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Post-Irradiation Total Cystectomy for Bladder Cancer

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Summary. Treatment with radiotherapy (6000 rad) followed by total cystectomy was carried out in 125 patients with T1-T3 bladder cancer, the tumour being poorly differentiated (grade III-IV) in 115 cases. Survival was significantly better, if the irradiation had resulted in complete tumour regression before cystectomy, and if the tumour at the initial examination was of category T1. The relative cumulative survival after 5 years for patients with T1-tumours was 60%, as opposed to 40% for patients with T3-tumours. 4 patients (2.4%) died within 30 days of the cystectomy, but 13 patients (10%) died within 3 years from complications of the treatment regime. 83 patients (66%) experienced non-fatal complications such as infected cavity and urinary or intestinal stenosis. 3 years after the cystectomy 62 patients (50%) were dead from recurrent tumour or from other causes.

Key words: Bladder cancer, Radiotherapy, Cystectomy, Survival, Complications.

In an attempt to improve survival of patients with invasive carcinoma of the bladder a combined treatment of radiotherapy and radical surgery was introduced at our institution in 1971, caused by the poor results from the various forms of local therapy used until then (2).

MATERIAL AND METHODS

Patients with carcinomas of the TNM-categories T1 - T2 - T3 (U.I.C.C.) were given a full course of radiotherapy (6000 rad/6 weeks), and 12 weeks later a total cystectomy with ileal loop diversion was done. No antineoplastic chemotherapy was given.

From 1971 - 1976 125 patients were treated according to these criteria. The follow-up examination was carried out during 1977, with a mean observation time of 3.5 years (9 months - 6.5 years). Table 1 shows the age and sex distribution of the patients. 54% were over 60 years of age, and 19% were females.

Stage and grade: In 46 patients the tumour was classified as category T1 at the initial examination, in 32 patients as T2, and 47 patients as category T3. In 115 patients (92%) the tumour was poorly differentiated (histological grade III-IV). In the remaining 10 patients the tumour was of histological grade II in 8 patients, and undetermined in 2, one of which was a squamous cell carcinoma.

RESULTS

In 32 patients (26%) the pathological examination of the removed bladder showed no sign of residual tumour after the irradiation. 4 of these patients (13%) died with recurrent tumour during the observation period. In 93 patients the bladder contained residual tumour tissue at the time of the cystectomy. 43 of these patients (46%) died with recurrent tumour. This difference is statistically significant ($P < 0.005$, chi-square test, Yates correction).

Mortality. 3 patients died within 30 days of the cystectomy (operative mortality 2.4%), while altogether 7 patients died during the stay in hospital (hospital mortality 5.6%). Of these 7 primary deaths 2 were caused by other unrelated diseases

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Table 1. Age and sex distribution

Age	Total No. patients	Females No.	Males No.
38 - 50	15	6	9
51 - 60	43	7	36
61 - 70	56	6	50
71 - 77	11	5	6
Total	125	24	101

Table 2. 3 year mortality rates from all causes

TNM-category	Total No. patients	Deaths No.	%	95% confidence limits (%)
Category T1	46	19	41.3	27 - 57
Category T2	32	16	50.0	32 - 68
Category T3	47	27	57.5	42 - 72
Total	125	62	49.6	40 - 58

while 5 were due to complications of the combined treatment. Later during the observation period a further 8 patients died from complications and 3 from other diseases, so that a total number of 18 patients died from causes other than recurrent tumour, equally distributed in the 3 TNM-categories. Of these 18 deaths 13 were due to complications arising from our treatment regime.

All the deaths from complications and from unrelated causes, and 94% of the deaths from recurrent tumour, occurred within the first 3 years after cystectomy, so that after 3 years 62 patients (49.6% of all, 95% confidence limits 40% - 58%) were dead from recurrent tumour or from other causes. In Table 2 the 3 year mortality rates are listed for all patients and TNM-categories. Figure 1 shows the cumulative survival (life table method) of the total number of patients, and of the patients who died from recurrent tumour (the "relative mortality"). This relative survival curve may be subdivided into relative survival curves for the 3 TNM-categories (Fig. 2). After 5 years 60% of the patients with T1-tumours were alive without recurrence, as opposed to 40% of the patients with T3-tumours ($P < 0.05$).

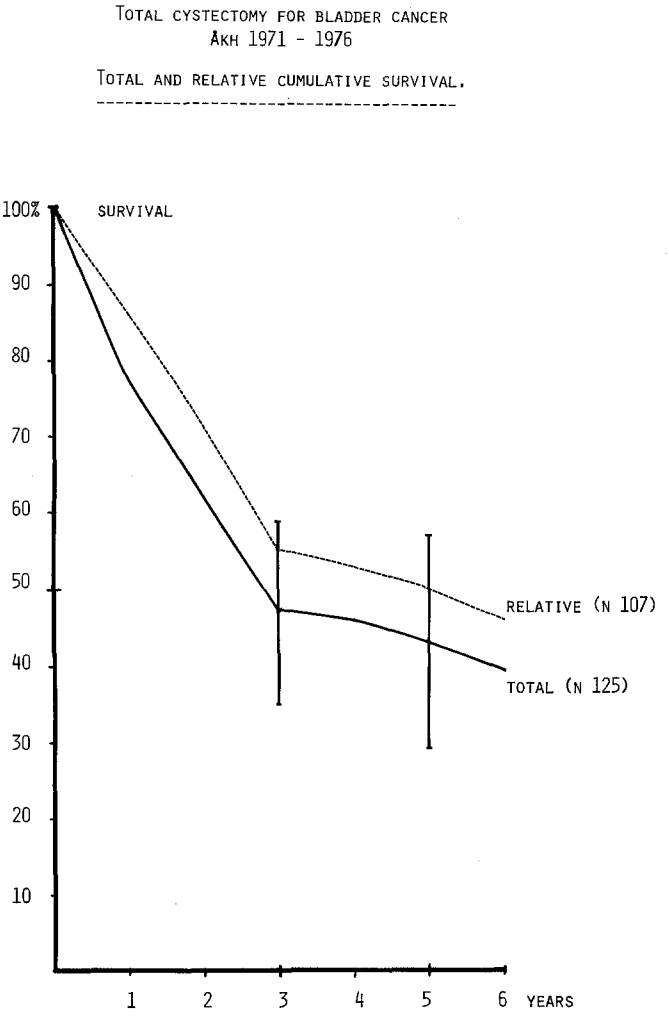

Fig. 1. The two curves represent cumulative survival rates after the life table method (actuarial), for the total number of patients, and after subtraction of the patients who died from other causes than recurrent tumour, ("relative survival"). For the total curve 95% confidence limits are indicated at 3 and 5 years

Complications, Fatal and Non-Fatal. In 28 patients (22%) the course was uncomplicated, and in another 2 patients the only complication was a small ventral hernia. 15 of these 30 patients died from recurrent tumour during the observation period.

The remaining 95 patients experienced one or more complications after the combined intensive therapy. The most frequent complication was an infected cavity after the cystectomy, with prolonged drainage in 55 patients (44%). 1 patient died from persistent infection. In 49 patients (39%) complications arose from the urinary diversion, and 6 of these persons died as a consequence of these complications. Twenty patients

had bilateral stenosis of the uretero-ileal-anastomoses, and in 15 cases the stenoses were corrected surgically. Twenty eight patients had unilateral stenosis, (18 L and 10 R), and in 10 cases reanastomosis had to be performed. 1 patient was operated upon because of a urinary fistula, so that altogether 26 of the 49 patients with urinary system complications had secondary surgery because of these.

The most serious complications were gastro-intestinal in the form of fistulae and/or stenoses. Thirteen patients experienced such complications; 10 patients were operated upon to correct the complication. Six cases died as a consequence of the intestinal problems.

Fifteen patients in the uncomplicated group and 48 patients in the group with a complicated course, i. e. a total of 63 patients (50. 4%), were alive and well at the follow-up examination.

DISCUSSION

Several modifications of therapy for bladder cancer have been suggested, all aimed at combining reduction of the frequency of tumour recurrence with a minimum of complications from the treatment itself. Local surgical treatment (2, 3) and pure radiotherapy (4, 8) have relatively few complications but, at least in the higher stage tumours (T2 and T3), poor long term survival. The common occurrence of multifocal tumours (in 20% of patients), and poor histological differentiation (92% of the tumours were of histological grades III-IV), seem to justify radical therapy. We decided to follow the principle of combining irradiation in curative doses with a total cystectomy in patients with bladder cancer of the TNM-categories T1 - T2 - T3. The same principle has been suggested by others, but usually with a lower preoperative dose of irradiation, such as 4000 rad (6, 8, 9), or 2000 rad (9) instead of our 6000 rad/6 weeks. The disadvantage of the high dose of irradiation is the number of complications following the cystectomy, often the result of the tissue changes caused by the radiotherapy. Our frequency of complications is unacceptable, although an operative mortality of 2. 4%, and a hospital mortality of 5. 6% compare favourably with other publications (1, 4, 5, 9). Our main concern was the late complications, such as infection and uretero-ileal stenosis (5, 6) that have required secondary surgery in 36 of our patients (29%), being fatal in 8 patients in addition to the 5 primary deaths from complications. For this reason we have decided to reduce the preoperative radiation to 4000 rad (7). A critical revision of our technique of anastomosing the ureters to the ileal loop has already reduced the frequency of stenoses.

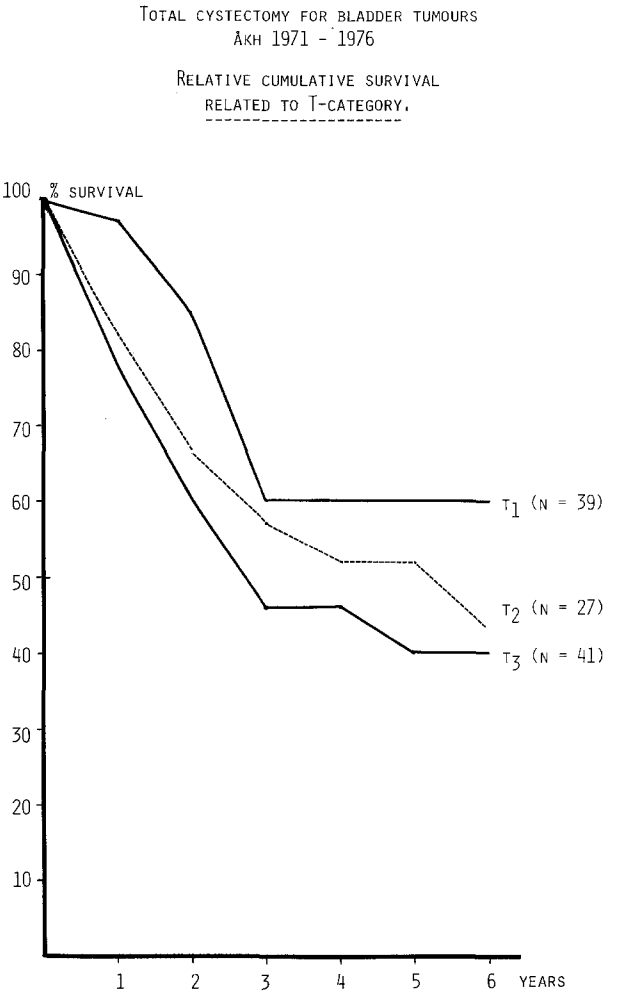

Fig. 2. The three curves represent the relative cumulative survival after the life table method for the patients in the three TNM-categories

Reviewing our results we feel that we have achieved the desired results on the tumour process itself, at least in the more advanced tumour stages (T2 and T3), with a 5 year survival of 40-50%. These results are better than the results after pure radiotherapy with a 5 year survival of about 15% (4), and of transurethral surgery with a 5 year survival of 15 - 30% (3), and are of the same level as other series undergoing the same combined and intensive treatment (1, 4, 8, 9). In low stage tumours (category T1) excellent results have been achieved by transurethral surgery with an elaborate technique (3), with a 5 year survival of 50 - 60%, i. e. the same level as after our combined treatment.

After 3 years, 44 of our 125 patients (35%) were dead from recurrent tumour. Two facts, however, seemed to reduce the risk of tumour recurrence. One factor was low stage of the

tumour at the initial examination, with a 5 year survival rate of 60% for T1-tumours, compared with 40% for the T3-tumours, as reported by others (8, 9). The other favourable indicator was a significant regression of the tumour after the radiotherapy, in which case only 13% of our patients died from recurrent tumour, as opposed to 47% of the patients with no or minimal regression in tumour stage. This same observation has been made in other publications (1, 4, 8), and it might suggest that one way to select the patients who will benefit most from the cystectomy is to find the ones with the most favourable response to the radiotherapy. The patients with no response or a poor response to radiotherapy have a poor prognosis no matter which treatment is added to the radiotherapy, - with the possible exception of the T1-tumours which may benefit from a careful, two-stage transurethral resection with very few complications (3).

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