Carcinoma Cervicis Uteri
Treatment Results from the Period 1953—1968

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During the course of 16 years, i.e., from 1953 to 1968 inclusively, a total of 2111 patients with carcinoma of the uterine cervix were treated at the Oncological Institute in Brno. Of these, 1829 patients, i.e., 86.6% were irradiated, 282, i.e., 13.4% underwent primarily a radical excision and subsequently were irradiated. During the past years, approximately 95% of all such patients are being given radical irradiation. The mean age is 52.7 years, the sixth decade being numerically the highest in incidence — 27.4%.

The distribution pattern according to the tumor stage: I — 29.3%, II — 14.3%, III — 48.2%, IV — 8.2%. This distribution remained practically unchanged over the follow-up period of 16 years. The fundamental method of treatment of practically 87% of all the patients was actinotherapy consisting in a combined application of radium and X-rays. Of the total number of 2111 patients, 1298, i.e., 61.5% have survived 5 years without any symptoms of the disease. 966 patients, i.e., 59.0% (out of a total of 1671 patients) survived 10 years. The five-year survival symptom-free period for the various stages is as follows: I — 82.5%, II — 77.1%, III — 52.8%, and IV — 9.8%.

A comparison of the results of treatment in patients radically irradiated and those primarily operated upon then subsequently irradiated, i.e., in 619 patients of stage I showed the 5-year recovery to be superior by almost 4% in the former than in the latter group — 84.1% as against 80.3%. Over the last 6 years of the follow-up, i.e., 1962—1968, this difference went up to 6.0% in favour of those radically irradiated — 85.1% as against 79.2%. An increasing mortality rate due to carcinoma is noted with advancing age.

Key words: Carcinoma cervicis uteri, treatment results.

The patients with carcinoma of the uterine cervix hospitalized in the Oncological Institute in Brno represented every stage of development of the disorder and included also such as had been operated upon at other institutions.

Material and Methods

Three basic procedures were used in the treatment of these patients: 1. combined mode of radium and X-rays, 2. supporting irradiation following radical excision, 3. irradiation as a palliative procedure in patients whose advanced age, a bad overall condition or advanced stage of the disorder precluded the use of the radical combined method — Radium + X-rays.
During the period 1953 through 1968 inclusively, a total of 2111 patients with Ca cervicis uteri were hospitalized and treated at the Institute. Of these, 1829 patients, i.e. 86.6% were irradiated and only 282 patients, i.e. 13.4% underwent primarily a radical operation and subsequently were irradiated.

In Fig. 1 the treatment with actinotherapy and by surgery with supporting irradiation is expressed graphically. The descending curve for the combined mode of treatment indicates that by far the greatest number of patients is treated with radical irradiation. For the last five years studied (1964—1968), this represented a total of 410 out of 440 patients treated, i.e. 93.2%.

From the case histories, the following points are of importance: In 1903 women, i.e. in 90.2% of the women, carcinoma was detected during subjective complaints (discharge, bleeding, pain). An exploratory probe or a gynecological investigation during the course of hospitalization for other complaints, carcinoma was detected in only 208 women, i.e. 9.8%.

At the first gynecological check up, carcinoma was revealed in over 90% of all cases.

The great majority of the women had given birth — a total of 1921, i.e. 91.2%.

145 had been nulligravid (6.8%) and 45 nullipar (2.0%).

Ectopia or lacerating ectropium had been detected prior to the onset of the carcinoma in only 109 patients (5.2%), and diabetes mellitus in 51 patients (2.4%).

Of the 2111 patients treated, 305 (18.2%) stated a tumorous affection in relatives, and 86 (4.0%) reported a tumor of direct gynecological origin. That means that 22.2% of the patients came from families in which one or several members had been treated for or died of some malignant process.

A second malignant tumor — carcinoma duplex — was found in 68 women (3.2%), the most frequent duplicity being Ca of the skin and of the uterine cervix (27.9%), Ca mammae and cervicis (17.6%), Ca of the digestive tract and of the cervix (11.7%). Carcinoma triplex was detected in 2 of the patients, viz. Ca mammae-cervicis-myeloma, and mammae-cervicis-corpus. One patient was treated simultaneously for lymphatic leukemia. The patient lives and has been in good condition without complaints for 15 years now. Her lymphatic leukemia, too has been in remission for the same period.

The mean age of the patients is 52.7 years (Fig. 2). Fig. 2 gives the
Carcinomas of the uterine cervix were assigned into the various stages of development by an exact clinical investigation before beginning with a definite therapy. This distribution is in Table 1 and 2.

The index according to Reiffenstuhl is high: \( Q = 132.3 \) [3].

As evident from Table 2, the number of patients in stages I and IV in all the 3 groups remains practically unchanged. Only the number increased in the stage II and decreased in the stage III. However, the index according to Reiffenstuhl in all the three groups remains almost the same — 131.9 in group one, 134.3 in group two, and 130.6 in group three.

The fundamental mode of treatment in practically 87% of the patients consisted of actinotherapy. Intracavitary radium applications combined with external X-ray irradiations were as far as possible individualized and indicated by the extent and localization of the tumorous lesion. Radium was applied with the aid of a colpostat containing 6 \( \times 5 \) mg Ra, with an separate setting of one ovoid in front of

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>619</td>
<td>29.3</td>
</tr>
<tr>
<td>II</td>
<td>301</td>
<td>14.3</td>
</tr>
<tr>
<td>III</td>
<td>1017</td>
<td>48.2</td>
</tr>
<tr>
<td>IV</td>
<td>174</td>
<td>8.2</td>
</tr>
<tr>
<td>Total</td>
<td>2111</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 1. Distribution of Ca according to the stage of progress

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>28.5</td>
<td>30.2</td>
<td>29.5</td>
</tr>
<tr>
<td>II</td>
<td>10.3</td>
<td>15.3</td>
<td>19.0</td>
</tr>
<tr>
<td>III</td>
<td>53.5</td>
<td>45.8</td>
<td>42.9</td>
</tr>
<tr>
<td>IV</td>
<td>7.7</td>
<td>8.7</td>
<td>8.6</td>
</tr>
</tbody>
</table>

\[ JR = 131.9 \quad JR = 134.3 \quad JR = 130.6 \]
\[ JR_C = 132.3 \]
suppository between the colpostat carriers; occasionally, even tamponade of the vagina was practiced with individual ovoids. The scope of the uterine probe and the amount of Radium were adapted to the size of the uterine cavity. The most frequently used probes were those containing 3 × 10 and 4 × 10 mg Ra. The mean Radium dose for vaginal and intrauterine application ranged between 5760 and 7440 mgh.

The X-ray irradiation was made with a middle-voltage therapy with four input fields — 2 anterior-hypogastric and 2 posterior gluteal, 150 cm² in area. The focal dose to the parametrium was stepped up over 16 years from 1500 T to 1900 R. In the case of patients with a broad pelvis and extensive infiltrates, the focal dose to the parametrium was further raised by the addition of one or two side fields, so that it ranged on an average between 1900—2400 R.

Patients primarily operated upon (for the most part outside our Institute) were irradiated with X-rays according to the same principles as in the case of radical actinic treatment, but the dose was adjusted to both the extent of the primary tumorous lesion and the scale and mode of the surgical intervention.

**Results and Discussion**

The success of these methods of treatment is evidenced by the 5- and 10-year rate of survival (Fig. 3).

Of the total number of 2111 patients, 1298 (61.5%) have survived 5 years, and 986 (59.0% out of a total of 1671 patients) have survived 10 years.

The mortality rate in patients treated with a radical actinotherapy is 22, i.e. 1.2% out of a total of 1829 irradiated patients. (This number does not include patients who died of an intercurrent disease, with Ca cervix uteri being cured.) These were only patients with stages III and IV of the disease (10 patients died of peritonitis — 45.4%, 10 of advancing tumor — 45.4%, 2 of embolism — 9.2%). A point that is not itself without interest is that of 71 patients who died of some other disorder with a cured Ca cervix uteri, 26, i.e. 36.8% died of some other form of carcinoma — carcinoma duplex; this number represents more than one third of these patients.

The stage of advancement of the disorder at which it was detected and treatment initiated has a decisive effect on the outcome of the therapy (Table 3).

To get a more exact picture of the growing number of cured patients, those of stages I to III were again divided into 3 groups: 1953—1957, 1958—1962, 1963—1968 (Fig. 4).

As evident from Fig. 4, the number of cured patients in stage I rose from 76.6% in the period 1953—1957 to 85.8% during the period 1963—1968. This percentage difference amounting to 9% is of statistical significance ($t = 2.4$, $p < 0.01$). In the

![Fig. 3. Ca cervix uteri 1953—1968. The 5- and 10-year survival rate.](image-url)
Table 3. Five-year survival according to the stage of disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total number</th>
<th>5-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>619</td>
<td>511</td>
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<tr>
<td>II</td>
<td>301</td>
<td>232</td>
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<tr>
<td>III</td>
<td>1017</td>
<td>537</td>
</tr>
<tr>
<td>IV</td>
<td>174</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>2111</td>
<td>1298</td>
</tr>
</tbody>
</table>

Table 4. Ten-year survival according to the stage of disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total number</th>
<th>10-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>499</td>
<td>403</td>
</tr>
<tr>
<td>II</td>
<td>219</td>
<td>159</td>
</tr>
<tr>
<td>III</td>
<td>823</td>
<td>414</td>
</tr>
<tr>
<td>IV</td>
<td>130</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>1671</td>
<td>986</td>
</tr>
</tbody>
</table>

stage II the percentage difference amounts to only 3% in these two groups and is nonsignificant ($t = 0.49, p < 0.01$). The evaluation has been done according to the formula [6]:

$$t = \frac{p_1 - p_2}{\sqrt{p(100 - p) \frac{n_1 + n_2}{n_1 n_2}}}.$$  

The best results have been achieved in the stage III where the difference between the 1st and 3rd group exceeds 12% (44.2 : 56.9%) and is of high statistical significance ($t = 3.26, p < 0.01$). The stage IV has not been evaluated because of the very small number of cures.

Success of radical actinotherapy and surgical investigation with a subsequent supporting irradiation was evaluated only in 619 patients of the stage I. The reason
is that a clinical determination of the stage I despite a higher relativity is the most exact and the number of 619 cases already permits certain conclusions to be made. Of that number, 365 patients (59%) were radically irradiated, and 254 (41%) were operated upon with a subsequent irradiation. In the former group, 58 patients — in the latter 50 patients died of the tumor. The percentage difference between the two groups amounts to 84.1 : 80.3%, i.e. 4% in favor of radical irradiation.

![Fig. 4. 1953—1968 Ca cervicis uteri. Five-year survival. a) 1953—1957. b) 1958—1962, c) 1963—1968.](image)

This difference is statistically nonsignificant ($t = 1.2, p < 0.01$) [4]. However, a comparison of these two groups over the period 1962—1968, reveals the 5-year cure to be better by 6% in those radically irradiated than in those operated upon, i.e. 85.1 : 79.2% ($t = 2.9, p < 0.01$). In the stage II this difference in the numbers of cures was even more striking.

In addition, we also followed the relationship between mortality rate due to tumor and patients' age.

There was a rising trend in the mortality percentage due to the tumor with advancing age of the patients. The least number of the patients — 26.8% — died of tumor in the fourth decade, i.e. between 31 and 40 years of age. However, from the age of 61, the death rate for all the patients due to tumor rose to 60% [1].

By its histological structure, the carcinoma of the uterine cervix was for the most part of the epidermoid type:

- Ca spinocellulare 1984 patients = 94.0%
- Adenocarcinoma 127 patients = 6.0%

Of the 127 cases with adenocarcinoma, 22 patients (17.3%) were primarily operated upon, and 105 (82.7%) were irradiated. Of the former, 17 patients (77.2%) survived 5 years, of the latter 45 patients (42.8%) only. This percentage difference is of high statistical significance ($t = 5.7, p < 0.01$). However, there is a considerable age difference between the two groups: while the mean age of patients operated upon was 47.2 years, that of those undergoing irradiation was 59.2 years. This age difference then considerably distorts the success of surgical treatment when expressed in per cents [2, 5].
From this statistical analysis of 2111 patients treated for carcinoma of the uterine cervix at the Oncological Institute in Brno over the years 1953 through 1968, it ensues that:

1. The percentage distribution of patients over the various stages of progress of the disease did not change over the 16 years' period followed. This implies that the great majority of patients, regardless of preventive check-ups, comes for treatment when in the stage III.

2. Likewise the age distribution remained unchanged over 31 years of treatment of carcinoma of the uterine cervix, as evident from a comparison of a preceding study (Čs. gynecologie, 1956, p. 191) which deals with this disorder for the period 1938—1952.

3. Therapeutic results have improved considerably over the years, thanks, principally to higher focal doses of X-rays irradiation (by as much as 37% — 46.2 : 82.5 — 1° — against the period 1938—1952).

4. In our material and our patients, surgical treatment for carcinoma of the uterine cervix of stage I proved less successful than actinotherapy. Consequently, we reserve surgery only for selected case, as for instance, adenocarcinomas, or to carcinomas associated with gravidity, with tumors of the adnexa or with myomatous uterus.

5. Mortality rate of tumor of the uterine cervix rises with advancing age of the patients, although an analysis and a correlation according to the various stages of tumor progress reveal a specially high percentage mortality of carcinoma in patients below the age of 30 years.

6. Curability is directly proportional to the stage of progress of the disease.

References