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Treatment of invasive cervical carcinoma using surgery and/or irradiation

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THE TREATMENT OF INVASIVE CERVICAL CARCINOMA USING SURGERY AND/OR IRRADIATION

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I. Carcinoma of the uterine cervix is now the second most common cause of death due to cancer in women in this country and should therefore be of concern to every physician having contact with female patients, no matter what his specialty may be. Although the early diagnosis of cervical carcinoma before it has become locally invasive or metastatic in nature is the ultimate goal in therapy, many cases of invasive carcinoma are still seen today for various reasons. Therefore, the treating physician must be aware of the possible methods of treatment that are available in managing cases of invasive cervical carcinoma.

Historically, the first treatment was operative and the first hysterectomy for carcinoma was done vaginally in 1821 by Sauter of Constance. Between the years 1821 and 1870 vaginal hysterectomy was in vogue and the first abdominal hysterectomy was not performed until 1879 but the operative mortality was so high that this type of operation was not favored. In 1898 Wertheim reported his first series of radical abdominal hysterectomy and his operation was adopted widely despite a general immediate mortality of 20%. Then in 1908 the Curies discovered radium and its benefical effects were widely explored. In 1912 Kelly and Burnham began elective treatment of early as well as late cases of

carcinoma of the cervix with radium. Between the years 1920-1940 radiation therapy was used almost exclusively throughout the world as the survival rates and complications of operative treatment pushed this form of therapy into disfavor.[16] In the past two decades some surgeons have returned to operative treatment as they feel they are able to achieve equal or better results than with radiation therapy alone.

This return of operative treatment has brought forth a great deal of controversy in relation to what type of treatment is best for invasive carcinoma. Some advocate only irradiation treatment, others advocate primary surgical treatment of different forms and others are beginning to advocate combined surgical-irradiation treatment.

Therefore, it is the purpose of this paper to review the recent literature concerning the various methods of treatment used today. The primary concern will be gross method of treatment, complications of treatment, and survival results. No attempt will be made to cover the exact details of each specific method of treatment but rather an attempt will be made to review why various authors may or may not prefer a particular method. This paper will also include case histories and follow-ups on those patients treated by radical Wertheim hysterectomy at University Hospital along with results of irradiation treatment between the years 1937-1952 at University Hospital.

II. Many problems are encountered when attempting to review the results of various authors especially when trying to compare surgical and irradiation treatment. Selection of patients can play a major role in final survival results as it is very easy to include or exclude certain patients, and thus color one's statistics. Clinical staging of the disease can also effect results as such things as including a number of advanced Stage II patients as Stage III will markedly improve ones Stage III survival results. There is also the problem of differences in the criteria for classification among various investigators. Another problem in evaluating studies is the lack of adequate and long term follow-up because of either loss of patient contact or insufficient length of study.

Despite these problems in evaluating studies, I feel that there are many excellent studies published in the literature and the following discussion covers some of these. Surgical treatment will first be discussed, followed then by irradiation treatment, and then combined treatment.

III. Surgical treatment of invasive cervical carcinoma is now becoming a generally well accepted means of treating certain patients. The reasons for consideration of definitive surgery are as follows:

1. Removal of the cervix prevents future recurrence of a primary cervical lesion.

2. Wide removal of tissue in the area prevents recurrence from neoplastic cells which may not have been destroyed by irradiation.

3. Certain cancers of the cervix are radioresistant.

4. There will be less bowel damage as adherance of either small bowel or rectum to the uterus predisposes to severe bowel damage.

5. There is a question concerning the reliability irradiation therapy in curing nodal metastasis.

The prognosis from any type of therapy is ultimately linked to the degree of spread to the regional lymph nodes. It is well established that metastatic cancer is more resistant to irradiation than primary growth and this may be the reason for the failure to salvage more patients with Stage I cancer. Various figures have been reported concerning frequency of metastatic spread, but many of these are based upon autopsy findings. These figures vary from 18% to 42 percent.

Mitani and associates conducted an operative study on 238 patients selected at random from 434 patients with cervical carcinoma. In all 3,324

nodes were removed and examined. His incidence of metastasis was as follows:

Stage I	30.2%
Stage II	29.8%
Stage III	46.3%
Overall	32.8%

Metastases were most frequently found in the hypogastric lymph nodes (9.8%) and then in order of frequency, in the parauterine, inferior iliac, obturator, superior iliac, and deep inguinal nodes. Meigs reported the incidence of positive nodes in Stage I to be 17.9% and 36.9% in Stage II. Way has reported figures of 34.0% for Stage I and 51.0% for Stage II while Morton reports an incidence of 14.8% and 23.8% for Stage I and II respectively. From these figures one can see that there is a great deal of variation from author to author although the accepted standard generalization for positive node percentage is 20% for Stage I, 30% for Stage II, and 40% for Stage III.[22]

Even though there is great variation in the reported incidence of metastasis, one can readily see that the problem isn't one in incidence of metatasis, but how are these metastatic lesions best treated along

with the primary lesion. Groups favoring surgery believe that the radiosensitivity of involved lymph nodes is too low while groups favoring radiotherapy feel that intensive irradiation therapy is sufficient to destroy tumor in lymph nodes. Thus, the question of actual effect of irradiation on lymph nodes now becomes quite controversial.

J.B.Llusia and his group conducted a study on 60 patients with Stage III carcinoma using four methods of treatment. In the groups having no irradiation and in the group receiving only 2000r, he found an incidence of positive nodes in 33.3 per cent of the cases. In the group receiving 6000r he found positive nodes in 20% and only 6.6% in the group receiving 8000r. From these results one can see that deep radiotherapy with high doses does diminish considerably the number of tumor bearing nodes, but sterilization is not total even with high doses. One also notes that 2000r per radium therapy is not sufficient to destroy tumor bearing lymph nodes.[19]

On the other hand, Dr. Gray and associates performed lymphadenectomy on 58 patients following treatment with radium and supervoltage irradiation. They found positive nodes in only 3 patients, and incidence of 5.2%. Two of these patients were Stage III

and only one patient of the group of Stage I and II had positive nodes. This incidence is the lowest in any series yet reported and Dr. Gray believes that modern irradiation is able to destroy lymph node tumor adequately and that surgery carries too prohibitive morbidity to be sound.[15]

Other authors have reported varying figures including Taussig's finding of a 26.8% incidence of positive nodes after therapy. Morton found 30.0% positive nodes before irradiation and 16.3% in those who had irradiation. Chen and associates at Detroit reported an incidence of residual carcinoma on 19 of 87 cases for an incidence of 20.5%. Residual carcinoma was found in the cervix in 16 of those 19 cases and lymph nodes were involved in 8 cases.[7]

Thus one can see that there is a marked difference of opinion concerning the actual incidence of lymph node metastasis, and the efficiency of irradiation in sterilizing nodes. The proponents of surgical treatment believe that the incidence of positive nodes is great enough to warrent operative treatment and consequently a number of surgical procedures have been described in the literature.

Three major types of primary surgical procedures are in use today with numerous specific modifications

being used by surgeon. These three major types of operations are radical abdominal hysterectomy (commonly known as the Wertheim operation), radical vaginal hysterectomy (commonly known as the Schauta operation), and pelvic exenteration. Each procedure has its own merits and complications, and each has been studied and tried by numerous surgeons.

The original radical hysterectomy as described by Wertheim is not the same type of hysterectomy that is usually done today as the so-called Wertheim operation. The modern radical hysterectomy includes the careful dissection of regional lymph nodes whereas the hysterectomy described by Wertheim did not include this prodecure. Many specific modifications of operative procedure have been proposed by such prominent men as Carter, Meigs, Morton, Brunschwig, and others, but all consist basically of the en bloc removal of the uterus, ovaries, tubes, as many regional lymph nodes as possible, and wide excision of the parametrial tissue.

Dr. Joe Meigs revived interest in radical surgery in the early 1940's for Stage I and most Stage II carcinomas. He believed it could occasionally be used in selected cases of Stage III patients. As a result of his great skill, few patients were excluded for medical reasons such as obesity or diabetes, and age per se was not considered as a

reason for rejection. He believed that each patient should have a very thorough evaluation including an intravenous pyelogram and proctoscopy to evaluate the status of renal function and possible bladder and rectal involvement. The patients were always examined under anesthesia prior to operation, and careful exploration of the abdomen was done in an attempt to evaluate the extent of the disease and decision made as to the resectability of the lesion. In his original pilot study of 100 cases of selected thin young women in good health he reported 81.8% survival for Stage I and 61.8% for Stage II. Of the 25 patients who died, 17 had positive nodes. He also reported 7 cases of ureter-ovaginal fistulae with one patient requiring nephrectomy and another nephrostomy. Since that time other surgeons have performed many more extensive studies.[23]

Brunschwig and Daniel have reported a study of surgical treatment of 348 patients with all stages of carcinoma. Of these 348 cases with definitive surgery, 190 are living after 5 years, for an overall survival of 54.6%. The overall surgical mortality (death within 30 days of operation) was 4 cases or 1.15%. Break-down of survival by stages was as follows: Stage I; 79%, Stage II: 50%, Stage III: 22%, and Stage IV: 19%.

These authors believe that one important advantage of surgical treatment is that a speciman is obtained which can be used to obtain information concerning lymph node involvement. The importance of lymph node metastasis in prognosis is shown by the fact that his overall survival was 66% in patients without nodal involvement and only 26% in those with positive nodes.

Urinary tract morbidity was 45 urinary tract fistulae (13%). He believes that immediate morbidity following operation is undoubtly greater than after radiation, but there is an appreciable morbidity from modern irradiation which is not manifested immediately. He believes that modern surgery is a highly effective method of attack on cancer and should be for the present, confined to institutions with adequate equipment for a surgical program whose personnel includes those who are truly interested in surgery of this type and who have adequate surgical skill.[3]

In 1961 Brunschwig and Daniel reported on a further continuation of the study reviewed above and they now had 523 patients included. The overall salvage on 523 patients was now 56% with a breakdown of 76.2%. for Stage I, 52% for Stage II and 27% for Stage III.[5]

Carter and his group reported on a study of 177 patients treated from 1944-1952 by radical hysterectomy and lymphadenectomy. He reported a survival of 81.5% for Stage I, 51.3% for Stage II, and 50% for Stage III. Thirty-three of his patients had positive nodes and the 5 to 13 year survival on these patients was only 36.3%. The overall salvage on those with negative nodes was 72.3%.[6]

Welch, Pratt, and Symmonds reported on 486 Wertheim operations done prior to 1961. Of these patients, 237 received pre-operative irradiation and 250 did not receive pre-operative irradiation. Their 5 year survival for 321 patients on whom follow up was possible is as follows: Stage I, 87.4%, Stage II, 74.3%, and Stage III 60.0% with an overall survival of 81.1%. They reported the lymph nodes to be involved with metastatic disease in about the same incidence whether or not the patient received pre-operative irradiation. One has difficulty in interpreting these figures as there is no effort to study what effect the X-ray therapy might have had on five year survival. There is also no mention of the incidence of complications.[33]

Parsons reports a study of 104 cases treated by surgery alone including 80 Wertheim hysterectomies with pelvic lymphadenectomy, 13 total pelvic exenteration

and 11 partial exenterations. His 5 year salvage rate for Stage I was 78.1% and 68% for Stage II with an overall survival of 73.6%. He found lymph node metastasis in 20% of the 94 cases or 19.2%. Surprisingly he found only 4 cases in Stage III and IV with positive nodes. This is a much lower incidence than is reported by most authors. Though his salvage was very good, it was achieved at the expense of 33 major complications in the 104 cases. Two-thirds of these were of urologic nature. Parson believes that surgery is a successful means of treating carcinoma and emphasis should be placed primarily on adequate excision of the paravaginal and parametrial tissue and not on node dissection. This is in contrast to most authorities thinking, as node dissection is of paramount importance in most surgeons' minds.[25]

Another very good study has been reported by Riva and associates on a study of 823 patients treated over a period of 15 years at Walter Reed Hospital. The study was divided into 5 year periods with a majority of patients receiving primary surgical treatment in the period from 1945-1950 and a majority receiving combined treatment during the two following periods. The total overall survival figure excluding Stage 0 was 62.3% survival for patients receiving only surgical treatment was 84.4% for Stage I and 57.1% for

Stage II. During the first 5 year period the incidence of ureterovaginal fistula and vesicovaginal fistulae was 16.3%. He firmly believes that surgical treatment is a good method of approach to nodal involvement, residual disease in the uterus and vagina, and to radioresistent disease. He also believes that combined therapy warrants further study.[28]

The incidence of complications following the radical hysterectomy with lymphadenectomy has been a problem to surgeons. Green and others made a study of 623 patients operated on between 1939-1961, with an operative mortality of 1.8%. This study included 396 cases of Stage I, 214 cases of Stage II, and 13 cases of Stage III. The incidence of ureteral complications was 12.5%, and of bladder complications was 6.6%. They found that some type of urologic disturbance was found in 20% of the cases. They found that during the past 10 years when they tried post operative bladder drainage for 6-8 weeks reduced the incidence of ureterovaginal fistulae from 11 to 5.6%. All of these patients were completely rehabilitated from a urologic standpoint and there were no permanent "urologic cripples".[14]

Another major type of surgical procedure that is used a great deal in Europe but rarely in this country is the radical vaginal hysterectomy. The

so-called Schauta-Amreich operation is used very little in this country although good results have been obtained by certain men.

Dr. Ernst Navratil, who was a pupil of Schauta, lists the following indications and advantages for the radical vaginal operation.

1. Vaginal operations are tolerated much better by patients and are rarely contraindicated on general medical grounds.
2. Operation post operative mortality is very low.
3. The author believes it is possible to remove at least as much parametrial and paravaginal tissue as by the abdominal approach.
4. Damage to the ureter, bladder, and rectum is almost entirely avoidable.
5. Follow up exam shows late complications are rare.

Hiss apparent 5 year survival rate for 510 cases operated upon without preoperative radiation in the period through 1956 was 69.8%. It was 94.9% for Stage Ia, 79.2% for Stage Ib, and 51.7% for Stage II. Between 1952-1961 he had only one fistula in 572 cases and his postoperative mortality was only 0.7%.[24]

McCall in this country performed 155 Schauta-

Amreich operations in which 116 patients has Stage I or early Stage II squamous cell carcinoma of the cervix. Forty-five of the 50 patients operated on 5 or more years ago are living and 108 of 116 are living free of disease. Serious morbidity was 6.9% and operative mortality was 0.86%. He believes that pelvic nodes may be removed extra-peritoneally at the time of operation or at a second operation. He also believes that when abdominal exploration is mandatory, the Schauta operation may advantageously precede the intraperitoneal portion.[21]

The main argument advanced against radical vaginal surgery is that it does not allow lymph node dissection and it is one of the puzzling feature of gynecological surgery that such good figures are obtained. Navratil believes that this is explained by the different incidences of node involvement in various histological and clinical stages of carcinoma. The rarity of node metastasis in very small carcinoma has been demonstrated according to him. He believes, however, that is cases with lymph node invasion or blood vessel invasion, the revocal of lymph nodes is indicated. As public awareness of carcinoma increases along with better diagnostic tools, we will have more cases of early carcinoma to treat and vaginal operation

is of real consideration for these early cases.

Another major operative procedure which was first proposed and developed by Brunschwig beginning in 1947 in that of pelvic exenteration. This relatively new approach to pelvic carcinoma in general represents the ultimate in radicalism of treatment. Total pelvic exenteration consists of the en bloc removal of uterus, adnexa, bladder, rectum, vagina, vulva, and bilateral pelvic lymphadenectomy. Posterior exenteration means leaving the bladder in place and anterior exenteration means leaving the rectum intact.[4]

Graham believes there are five indications of which all must be present before this operation is used. These indications are: 1. The growth is resistant to a full course of irradiation, 2. The tumor occupies the central pelvis, 3. The tumor must be completely removable, 4. Regional nodes are not involved, 5. The patient must be alert and capable of handling diverted urinary and fecal streams. This set of criteria rules out the patient with pelvic wall invasion, involvement of nerves and veins to the legs, and in whom a cure is not possible.[13]

Dr. Brunschwig first proposed the operation as one of palliation; but as more experience was gained, he and other authors found that definite cure was possible. The rationale of this procedure is based

on the fact that carcinoma of the cervix is primarily a local disease and it may be possible to excise all of the malignancy.

Brunschwig reported in 1960 on a series of 592 cases of exenteration done in the period 1947-1950. Of these procedures, 135 were done for other forms of malignant neoplasms in the uterus or adjacent sites. His surgical mortality was 17.2% with shock being the most frequent cause. He believes that this high mortality can be reduced by more rigid selection of patients as this series included patients with positive aortic nodes in whom palliation was the only surgical possibility.

Of the patients with carcinoma of the cervix, he has 381 cases of 457 operated who have lived 2 years or more. In this group there was a surgical mortality of 77 patients. He uses a wet colostomy for urinary tract diversion as he believes that construction of an ideal conduit is very time consuming. The problem of prolonged stay in the hospital is not great as most leave the hospital by the 4th week. Brunschwig firmly believes that the operation has a definite plan in treatment as he has been able to achieve a 33% five year survival in those patients with Stage III & IV lesions in whom there were no distant metastasis. This is much higher than the cure rate for irradiation.[4]

Bricker and his group reported on a series of 218 exenterations for advanced pelvic carcinoma of which 150 exenterations were for carcinoma of the cervix. There were 15 operative deaths on the series of cancer of the cervix. Of these 150 patients, only three underwent primary surgery and the rest being irradiation failures. Nineteen of 75 operated upon 5 to 9 years ago are still alive and free of disease. The five year accumulative survival rate for the entire group who underwent operation was 34 per cent. As a control they compared a series of 138 women undergoing pelvic exenteration with 118 women treated for persistant cancer by other means and found the survival rate in the exenteration patients to be significently higher. Thus they concluded that their 34 five year accumulative survival was the result of operative treatment and not simply patient selection. The rate of complication was quite high as 69 of the 150 patients had 94 post operative complications of which 15 were fatal. Wound infection and bowel obstruction were the most frequent complication. This group believes that properly selected patients with advanced carcinoma can be helped by this operation as 53.1% of the total patients seen in consultation for carcinoma of the cervix had exenterations performed.[2]

IV. Radiation therapy has been the choice of therapy for most patients with cervical carcinoma for most gynecologists in the past. After radium was in use clinically after about 1918, it became obvious that radium was ineffective against lesions that has spread laterally. This is due to the fact that the effect of radium decreases in geometric proportion as the square of the distance from the central point of application. This necessitated the use of external irradiation, therefore combined use of radium and X-ray has been the accepted method of therapy in the past twenty-five years.

Various refined methods of treatment have been developed including the Stockholm method in 1914, the Paris method in 1919, and the Manchester method in 1938. It was also at Manchester that Tod and Meredith developed the concept of Point A and Point B which has proved to be very useful in calculating and thinking of dosage. There is no standard dosage given in each type of treatment as individuality is stressed especially in the Stockholm method where the usual range of dosage is 7200 to 8000mgm hr. of radium. In the Manchester method, the dosage is calculated to be that received at Points A and B.[26]

In the annual report of the Radiumhemmet in Stockholm the results of the 5 year recovery ratio in

over 42,000 patients treated in 84 centers of the world during the period 1947-1951, the average salvage rate for Stage I through Stage IV was 43%. By individual stages the salvage rate was as follows: Stage I, 70%, Stage II, 49%, Stage III, 27% and Stage IV, 7%.[26]

Kottmeier, who was head of the Radiumhemmet, presented a study of cases treated at the Radiumhemmet for the years 1938-1951. The following table shows the marked improvement of survival rates with each period of the study. From Table I, Page 250 American Journal of Obstetrics and Gynecology Volume 76.

Five Year Apparent Recovery Rate For The Years 1938-1945, 1946-1948, and 1949-1951 in Cases Treated At The Radiumhemmet.

	1936-1945		1946-1948		1949-1951	
Stage	No.of Cases	5 Yr.Cure Rate (%)	No.of Cases	5 Yr.Cure Rate (%)	No.of Cases	5 Yr.Cure Rate (%)
I	299	69.3	155	74.8	155	89.0
IIA	537	63.3	228	58.3	295	64.4
IIB	503	44.3	235	37.0	310	45.2
III	787	24.3	254	26.0	230	33.5
IV	230	11.3	78	2.5	91	7.8
I-IV	2756	42.3	950	42.5	1081	51.1
No Treatment	119		34		11	

There has been a significant increase in the survival in Stage I especially, but one will notice

the lack of improvement in survival in Stage IV. Kottmeier is firmly convinced that irradiation should be the primary treatment of all cases of invasive carcinoma as the price of surgical procedures is too high in view of the complication. Although he makes no definite mention of the actual incidence and types of complications in his study, he states that severe injuries have occurred in 1.1% of his cases.[17]

Makowski reported in 1962 on a series of 1,178 patients treated over a period of 1939-1956. External irradiation was used first over a period averaging 25-42 days with a tumor dose at 1800-2500 tissue roentgens at first but after 6 months this was upped to 3000-3500 tissue roentgens. On the last day of external irradiations, radium was inserted in the vagina, cervix and uterus using a total of 5000mg/hr. of treatment. His results are tabulated as follows:

Stage	No. of Patients	Cure-5 Years
I	422	81%
II	426	60%
III	286	35%
IV	59	3%

Overall Survival 58.8%

Seventeen (1.4%) developed fistulae and 7 (.1%) died during or immediately after therapy as patients with associated PID were accidentaly treated.

Aseptic necrosis of the femoral head and neck was also seen in 13 (1.1%) of his patients.[20]

Decker and Herick of the Mayo Foundation have reported a series of 1,143 patients treated by irradiation during the period 1940-1949. Therapy was begun with radium inserts and several days later roentgen or cobalt external therapy was started. A small tumor would receive 5,500 mg/hr. of radium and a large tumor would receive approximately 7,300 mg/hr. By use of cobalt therapy a tumor dose of 3,500 to 3,700 roentgens was also supplied. By stages the five year survival was as follows: Stage I, 82.9%, Stage II, 72.8%, Stage III, 51.7% and Stage IV, 22.9%. His five year survival was 57.7%, which is quite good considering the fact that only 42 of his 880 cases were Stage I. He also had 325 cases of Stage II, 357 cases of Stage III, and 156 cases of Stage IV. No mention is made of the frequency or severity of complication in the article.[12]

Blaikley of England reports a survival rate of 72.9% for Stage I, 50.0% for Stage II, and 17.4% for Stage III with an overall survival of 39.1% for 5 years. The fistulae rate was 1.4% in his studies at the Chelera Hospital for Women. In the same hospital, a 5 year survival rate of 68.0% for Stage I and 57.9% for Stage II was achieved with the use of the Wertheim

hysterectomy on 51 cases. This study was done between the years 1952-1955.[1]

Clayton reported an overall survival of 26.4% on patients treated primarily by irradiation at Parkland Memorial Hospital in Texas. This seems like a very low survival rate , but 33.6% of his patients were Stage IV and only 5.4% of these survived 5 years. His survival for Stage I was 81.2% and 40% for Stage II. There was no mortality and morbidity of moderate nature was 14.5%.[9]

Radiation therapy complications occur mainly several months to years after therapy and the actual incidence of complications is hard to determine as many patients are lost to follow-up study. Complications of radiotherapy include proctitis, rectal ulcer, radiation cystitis, bladder ulcer, sigmoiditis, fistula formation, small bowel nerosis, vault necrosis, pelvic bone injury, and excessive pelvic fibrosis with ureternal structures.

Dr. P.M. Chou and his group made a study of complications using supervoltage therapy and compared this to treatment in the Pre-super voltage era. These patients were all followed at least 2 years. He found the incidence of minor rectal and bladder complications and fistulae formation to be similar in

both senei of patients. Severe recto-sigmoiditis is a complication to be expected with intense super-voltage treatment. The most severe complication of radiation treatment is small bowel necrosis which usually appears approximately 1 year after treatment. The prognosis in this complication is quite poor. He also found that high dose radiation of the pelvic did not produce excessive fibrosis unless a surgical procedure was used in conjunction with therapy.[8]

Kottmeier and Gray reported on five hundred cases treated at the Radiumhemmet who had been followed more than five years. They found a direct correlation between dosage levels and incidence of bladder and rectal injuries. They found a quite high incidence of rectal injuries in dosages over 6000r and a high incidence of bladder injuries in dosage over 9000r. Most rectal injuries develop in the first 18 months and the bladder injuries develop 2-3 years after treatment. Their incidence of permanent disability due to therapy in this series was 1% of all patients treated with an over-all 5 year survival of 54.5%.[18]

V. The use of irradiation combined with surgery can be done in several different forms. The idea of lymph node dissection following a full course of irradiation has been under investigation for several years. The use of radical surgery and full irradiation is a relatively new idea and as yet, there are no large series of cases available for statistical review.

Lymph node dissection following a full course of irradiation is based on the assumption that irradiation may not destroy malignant disease in lymph nodes and removal will improve survival results. Their assumption itself is subject to a great deal of debate and was discussed earlier in this paper.

Taussig first advocated the use of lymphadenectomy and leaving the primary to be treated by irradiation. Two approaches can be used, namely the transperitoneal and extra-peritoneal. In the study done by Claiborne and his group, bilateral retroperitoneal pelvic lymph node dissection was done through an inguinal incision he described by Nathanson. No good valid survival rates were presented in this report, but is was stated that 38 to 40 Stage I patients treated in this manner are living from 3 months to 7 years without recurrence. Of 17 Stage II patients, 15 are still living for the above stated period. The operative mortality was 1.6% and no cases of lymphocoele

were encountered postoperatively.

Rutledge and Fletcher performed a series of 100 transperitoneal lymphadenectomie for Stage III carcinoma in patients first receiving high loses of irradiation. Node dissection was done transperitoneally beginning at the inguinal ligament and proceeding upward to the aortic birfurcation. Pathologic study showed 5 cases of positive nodes within the radiated field, 8 cases of positive nodes outside the field and 9 cases of positive nodes both inside and outside the indicted field. Thirty one cases of lymphocoele were noted postoperatively.[29]

Gray, in the study previously referred to, believed that lymphadenectomy is not therapeutically sound in view of the complication. She also believes that modern radiation is able to destroy metastatic cervical carcinoma as she found only 2% incidence of positive nodes following intensive radiotherapy.[15]

The use of radical surgery following full irradiation therapy is based on the fact that too many local recurrences appear after full irradiation. This is a relatively new method of treatment and only a few good long term studies are available at this time. Most of the series reported so far are quite small and are selected cases.

Sweeney and Douglas reported on 102 cases treated by a full course of X-ray and radium therapy

followed by radical hysterectomy. This was a selected group of those in good physical condition and of a relatively young age group. Their study includes 39 cases of Stage I, 54 Stage II, and 9 in Stage III. The 5 year survival was 82.1% for Stage I, 66.7% for Stage II, and 22.2% for Stage III. The 5 year survival in patients with positive nodes was 35.2%. Operative mortality was 2.9% and complications ranged from minor ileus in 3 cases to 15 cases of fistulae. Although his series is small, he believes this treatment has substantically increased the 5 year survival rates.[31]

Stevenson has reported a series of 95 cases treated with full irradiation followed in six to eithe weeks by a complete radical Wertheim hysterectomy. Only 12 Stage I and 16 Stage II cases have qualified for 5 year study and in these he has achieved a 92% and 81% survival rate respectively. His incidence of residual carcinoma was 28% following irradiation therapy. The operative mortality was zero and the incidence of fistulae was 15%, which is quite high.[30]

Crawford and his group have reported on a series of 105 cases treated by combined therapy. This was a selected group of patients consisting of young females in good health. Over-all, they found residual carcinoma in 21.9% of patients in this series.

Of the patients having been studied at least 5 years, the survival for Stage I was 82.2% and .75% for Stage II, with an overall survival of 79.2%. The overall survival was 91.7% if no residual cancer was found but only 25% if the nodes were positive at the time of operation. Their operative mortality was 1% and they have had no fistulae but have two cases that they consider "urologic crippls".[10]

Other investigators are working on this approach including Hollenbeck who has reported a survival of 95% for Stage I and 85.7% for Stage II. Dahle of Norway is currently using this form of therapy on selected patients but has not reported on survival rates. Thus, one can see the work on combined treatment is in the initial stages only and needs much more investigation in order to evaluate its use today.[11]

VI. Survey of Wertheim Radical Hysterectomies done at University of Nebraska Hospital from April, 1955 to July, 1963. All Stage I.

Patients	Age	Date of Operation	Nodal Status	Follow-Up
A.H.	75	4/55	Neg.	L&W-9/58
M.B.	23	5/57	Neg.	Lost to follow-up
J.N.	37	11/57	Neg.	L&W-3/59
V.D.C.	35	9/58	Neg.	L&W-6/59
U.S.	42	10/58	Neg.	L&W-1959
I.S.	28	4/59	Neg.	L&W-7/59
F.G.	25	8/57	Neg.	L&W-11/59
H.H.	41	5/59	Neg.	L&W-9/59
B.M.	31	8/59	Neg.	Lost to Follow-up*
D.M.	32	10/59	Neg.	L&W-1/63
R.S.	37	10/59	Neg.	L&W-1/63
V.M.	33	4/60	Neg.	L&W-3/63
R.G.	34	9/60	Neg.	L&W-12/62
C.B.	42	2/61	Neg.	L&W-4/63 **

Six other Wertheim hysterectomies were performed on patients who had received prior irradiation treatment. Four of these were done for persistent tumor: Two were planned combined therapy. One of these patients died of metastatic desease and another has metastatic disease. The rest are living and well as of late 1963.

* Senior Thesis U.N.H. by Francine Wismer, April, 1960

**Personal Communication, Dr. Donald A. Ritchie. Instructor OB-Gyn. U.N.H.

RESULTS OF TREATMENT ON INVASIVE CARCINOMA USING IRRADIATION AT UNIVERSITY OF NEBRASKA FROM 1937-52 *

1937-1947, (Radium and X-ray Therapy)

Stage L of N	No. (Cases)	Per Cent	No. (Survival)	Per Cent
I	64	27	44	68.8
II	101	44	44	43.8
III	40	17	5	12.3
IV	27	12	2	7.4
All	232		95	41.0

1948-1952, (Radium and X-ray Alone 102, Surgery 4, Combined 5)

Stage L of N	No. (Cases)	Per Cent	No. (Survival)	Per Cent
I	38	35	33	87.0
II	40	37	22	55.0
III	18	16	7	38.8
IV	15	12	0	0.0
All	111		62	55.8

* Hunt, Howard, McGoogan, L.S., Bunting, R.A., Waggener, Ronald E., Nebraska State Med. Journal. Febr. 1959, Vol. 44, No. 2 Pg. 53 from Table I.

CONCLUSION

VII. Several conclusions can be drawn from this review of the literature concerning the present ideas on treatment of invasive cervical carcinoma. The treatment of invasive carcinoma is now undergoing a change in the accepted standards of treatment. Surgery was the earliest form of treatment and was followed by irradiation as the accepted method of treatment. There is currently much intensive work being done concerning the use of combined therapy and radiation is no longer considered the only method of treatment.

The incidence of positive nodes in Stage I has been found to vary from 15% to 35% and from 23% to 51% for Stage II. The incidence of positive nodes after irradiation therapy has been found to vary from 5% to 20% for Stages I and II. By use of radical abdominal hysterectomy results as high as 84% 5 year survival for Stage I and 57% for Stage II have been achieved. The problem here is a high incidence of urinary tract complications. With use of the radical vaginal hysterectomy results of 87% for Stage I and 51% for Stage II have been achieved. Pelvic exec-teration is now considered to be a method of curing as high as 33% of Stages III and IV patients, but

here again is the problem of high operative mortality and post operative morbidity.

Radiation therapy has been the accepted treatment for the past several decades and results with this type of treatment have improved slightly in the past several years especially in the early stages. Results varying from 72% to 89% for Stage I and 40% to 64.4% for Stage II have been reported. With the use of higher and higher dosage, the incidence of complications has risen.

Combined therapy is a relatively new concept and the reported series reported so far are small and selected cases. Results as high as 92% 5 year survival for Stage I and 81% survival for Stage II have been reported. The incidence of complication is also quite high.

Thus, one can readily see that there is no one form of treatment for all invasive carcinoma patients and we are quite fortunate to have two good methods of treatment available. It would appear that in the hands of highly skilled individuals, surgery is an acceptable form of treatment for the earlier stages of carcinoma. For the less experienced surgeons, irradiation remains the best mode of therapy. In the later stages, pelvic exenteration offers more hope than irradiation, but here again an experienced.

team of surgeons is required. The use of combined treatment is a rapidly expanding field and requires more intensive work, but it appears that this form of therapy may become a widely accepted method of treatment in the future.

SUMMARY

VIII. This paper is a review of the modern day thinking concerning treatment of invasive cervical carcinoma. A brief historical review of the trend in therapy is presented followed by a rational behind the revival of surgical treatment. The works of several outstanding men are presented in relation to the Wertheim hysterectomy, vaginal hysterectomy, and pelvic exenteration. Complications of each type of therapy are reviewed. The results of irradiation treatment at several different centers are presented along with complications of intensive irradiation. The use of combined therapy is also reviewed although the series of cases are small. The case reports on patients undergoing radical Wertheim hysterectomy at the University Hospital are presented along with survival figures for patients treated by irradiation at the University Hospital for the years 1937-1952.

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