin
at the leison and work laterally only as necessary. This, of

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course, is to prevent iatrogenic metastases, if possible. It
is necessary to do a wide excision, removing uterus, adnexa, and
all areolar tissue and lymph nodes in the common iliac, hypogastric,
external iliac, and obturator regions. A wide vaginal cuff is
taken to guard against local metastases. The ureters are dissected
free from the bifurcation of the aorta to the bladder entrance.
The bladder is mobilized from the vagina so that the block of
lymphatic tissue which runs from lateral pelvic wall to the
paracervical and paravaginal areas may be removed. The vesical
nerve supply will be damaged by this maneuver and bladder atony
will occur for some time in an adequate operation.[14]

Schauta Hysterectomy. (Radical Vaginal Hysterectomy). This
operation, a radical vaginal hysterectomy, supposedly has the
advantage of less operative hazard than the abdominal approach,
and there are fewer ureteral injuries. Also, the primary mortality
is supposedly lower and there are fewer post operative fistulae.[25]
However, this operation has not gained favor in the United States
because the pelvic lymph nodes cannot be removed by this approach.[26]

Pelvic Lymphadenectomy. This procedure, which has not found
wide acceptance in this country, consists of bilateral pelvic
lymph node dissection without the removal of the primary lesion.
In 1952, Kimbrough treated a small series of patients with
lymphadenectomy followed by full radiation to the cervix.

His Stage I patients had 20.3% incidence of positive nodes, and his Stage II patients had a 34.8% incidence. After 5 years, 87% of Stage I patients and 62% of Stage II patients were alive without recurrence.[22] Gray found that preoperative radiation reduced the number of positive nodes to the extent that operative lymphadenectomy should not be necessary.[16]

Exenteration. These operations were originally meant to be only palliative and were used to relieve the patient from necrotic fistulae, pelvic sepsis, and the possibility of sudden massive hemorrhage. They were originally done by Brunschwig in 1947. At the present time, however, they are known to be curative in a small number of cases.[27]

These radical operations are an attempt to salvage patients with Stage III or IV carcinomas of the cervix who would otherwise have no hope of recovery. In the total exenteration, all pelvic organs including the vagina, bladder, uterus, adnexa, and rectum are removed. A colostomy is done, as well as some means for urinary drainage. The anterior exenteration is done when the bladder is involved but the rectum is free. The posterior exenteration is done when the bladder is free but the rectum is involved.[14] The initial mortality rate is 20-30%, but it must be remembered that patients selected for exenteration would

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ordinarily live only 1-2 years without the operation. The survival rates are about 20% at best[37] and complications are extremely frequent, but the proponents of exenteration feel that since these figures are comparable to those in lung and stomach cancer, the operations should continue to be done when indicated.

RESULTS OF SURGICAL TREATMENT OF CARCINOMA OF THE CERVIX

Stage 0. In Stage 0, there was a total of 38 patients treated between January 1, 1958 and October 1, 1963. The average age of these patients was 35.8 years. All of these patients except one were treated by surgical means. One patient (2.6%) was treated by irradiation because she had severe heart disease which was considered a contraindication to surgery.

Total abdominal hysterectomy was the treatment in 26 of the 38 patients (68.4%). Six patients (15.8%) were treated with total abdominal hysterectomy with bilateral salpingoophorectomy, and two patients (5.3%) were treated by total abdominal hysterectomy with unilateral salpingoophorectomy. Three patients (7.9%) were treated with only cervical conization. These methods of treatment are summarized by years in Table 6.

Year	# Patients	TAH	TAH with BSO	TAH with USO	Cervical Cone	Rad.
1958	3	1	-	1	-	1
1959	7	7	-	-	-	-
1960	10	6	3	1	-	-
1961	7	5	1	-	1	-
1962	5	3	1	-	1	-
1963	6	4	1	-	1	-

Table 6-Methods of Treatment of Stage 0 Carcinoma of the Cervix.

In the 26 total abdominal hysterectomies which were done, operative time ranged from 1-3½ hours, with a mean operative time of 2.6 hours. No blood was required in 15 patients, but 11 patients had transfusions 6f from one to three units.

In the six total abdominal hysterectomies with bilateral salpingoophorectomies, operative time ranged from two to three hours, with a mean operative time of 2.6 hours. Only one patient required a unit of blood.

In the two total abdominal hysterectomies with unilateral salpingoophorectomies, the operative time was two hours. Neither of the patients required blood transfusions.

Complications. In the 37 patients who were surgically treated for carcinoma in situ (Stage 0) carcinoma of the cervix, seven (18.9%) had postoperative complications. These were infectious in nature, for the most part, and are listed below.

1. Infected hematoma of vaginal cuff   (1 case)

2. Intraabdominal abscess   (1 case)

3. Wound infection   (3 cases)

4. Cystitis   (2 cases)

All complications occurred in patients who had hysterectomies, while none occurred in patients who were treated by cervical conization only.

Results. Of the 37 patients treated surgically, all are alive today. In no case has there been any evidence of recurrence. The one irradiated patient is also alive and free of recurrence.

Stage I. In Stage I, there was a total of 25 patients treated between January 1, 1958 and October 1, 1963. The average age of these patients was 45.4 years. Thirteen of these patients (52.0%) were treated by surgical means alone. Of these, ten had Wertheim hysterectomies, two had simple total abdominal hysterectomies, and one a vaginal hysterectomy with anterior and posterior repair of uterine prolapse. Three patients (12.0%) were treated with a combined program of radiation and surgery. Of these, one had radiation and an anterior exenteration, one had a simple total abdominal hysterectomy and radiation, and one had a Wertheim hysterectomy and radiation. Nine patients (36.0%) were treated with radiation alone. These methods of treatment are shown in tabular form in Table 7.

Year	# of Patients	Wertheim	TAH	Vaginal Hysterectomy	Radiation & Surgery	Radiation Alone
1958	3	2	—	—	1	—
1959	9	5	—	1	—	3
1960	6	2	1	—	1	2
1961	7	1	1	—	1	4
Total	25	10	2	1	3	9

Table 7-Methods of Treatment, Stage I Carcinoma of Cervix, 1958-1963.

In the 11 Wertheim hysterectomies which were done, operative time ranged from $2\frac{1}{2}$ to $5\frac{1}{2}$ hours, with a mean operative time of 3.8 hours. All patients required blood transfusions, ranging in amounts from one to four units. The average amount of transfused blood per patient was 2.5 units.

In the three total abdominal hysterectomies, operative time ranged from $1\frac{1}{2}$ to $3\frac{1}{2}$ hours, with a mean operative time of 2.3 hours. Only one patient required a unit of blood.

The vaginal hysterectomy with repair of a uterine prolapse took 2 hours. No blood was required.

The anterior exenteration with sigmoid ureterostomy took $5\frac{1}{4}$ hours.

Complications. In the 11 Wertheim hysterectomies which were done in Stage I, there were three complications (27.2%). These are listed below.

1. Postoperative infection leading to adhesions, finally resulting in bowel obstruction.

2. Postoperative cystitis.

3. Postoperative pyelitis and hydronephrosis.

The vaginal hysterectomy with repair of uterine prolapse was complicated by breakdown of the vaginal cuff and infection.

There were no complications in the three total abdominal hysterectomies or in the anterior exenteration.

Hence, there was a total of four operative complications in the 16 surgically treated patients, or an incidence of 25%.

Results. Ten patients were treated by Wertheim hysterectomy alone, and all of these patients are alive today with no evidence of recurrence. One patient who was operated upon in 1958 has survived 56 months. The most recently treated patient has survived 33 months. This results in a 2 year survival rate of 100%.

Two patients were treated by total abdominal hysterectomy only. Both of these patients are alive today, but the patient treated in 1961 is currently being treated for recurrence of the neoplasm after 28 months. The two year survival rate is 100%.

The one patient whose Stage I cancer was detected as an incidental finding after hysterectomy for other reasons is alive today, 45 months post operatively. This is a 2 year survival rate of 100%.

Two of the three patients who were treated with radiation and surgery are dead of cancer of the cervix. These are the patient who had a simple hysterectomy plus radiation, and an anterior exenteration plus radiation. The patient who had a Wertheim

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hysterectomy with radiation is alive and free from recurrence after 34 months. The two year survival rate is 33 1/3%.

Of the patients (9) who were treated with radiation alone, one is dead (after 2 months) of her tumor. Another died of a myocardial infarction, but at the time of her death, she was 30 months post-treatment, and free of carcinoma. The two year survival rate is 88.9%. The above results for Stage I are shown in Table 8.

PROCEDURE	# Patients	Alive & Well after 2 yr.	2 yr. Survival Rate
Wertheim hysterectomy only	10	10	100%
TAH alone	2	2*	100%
Vaginal hysterectomy only	1	1	100%
Radiation & surgery	3	1	33.3%
Radiation only	9	8	88.9%
Totals	25	22	88%

*Recurrence after 28 mo. in one patient.

Table 8-Survival of Patients Treated for Stage I Carcinoma of the Cervix, 1958-1963.

Stage II. In Stage II, a total of 17 patients was seen between January 1, 1958 and October 1, 1963. The average age of

these patients was 54.1 years. None of these patients were treated
by surgery alone. Two patients (11.8%) were treated with a
combination of radiation and surgery. One of these had radiation
and an anterior exenteration which lasted 8 hours, and the other
had radiation and a Wertheim hysterectomy. Fourteen of the
patients (82.4%) received radiation therapy alone, and one
patient (5.8%) refused any therapy and was lost to follow-up
in 1961.

Results. The two patients who were managed with radiation
and surgery combined are both alive at this time. The patient who
had radiation and an exenteration is alive after 48 months, but
recently developed pulmonary metastases, presumably from the
cervical tumor. The patient who had a Wertheim hysterectomy
is alive at 24 months, but has just had recurrence of the disease
in her pelvis.

Of the 14 patients treated with radiation alone, seven
(50.0%) are now dead of the carcinoma. Seven others are alive
and free of the disease at post-treatment time spans ranging
from 6 to 48 months.

The one patient who refused treatment was lost to follow-
up in 1961.

These results are shown on Table 9.

PROCEDURE	# PATIENTS	LIVING	DEAD	% SURVIVAL
Radiation & exenteration	1	1	—	100%
Radiation & Wertheim	1	1	—	100%
Radiation alone	14	7	7	50%
Totals	16		7	56.25%

Table 9-Results of Treatment in Stage II.

Stage III. In Stage III, there was a total of 14 patients treated between January 1, 1958 and October 1, 1963. All of these patients were treated by radiological means. Of these 14 patients, 13 (92.8%) are dead. These deaths occurred from two to 40 months after treatment, with an average survival time of 15 months. The one surviving patient is now alive 42 months after treatment.

Stage IV. In Stage IV, there was a total of 5 patients treated between January 1, 1958 and October 1, 1963. The average age of these patients was 61.8 years. Two patients (40%) refused therapy. One patient (20%) was treated with an anterior exenteration alone. One (20%) had an exenteration and radiation. Another (20%) was treated with radiation only. These methods of treatment are shown in Table 10.

YEAR	# PATIENTS	ANTERIOR EXENTERATION	RADIATION & EXENTERATION	RADIATION ONLY	REFUSED THERAPY
1959	2	—	1	—	1
1960	3	1	—	1	1
Totals	5	1	1	1	2

Table 10-Methods of Treatment of Stage IV Carcinoma of the Cervix, 1958-1963.

The anterior exenteration in 1960 took seven hours. The patient required 23 pints of blood. Complications in this case included a wound infection and a rectoperineal fistula.

The exenteration with sigmoid colostomy took five hours to perform and the patient required five units of blood.

Results. The two patients who refused therapy are both dead at two weeks and four months after treatment was offered.

The patient treated with anterior exenteration alone is living 35 months after surgery.

The patient treated with radiation and exenteration with sigmoid colostomy died 17 months after treatment, and the patient treated with radiation only died 14 months after treatment. These results are summarized in Table 11.

MANAGEMENT	# PATIENTS	LIVING	DEAD	% SURVIVAL
Refused therapy	2	—	2	0%
Anterior exenteration	1	1	—	100%
Radiation & exenteration	1	—	1	0%
Radiation only	1	—	1	0%
Totals	5	1	4	20%

Table 11-Two year Survivals in Stage IV Carcinoma of the Cervix.

DISCUSSION

Stage 0. In our study, there were 37 patients treated
surgically for carcinoma in situ of the cervix. All of these are
now alive and there has been no recurrence in any case. This
100% survival rate is excellent compared to the results of other
centers.

At the Mayo Clinic, there were 1,290 patients treated for
carcinoma in situ between 1932 and 1960. In this group there
was one operative death, and there were three deaths from recurrent
carcinoma in the vagina.[36] This gives a survival rate (excluding
37 patients who have died of unrelated causes) of 99.8%. Surgical
procedures done in this group of patients included total abdominal
hysterectomies and definitive conizations. In a smaller group of
Stage 0 patients done at Rochester, 12 patients were subjected to
Wertheim hysterectomies with a five year survival rate of 100%.
There were no recurrences in this group.

At the University of Oklahoma, somewhat more unfortunate
results were obtained. In this study of 74 patients with Stage 0
cancer, there were six recurrences of the neoplasm in the vagina
after total abdominal hysterectomy. This is attributed in part
to lack of removal of an adequate vaginal cuff.

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In our series of surgical patients, there were a number of
complications attributed to surgery. In the 34 total abdominal
hysterectomies done in Stage 0, there were 7 complications. They
were, for the most part, minor. There were three wound infections,
two cases of cystitis, one intra-abdominal abscess, and one
infected vaginal cuff.

Invasive Carcinoma. Table 12 shows results of purely surgical
therapy. Table 13, included only for reference, shows results
of pure radiation therapy, and will not be discussed since this
report is intended to discuss surgical results only.

STAGE	# SURGICAL PATIENTS	L & W AFTER 2 YEARS	2 YEAR SURVIVAL RATE
I	13	13	100%
II	-	-	-
III	-	-	-
IV	14	14	100%

Table 12-Survival of Surgically Treated Patients.

STAGE	# IRRADIATED PATIENTS	L & W AFTER 2 YEARS	2 YEAR SURVIVAL RATE
I	9	8	88.9%
II	14	7	50.0%
III	14	5	35.7%
IV	1	0	00.0%
Totals	38	20	52.6%

Table 13-Survival in Radiation Program.

At first glance, it seems that our 2 year survival rate of 100% in patients treated only by surgical means is remarkably good. Our elation must be tempered by the fact that we are comparing this survival rate to an exceedingly small group of combined therapy and radiation patients, and that our surgical group itself is small. Even though this is true, the good results are encouraging and warrent continued investigation in purely surgical treatment.

In reviewing the literature regarding the survival of surgical patients, the results of several investigators were studied. The operative procedure used most frequently was the radical abdominal hysterectomy with bilateral pelvic lymphadenectomy (Wertheim hysterectomy). The best results were obtained in a group in Japan reviewed by Magara.[24] In Stage I, the five year survival rate in his 28 patients was 100%. In Stage II, it was 74.1% and in Stage III it was 47.2%. The poorest results in the Wertheim hysterectomies were obtained by Blaikly[3] whose 5 year survival rate in Stage I was 66.1%. In Stage II it was 48.9% and in Stage III it was 20%. These results, along with those of other investigators are shown in Table 14.

INVESTIGATOR	STAGE I	STAGE II	STAGE III	STAGE IV
Blaikly[3]	66.1%	48.9%	20.0%	- - -
Carter[9]	81.5%	57.3%	50.0%	00.0%
Green[17]	85.5%	57.3%	10.0%	- - -
Magara[24]	100%	74.1%	47.2%	- - -
Welch[35]	89.2%	74.3%	60.0%	00.0%
TOTAL	86.4%	63.7%	45.9%	00.0%

Table 14-Results of Several Investigators of Radical Hysterectomy

      with Lymphadenectomy in Various Stages of Cancer of the

      Cervix.

Kimbrough[22] summarized the results of four other investigators
who used Wertheim hysterectomies in Stages I and II. These results
are roughly comparable to the totals in Table 14, and are shown
in Table 15.

INVESTIGATOR	STAGE I	STAGE II
Kelso	85.9%	71.1%
Rauscher and Spurny	87.4%	58.0%
Phillip	86.0%	53.8%
Meigs	81.8%	61.8%

Table 15-Five Year Survival Rates, Wertheim Hysterectomies.

Brunschwig[16] published results in 1958 of his 269 Wertheim

procedures, giving an overall 5 year survival rate for all stages of 58%. Combining this with the results shown in Table 14, we find that there was a total of 1,335 patients treated by Wertheim hysterectomy and 959 were alive at the end of 5 years. This is a survival rate of 71.8%. This survival rate is deceivingly high because it is biased with regard to the number of patients in Stages I and II.

McCall[25] treated 116 patients in all stages with the Schauta-Amreich radical vaginal hysterectomy and found that 108 (98%) survived five years. Brunschwig[6] found that 17 (68%) of his 25 patients treated with radical vaginal hysterectomy survived five or more years. Combining the data of these two investigators of the radical vaginal operation, we find that of 141 patients in all stages, 125 (88.6%) survived five years or more.

With regard to the pelvic exenteration procedures for far advanced carcinoma of the cervix, the results of two investigators were studied. In 1957, Schmitz[31] published results of various procedures which included results of 34 exenterations. Of the 34 patients, eight (23.5%) survived five or more years. Between 1947 and 1957, Brunschwig did 552 exenterations and found that 116 or 21.0% survived five years or more.[37] These results are combined and presented in Table 16.

INVESTIGATOR	# PATIENTS	# SURVIVORS	5 YEAR SURVIVAL RATE
Schmitz[31]	34	8	23.5%
Brunschwig[37]	552	116	21.0%
TOTALS	586	124	21.2%

Table 16- Results of Pelvic Exenteration Procedures.

In our study at the University of Nebraska, six patients
were treated with a combined radiation-surgery program. The
results of this management are seen on Table 17.

STAGE	# CASES	# 2 YR. SURVIVALS	2 YR. SURVIVAL RATE
I	3	1	33.3%
II	2	2*	100%
III	—	—	—
IV	1	0	00.0%
TOTAL	6	3	50.0%

*Now recurring in both patients.

Table 17-Survival in Combined Therapy Program

Several investigators studied the effects of pre-operative
radiation on five year survival rates. Blaikly[3] found that
a combination of radiation and surgery produced identical five
year cure rates to either method alone in Stage I. Brunschwig[6]
concluded in 1958 that preoperative radiation was of no value,
although his later statistics showed that this was not true.

Sweeney[32] did Wertheim hysterectomies on previously irradiated
patients and got a five year survival rate in all stages of 68.6%.
In 1961, Brunschwig[7] published a report on survivals of 404 patients
without pre-operative radiation and 110 patients who were irradiated
prior to surgery. He found that pre-operative radiation contributed
to the survival rate. This was also the conclusion of Welch[35]
who studied 153 non-irradiated surgical patients and 144 irradiated
ones. The results of these two investigators are tabulated and
combined in Table 18.

INVESTIGATOR	STAGE I		STAGE II		STAGE III		STAGE IV	
	NO RAD	RAD	NO RAD	RAD	NO RAD	RAD	NO RAD	RAD
Brunschwig[7]	76%	84%	52%	53%	27%	20%	15%	27%
Welch[35]	88%	91%	80%	72%	50%	67%	—	00%
TOTALS	81%	88%	56%	64%	31%	45%	15%	23%

Table 18-Five Year Survival Rates in Surgical Patients with and

without Pre-operative Radiation.

All of our Stage I patients who were operated upon had pelvic
lymph nodes which were free of metastases, as proved by pathologic
examination. Other investigators have found a higher percentage
of positive nodes. Green[17], Carter[9], and Brunschwig[6] have found
that 14% of their Stage I patients have positive nodes. Riva[24]
and Kimbrough[22] have a 19% incidence of positive nodes in Stage I.
It has been shown that the presence of pelvic lymph node metastases

markedly affects the five year survival rate. For example, Green[17] found that his five year survival rate in Stage I surgical patients with negative nodes was 89%, but in those with positive nodes it was only 44%. Brunschwig[6] found that 82% of his Stage I patients with negative nodes survived five years, while only 61% of those with positive nodes did. Cosbie's[10] results were 75% and 22% respectively. Our 100% survival rate is no doubt a result of the absence of node metastases.

In our series of surgical cases, there were no operative mortalities. In comparing this to the operative deaths of others, we find that McCall[25] had an 0.86% immediate mortality in radical vaginal operations. Riva's[28] Stage I operative mortality rate was 0.8% for Wertheim hysterectomies. Brunschwig[7] found an operative mortality of 0.7% for all operations exclusive of exenterations. The immediate death rate for his exenterations was 11%.

In the 11 Wertheim hysterectomies done here in Stage I, there were three complications (27.2%). One patient had post-operative cystitis, another developed pyelitis and hydronephrosis, and another developed adhesions which finally resulted in bowel obstruction. There were no fistulae. In Stage IV, there were two exenteration procedures done. In one of these, there was a wound

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infection and a rectoperineal fistula.

Our low incidence of major complications compares favorably
with the findings of other investigators. Most found that their
major complications were fistulae. In 447 Wertheim hysterectomies,
Brunschwig[7] had a 9% incidence of ureterovaginal fistulae and a
7% incidence of vesicovaginal fistulae. These findings are similar
to those of Green.[17] Green found that his 11% incidence of all
fistulae was reduced to 5.6% by prolonged post-operative bladder
drainage. Schmitz[31] had an 11% incidence of complications (including
fistulae, infection, and evisceration) in 24 Wertheim hysterectomies
on patients who had had no pre-operative radiation. His incidence
of complications in patients who had pre-operative radiation was
30%. Schmitz also had an incidence of 17.1% fistulae in 35
exenterations. Decker, in an interesting paper on sexual function
after surgical treatment of carcinoma of the cervix found that
sexual function was diminished or abolished in 18.8% of his 37
patients, but was increased or remained unchanged in the remainder.[11]

SUMMARY

In this report, we have attempted to discuss the results which can be expected in the surgical treatment of carcinoma of the cervix.

The study group was a group of 99 patients treated by various means at the University of Nebraska Hospital between January 1, 1958 and October 1, 1963. Patient distribution by stage of carcinoma, age, blood group, and parity was presented. Initial symptoms and delay between the onset of symptoms and the patient's seeing a doctor were discussed.

The general aspects of surgery of carcinoma of the cervix were presented, and the indications and various procedures were discussed. These included the Wertheim radical hysterectomy, the Schaunta radical vaginal hysterectomy, pelvic lymphadenectomy, and the exenteration operations.

Results of surgical treatment at the University of Nebraska Hospital were tabulated and discussed, and complications were mentioned. A short literature review showing results of other investigators was also included.

CONCLUSIONS

It is apparent from the results of our study and from the
results of others that the most widely accepted method of treat-
ment for carcinoma in situ of the cervix is a total abdominal
hysterectomy with removal of a wide vaginal cuff. Our two year
survival rate, recurrence free, was 100%. From the results of
other investigators we can see that the expected five year
survival rate is virtually 100%. If the patient is pregnant,
or wishes to become pregnant, it is acceptable to treat her by
conization and adequate follow-up.

The advantages of surgery in the treatment of invasive
cervical carcinoma are basically twofold. First, surgery allows
direct exploration so that the extent of the disease can be seen.
Second, the cervix, uterus, and node-bearing areas can be removed,
precluding recurrences in these areas.

In our Stage I patients there were ten Wertheim hysterectomies,
two total abdominal hysterectomies, and one vaginal hysterectomy.
The two year survival rate is 100%. Complications after the
Wertheim procedure included adhesions,(1); cystitis,(1); and
hydronephrosis,(1). The Stage I surgical cases were obviously
early invasions as shown by the fact that there were no positive

lymph nodes in any case. In Stage II, there were no patients
treated by surgery alone, but two were treated with radiation
and surgery, and they both have survived at least two years.
No surgery was performed on Stage III patients. In Stage IV,
one patient had an anterior exenteration and is alive after
two years. Another had an exenteration and radiation and is
dead.

The Wertheim hysterectomy, or radical hysterectomy with
bilateral pelvic lymphadenectomy is the most widely used operation
in the attack against invasive carcinoma of the cervix. After
reviewing the literature, we find that we can expect a five year
survival of about 86% in Stage I, 64% in Stage II, 46% in Stage III,
and 0% in Stage IV. If there are pelvic nodal metastases, we can
expect our survival rates to be halved. The Wertheim procedure
carries with it an operative mortality of 0.8% and a 16% incidence
of fistulae.

The pelvic exenteration procedures for far advanced carcinoma
of the cervix may be expected to provide a five-year survival
rate of approximately 20%.

It has been shown that modern surgery is not to be disregarded
in the attack upon carcinoma of the cervix. It is a highly effective
method of treatment which deserves further study.

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