Current status of preoperative and adjuvant radiation therapy in cervical carcinoma

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The conventional treatment of patients with stage Ib and IIA cervical carcinoma consists of either radical hysterectomy and bilateral pelvic lymphadenectomy or radiation therapy combining the whole pelvic external irradiation with local brachytherapy. These treatment modalities are recognized as equally efficacious with respect to local control and survival.

However, in younger patients surgery is often preferred to radiotherapy, because after irradiation ovarian function is eliminated and sexual function is often compromised. In addition, late complications of radiation are avoided. Further, it is necessary to choose the type of treatment depending on the patient’s condition, the skill and ability as well as the technical conditions of the team for either method of treatment.

Operative treatment has been the treatment of choice in stages IB, IIA and early IIB of cervical carcinoma at the Department of Obstetrics and Gynecology in Ljubljana for decades. Our experience in this field is based on over 3000 cases treated by Wertheim operation and goes back to the year 1907 when the first Wertheim operation in Ljubljana was performed. In spite of the fact that our principal method of treatment has been the surgical one, we have been of the opinion that in high risk cases with bad prognostic factors the operative treatment should be combined with radiation. At least four major prognostic factors have been identified:

1) Size and extent of the primary tumor
2) Tumor grade
3) Lymph – vascular space invasion
4) Presence of lymph node metastases

Of these four variables, nodal metastases appear to be the most important prognostic indicator with the remaining factors influencing survival mainly as a reflection of the risk of nodal spread.

Preoperative brachyradiotherapy and/or external irradiation has been applied in cases of large exophytic tumors in order to reduce tumor size, making the operation easier and in hope to avoid the central recurrence following radical hysterectomy. Adjuvant postoperative whole pelvic irradiation, based on pathohistological examination of the surgical specimen, has been applied to improve pelvic control and presumably survival in patients at increased risk of recurrence following radical hysterectomy and pelvic node dissection. It has been believed that microscopic extracervical metastases could be treated with external irradiation.

At our Department over the last 25 years the number of cases treated with preoperative irradiation for big size tumors has diminished, but postoperative adjuvant radiotherapy is still applied in stages IB or IIA of cervical carcinoma when these adverse factors are present: positive lymph nodes, close or involved surgical margins, deep stromal invasion (more than half of cervical depth), exophytic lesions greater than 3 cm in diameter, or microscopic parametrical involvement. Surgical procedure consists of Wertheim-Meigs-Novak radical hysterectomy (Piver III) with pelvic lymphadenectomy.

The 5-year survival of patients with cervical carcinoma stage Ib treated in two different periods (1965-72 and 1978-87) is shown in Table 1. (1, 2).

<table>
<thead>
<tr>
<th>Period</th>
<th>No</th>
<th>Surgery + irradiation</th>
<th>Survival No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965-72</td>
<td>259</td>
<td>38%</td>
<td>192</td>
<td>74</td>
</tr>
<tr>
<td>1978-87</td>
<td>248</td>
<td>54%</td>
<td>192</td>
<td>77</td>
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Of the 259 operations (1965-72) there were 49 cases (19%), and of the 248 operations (1978-87) there were 7 cases (3%) of Schauta-Amreich procedure, all other operations were Wertheim. In the period 1965-72 Wertheim operation was combined with irradiation in 38% of cases, and in the period 1978-87 in 54% of cases. Preoperative brachytherapy consisted of one application of 4000 cGy to point A (in the first period radium...
according to Manchester scheme, and in the second cesium with afterloading technique. Postoperative external radiation was delivered to the pelvis at a dose of 5000-5600 cGy in 4 weeks. The difference in the 5-year survival between the two periods is not significant, although in the second period significantly more patients were submitted to the combined treatment (15% preoperative, 34% postoperative, and 5% pre- and postoperative irradiation). The percentage of positive lymph nodes was about the same in the two compared periods (18%). Irrespective of postoperative irradiation, the overall survival in these cases was 56%, whereas in cases of three or more positive pelvic nodes it was only 18%.

In women younger than 35 years the share of cervical carcinoma related to the total number of cases increased from 4.9% in 1965 to 17% in 1989 (3). The number of cases of cervical adenocarcinoma has raised from 5.8 to 22% of all cervix carcinoma cases in the last 15 years. Younger age and the histologic type of cervical carcinoma have not changed our treatment policy substantially, and the 5-year survival is comparable with that of older patients and squamous type carcinomas.

Our analysis (4) on 174 Wertheim and 29 Schauta operations demonstrated that severe urological complications were significantly more frequent in cases undergoing combined treatment. No case of permanent hydronephrosis was observed in only surgery group. However, permanent hydronephrosis requiring surgical treatment was observed in 8.3% of preoperatively irradiated cases, in 8% of postoperatively and in 12% of pre- and postoperatively irradiated cases. The percentage of ureterovaginal fistulas was 2.5%, irrespective of radiation therapy. We have no evidence of major gastrointestinal complications.

The question remains whether pre- and/or postoperative pelvic radiotherapy improves survival. Morrow et al (5) presented a retrospective series with a review of the literature and he could not identify a significantly improved survival in patients with positive lymph nodes who received postoperative irradiation. Postoperative radiotherapy may control local pelvic disease, but does not improve the overall survival, because more than 60% of recurrences were outside the radiation field (5-7). Other authors (8-10) suggest that adjuvant radiotherapy after radical hysterectomy produces favorable survival results with limited morbidity, especially in high risk cases with only one or two adverse factors. According to the published data (8-9) the major morbidity after combined therapy is genitourinary and gastrointestinal, and varies from 3 to 30%. In our analysis severe complications after combined treatment were mainly urological (from 8 to 12%).

Our data demonstrate that in patients with positive nodes, especially in cases with three or more positive nodes, the prognosis is significantly worse, and the overall 5-year survival was about 55-60%, irrespective of the combined surgical-radiotherapy.

In conclusion, there remains the unresolved problem of the efficacy of adjuvant pelvic radiotherapy in cervical carcinoma. Because in patients treated with combined therapy recurrences are mainly distant, not only adjuvant regional radiotherapy, but also systemic chemotherapy should be considered in cases at high risk for subclinical metastatic disease, especially because there has been little improvement in survival in cervical carcinoma in the past decades.

REFERENCES