Radiol Oncol 1993; 27: 115-9.

Invasive cervical adenocarcinoma: An analysis of 67 treated cases vs squamous carcinoma

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Adenocarcinoma (AC) of the cervix uteri has become an important clinical entity owing to its increasing incidence, high malignant potential, and relative radioresistance. The treatment results of 67 patients treated at the Institute of Oncology, and University Department of Gynecology in Ljubljana between 1973–1978 are presented in correlation with the results of 835 patients with squamous cell carcinoma (SC) treated in the same period. The rate of adenocarcinoma among all cervical cancers is 7%. Five-year survival was analysed according to the mode of treatment and stage of the disease. The survival in stage I was not influenced by treatment modality. There was also no difference as to the histologic type; in both studied types the survival was 79.3%. However, in advanced stages the mortality rate was alarmingly high: only 7.9% of patients with adenocarcinoma in stages II, III and IV survived 5 years, whereas the corresponding survival rate in patients with squamous cell carcinoma was 37.8%. Radioresistence of adenocarcinoma was evident in the group treated by irradiation alone: their 5-year survival was 9.1% vs 36% observed in squamous carcinoma. The overall 5-year survival of patients with adenocarcinoma was 38.8% vs 54.6% in squamous carcinoma.

Key words: cervix neoplasms-therapy; adenocarcinoma; squamous cell carcinoma; survival rate

Introduction

Adenocarcinoma (AC) of the uterine cervix is a relatively rare form of cancer. Its epidemiologic characteristics are similar to those observed in squamous type. During the past decades the incidence has been increasing.

Carcinoma shows prevailingly infiltrative growth (barrel shaped cervix), and it is relatively radioresistant. This renders the prognosis extremely unfavourable, particularly in the advanced stages of disease and poorly differentiated types.

The presented report analyses 5-year survival of patients with adenocarcinoma of the cervix with respect to the stage and treatment approach. The results are compared with those obtained in patients treated for squamous carcinoma (SC) in the appointed period.

Patients and methods

The presented analysis was carried out in patients with carcinoma of the uterine cervix treated at the University Department of Gynecology and/

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UDC: 618.146-006.6-08-036

or the Institute of Oncology in Ljubljana from 1973 to 1978. The total number of treated patients was 979; 29 patients were excluded from the analysis because they had been lost to follow up or had died of unknown causes. In the group of 950 patients there were 67 (7.1%) with adenocarcinoma.

Distribution by stages and comparison with squamous cell carcinoma are presented in Table 1 (staging according to FIGO classification

Table 1. Distribution of patients according to histologic type of carcinoma by stage.

Histologic type	Stage					
	I.	II	III	IV	All	
	No.	No.	No.	No.	No.	%
SC	338	218	234	45	835	87.9
AC	29	14	17	7	67	7.1
Other ca	21	5	18	4	48	5.0
Total	388	237	269	56	950	100.0

1972, confirmed 1978). Thus the rate of Stage I is 43,3% vs 40,4% for sqauamous cell carcinoma. There is no difference in age distribution between both histologic types. Median age of patients wiht AC was 54 years, and of those with SC 56 years.

Histological typization of AC was not performed, and there were no data on tumor differentiation or grade (G) available.

The treatment aproach was as follows (Table 2):

Table 2. Five-year survival of patients by treatment method and stage of adenocarcinoma.

Therapy Stage	Surg.		Surg + RT		RT		All	
	No.	%	No.	%	No.	%	No.	%
I	18/21	79.9	3/5	–	2/3	–	23/79	79.3
II	0/2	–	2/3	–	0/9	–	2/14	14.3
III	–	–	0/2	–	1/15	–	1/17	5.9
IV	–	–	0/1	–	0/6	–	0/7	–
Total	18/23	78.3	5/11	–	3/33	9.1	26/67	38.8

* percentages are not given when the number of patients is below 20.

– 23 patients underwent Wertheim-Meigs surgical procedure (radical or extended hysterectomy with pelvic lymphadenectomy);

– 5 patients preoperatively received intracavitary ^{226}Ra applications using Manchester technique; TD 40 Gy was delivered to point A prior to Wertheim-Meigs operation.

– 3 patients were postoperatively treated by external irradiation; TD 40–56 Gy (2 Gy daily) were delivered to the whole pelvis;

– 33 patients received a combined tele- and brachyradiotherapy in the following order: external irradiation – TD 40 Gy to the whole pelvis, followed by brachytherapy – TD 40 Gy to the point A, ending with additional irradiation to the parametrium and lymph nodes – TD 20 Gy with shielding of the center.

– 3 patients were hysterectomized because of local recurrence after radical irradiation.

The data were processed at the Institute of Biomedical Information of the Medical Faculty, University of Ljubljana, using their own software program STAT installed in a DEC 10 computer system.

The following two types of analysis were used:

1) basic statistic description of variables

2) analysis of variables with distribution of cases into subgroups

Crude five-year survival rate was calculated by direct method. All patients were followed for 5 years; those lost to follow up were not included in the analysis.

Results

In the investigated group of 67 patients 26 (38.8%) survived 5 years. Table 3 presents a comparison with SC where 5-year survival was 54.6%. Graphic comparison of the survival results in both histologic types is shown in Figure 1. The same rate of survival in both histologic types, i.e. 79.3%, was achieved in stage I patients only. In more advanced stages 5-year survival for SC was 37.8%, whereas in AC it was only 7.9%. The difference was statistically significant ($p<0.001$).

Table 3. Five-year survival by histologic type and stage of the disease.

Histologic type	Stage									
	I		II		III		IV		All	
	No.	%	No.	%	No.	%	No.	%	No.	%
SC	266/388	79.3	117/218	53.2	69/234	29.5	3/45	6.7	456/835	54
AC	23/29	79.3	2/14	–*	1/17	–	0/7	–	26/67	38
Other ca	18/21	85.7	3/5	–	4/18	–	0/4	–	25/48	52
Total	310/388	79.9	122/237	51.5	74/269	27.5	3/56	5.4	409/950	53

* percentages are not given when the number of patients is below 20.

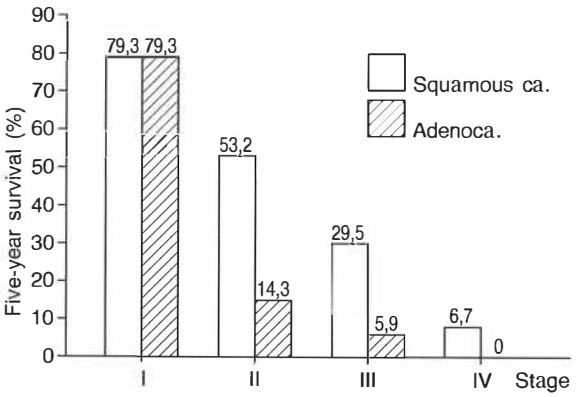

Figure 1. Five-year survival of 902 patients with cancer of the uterine cervix by histological type and stage of carcinoma.

Table 2 presents the survival with respect to treatment approach and stage. Thus, surgery alone proved effective in 78.3%, whereas a combination of surgery and radiotherapy was successful in 5 of 11 patients (45.5%), and radiotherapy alone in 3 of 33 (9.1%) patients only.

There was no difference between AC and SC patients treated by surgery alone. The difference is, however, evident in irradiated group where 182 of 513 (36%) SC patients survived 5 years. In the group of 141 SC patients treated with a combination of surgery and radiotherapy there were 102 (72%) 5-year survivors vs 45.5% in AC group; the difference is statistically significant.

Discussion

Recently, the rate of AC among cancers of the uterine cervix has been showing tendency to increase. Thus the rate of about 5% reported fot the past few decades has increased to almost 10% (9%, according to the data from Ann Rep No 21).[1] Some authors even report rates as high as up to 35%.[2] There are two possible interpretations of these values:

1) the incidence of invasive SC has been decreasing owing to successful screening using Papanicolaou test, whereas in AC this test fails to detect the disease in 25–50% of cases,[3, 4]

2) the number of AC cases is absolutely on increase.

Epidemiologic characteristics are the same as in SC, whereas possible influence of obesity, diabetes and hormonal treatment are still subbject to investigation, likewise in endometrial carcinoma.[4]

The clinical picture is similar as in SC, though AC often starts endocervically and therefore remains concealed. Barrel-shaped cervix is a typical result of its infiltrative growth.

Prognosis mainly depends on the stage of disease, being extremely poor in advanced carcinomas (Figures 2, 3).[1] There are no significant differences in the survival between Stage I AC and SC patients when our results (approximately 80% 5-year survival) are compared with those reported by other authors. On the other side, in advanced stages the mortality rates for AC are significantly higher. This difference is most apparent in patients treated by radiotherapy alone. The survival in our patients was only 9.1%, according to Ann Rep 20%, the mortality therefore being 2–5 times higher than in SC. With the use of combined surgical and

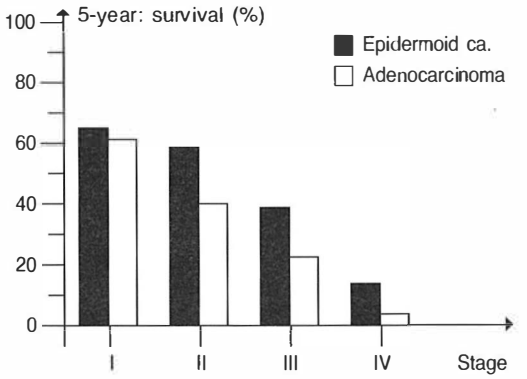

Figure 2. Carcinoma of the uterine cervix, 1982–1986. Five-year survival by histological type and stage for patients treated by radiation alone.

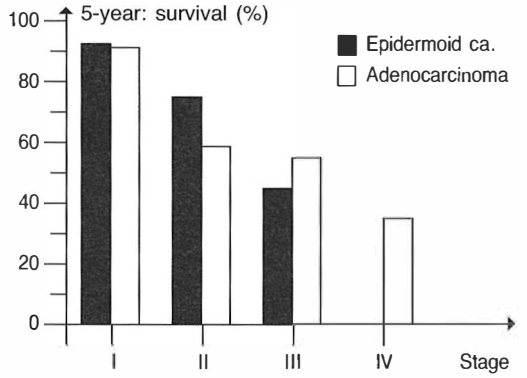

Figure 3. Carcinoma of the uterine cervix, 1982–1986. Five-year survival by histological type and stage treated by surgery alone.

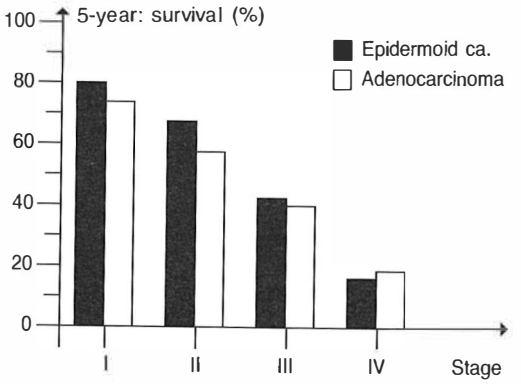

Figure 4. Carcinoma of the uterine cervix, 1982–1986. Five-year survival by histological type and stage for patients treated by surgery and postoperataive radiation.

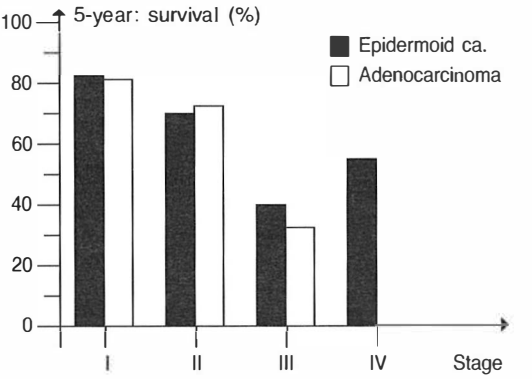

Figure 5. Carcinoma of the uterine cervix, 1982–1986. Five-year survival by histological type and stage for patients treated by preoperative radiation and surgery.

radiation treatment these differences are not so marked (Figures 4,5).[1]

Obviously, AC is a relatively radioresistant tumor, which is particularly the case with bulky tumors. The treatment of choice is therefore surgery which is indicated even in the cases of borderline operability. When radical surgery is not feasible, the therapy is completed with additional irradation. A signaficantly better survival is reported in patients with Stage II of the disease who have had histerectomy and irradiation than in those treated by radical hysterectomy or irradiation alone.[2] In primarily inoperable patients residuum after radiotherapy should be surgically removed (histerectomy after irradiation).

In our patients with AC the data on tumor type and differentiation were missing. According to the data from literature, the worst prognosis is associated with mucoepithelial and mucinous type of AC (Ferenczy's classification),[5] and the best with endometroid type. Poorly differentiated AC metastasizes faster, and the mortality in G3 is three times higher than in G1.[3] The survival in SC is not significantly influenced by tumor type and grade.

In clinically operable tumors, as in SC, lymph node status is the most relevant prognostic factor, though in AC the survival is two times

lower (approximately 30% vs 60%), which corresponds to the systemic nature of the disease[3]. Chemotherapy is not effective.

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