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## RESULTS OF CYSTECTOMY WITH AND WITHOUT PREOPERATIVE RADIOTHERAPY IN CARCINOMA OF THE URINARY BLADDER

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### Abstract

During a period of 13 years, 84 patients underwent total cystectomy for transitional cell carcinoma of the bladder. The corrected 5-year survival rate was 58%. The operative mortality was 5 patients (6%). The 5-year survival rate of 42 patients who were treated by surgery alone was 53%, whereas that of 42 patients who received preoperative radiation of 30–40 Gy was 65%. The prognoses of the patients were dependent on the histological differentiation and the extent of the primary tumour within each treatment group.

*Key words:* Bladder carcinoma, preoperative radiotherapy, cystectomy.

Total cystectomy has an important role in the primary treatment of invasive bladder carcinoma and sometimes in the final treatment of rapidly recurring non-invasive carcinoma. Preoperative radiotherapy has been widely used with a tumour dose of 12–50 Gy (1). However, the value of radiotherapy remains uncertain (2) and equivalent results with and without preoperative irradiation have been reported in some series (3, 4). The present report is a retrospective study of treatment results and main prognostic factors in 84 patients who underwent cystectomy for bladder carcinoma.

### Material and Methods

From 1972 to 1984, 106 patients underwent total cystectomy for bladder carcinoma at the Department of Surgery, University of Turku, Finland. Nineteen patients who underwent salvage cystectomy after radical radiotherapy and 3 patients with squamous cell carcinoma were excluded from this study. The remaining 84 patients had

invasive or recurrent transitional cell carcinoma. There were 18 women and 66 men with a mean age of 65 years (range 32–79 years). All patients were followed up until death or the end of 1986. All medical records were checked, and the preoperative biopsy specimens and cystectomy specimens were reexamined for histological grading and pTNM-classification by one pathologist (T.E.). The main clinical features, TNM-classification and pTNM-classification are presented in Table 1.

Survival rates were estimated by means of the life-table method. The statistical significances of differences between survival curves were calculated with the log-rank test. The time of survival was measured from the operation. The observed survival rates were calculated for all patients, but for further analysis we also used survival rates corrected for deaths from causes other than bladder carcinoma according to autopsy or firm clinical evidence. The operative mortality was included in all calculations.

The operation consisted of cysto-prostato-vesiculectomy in men and cysto-urethrectomy and total hysterectomy in women. Three men underwent simultaneous urethrectomy because of tumour growth in the prostatic urethra. In every case a single stage ileal conduit urinary diversion was performed according to the method of Bricker (5). Lymphadenectomy was not performed but lymph nodes were biopsied.

Preoperative radiotherapy was administered to 42 patients: the total tumour dose was 40 Gy in 35 cases and 30 Gy in 7 cases; 42 patients received no irradiation. There was no prospective randomization into treatment groups. The similar number of cases with and without preoper-

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**Table 1**

Main clinical features of patients and classification of tumours in 84 cases of transitional cell bladder carcinoma

	No radiotherapy	Radiotherapy
Men	32	34
Women	10	8
Mean age (years)	63	66
G1	8	4
G2	19	18
G3	15	20
Tis	7	3
T1	11	9
T2	15	11
T3	8	17
T4a	1	2
pT0	2	9
pTis	4	7
pT1	17	4
pT2	9	6
pT3a	1	4
pT3b	5	10
pT4a	3	1
pT4b	1	1

ative radiotherapy was only a result of chance. Radiotherapy was delivered with a cobalt machine in 4 cases, with 6 MV photons in 15 cases and 10 MV photons in 23 cases using a 4-field 'box-technique' with 2 lateral and 2 antero-posterior opposed fields. Radiotherapy was given as 5 fractions weekly, 1.9–2 Gy per fraction. During the first years only 2 fields were treated daily but since 1981 all 4 fields. Until 1979 the standard preoperative dose was 30 Gy and thereafter 40 Gy. The treatment volume included the bladder and regional lymph nodes. Cystectomy was performed about 3 weeks after the last preoperative radiotherapy session.

### Results

The corrected 5-year survival rate after cystectomy for 84 patients was 58%. If deaths from unrelated causes were also counted, the corresponding figure was 48%. The 5-year survival rate for men was 54% and that for women was 59%. The 5-year survival rates for patients with well, moderately and poorly differentiated tumours (G1, G2, G3) were 84%, 65% and 43% respectively. The differences between the survival curves were not statistically significant ( $p > 0.05$ ). The 5-year survival rates according to the extent of the primary tumours were 74% for pTis–pT1, 64% for pT2–pT3a and 9% for pT3b–pT4a. The difference between survival curves for patients with pTis–pT1 and pT2–pT3a was not significant ( $p > 0.1$ ) but it was significant ( $p < 0.01$ ) between pT3a–pT4a and the other two groups.

**Table 2**

The 5-year survival rates according to the T-category of the tumour

Category	No radiotherapy		Radiotherapy	
	Number	Survival %	Number	Survival %
Tis–T1	18	67	12	100
T2	15	69	11	62
T3	8	13	17	52

**Table 3**

The 5-year survival rates according to the pT-category of the tumour

Category	No radiotherapy		Radiotherapy	
	Number	Survival %	Number	Survival %
pTis–pT1	21	64	12	100
pT2–pT3a	10	60	9	78
pT3b–pT4a	8	13	11	15

**Table 4**

Occurrence of pelvic recurrences, distant metastases and subsequent urothelial carcinomas

	No radiotherapy	Radiotherapy
Pelvic recurrence	4	6
Distant metastasis	7	4
Urethral carcinoma	4	4
Renal pelvic carcinoma	1	1

The 5-year survival rate was 53% for 42 patients who did not receive radiotherapy and 65% for those 42 who received preoperative irradiation ( $p > 0.1$ ). The 5-year survival rates according to the pretreatment clinical classification (TNM) of patients in these treatment groups except 3 patients who had tumour of pT4-category, are presented in Table 2. The 5-year survival rate of patients with muscle invasive bladder carcinoma (T2–T4a) was 41% for those who did not receive radiotherapy and 59% for those who received preoperative irradiation ( $p > 0.1$ ).

There was no residual tumour in cystectomy specimens of 9 patients who had received 40 Gy. In the clinical staging the extent of these pT0 tumours had been Tis in one, T1 in one and T2–T3 in 7 cases. The histological differentiation had been high in one, moderate in 4, and poor in 4 cases. Only one of these patients died of metastatic disease. The 5-year survival rates for patients with tumours of pTis–pT4a categories are presented in Table 3. Three patients whose tumours were of pT4b-category died within 2 years of metastatic disease.

The 5-year survival rates were correlated to histological differentiation in all TNM and pTNM categories. However, the differences were not statistically significant.

In 31 patients recurrence or metastasis of transitional cell carcinoma appeared within 5 years. The location of first recurrence is presented in Table 4.

Five patients (6%) died within 30 days of surgery. The cause of postoperative death was pulmonary embolism in 2 cases, myocardial infarction in 2 cases and small bowel gangraena in one case. Two of these patients had received preoperative radiotherapy.

Twenty-nine out of 42 patients who received preoperative radiotherapy complained of voiding symptoms (frequency and/or urgency) and/or diarrhoea during or some weeks after the radiotherapy. In most cases these symptoms did not require any treatment. No severe late complications of radiotherapy could be observed.

### Discussion

The overall 5-year survival rate of 58% is well comparable with most recent series that report figures 30–60% for patients with bladder carcinoma treated by cystectomy (3, 4, 6, 7). The observation that the prognosis depends on the grade and the stage of the tumour is also compatible with other studies (7).

In reporting results of treatment the pretreatment clinical classification (TNM) has been rated most important (8). However, in the present study the extent of the tumour is also reported according to the postsurgical histopathological classification (pTNM), because it has been shown that there is considerable uncertainty in assessment of the preoperative stage, especially the separation between T2 and T3 categories (9). This separation is probably of clinical importance since there seems to be a considerable impairment of the prognosis when the tumour grows through the bladder wall, e.g. advances from category pT3a to pT3b.

The use of preoperative radiotherapy has been based on the observation that the survival rate for patients who received radiotherapy was on average twice as high as that for patients who did not receive irradiation (10, 11). However, the indications and doses of preoperative radiotherapy are not clear at present (2). Similar results have been published in two series, one treated without preoperative radiotherapy (3) and another with 16 Gy delivered in 4 days followed immediately by surgery (4). Whitmore et al. (10) proposed that 20 Gy in 1 week and 40 Gy in 4 weeks are equally effective. Anderström et al. (12) assumed according to their prospective study that preoperative radiotherapy exceeding a CRE-value ('cumulative radiation effect') of 1400 (tumour dose 40 Gy) might improve the results. It has been shown that in some cases a considerable reduction of the tumour has been achieved by radiotherapy and that these patients have a better prognosis than expected after surgery alone (12–15).

In the present series, with a limited number of cases, the patients who received preoperative radiotherapy had the best survival rate. Furthermore, these patients had slightly higher age, higher grade and more advanced T-category than those who did not receive radiation (Table 1). Since 9 patients had no residual tumour after radiotherapy, and the majority of these had had invasive carcinoma in preoperative biopsy before irradiation, the favourable survival rate was possibly related to the pronounced effect of irradiation on the tumour.

It has been proposed that preoperative radiotherapy might decrease the frequency of local recurrences (16). However, in the present study no such effect was observed, but the patients who did not receive radiotherapy developed distant metastases somewhat more often (7/42) than the patients who received irradiation (4/42). Because of the fact that both local recurrences and distant metastases probably follow non-detectable micrometastases present already at the time of surgery, trials with preoperative chemotherapy have been conducted recently (17).

During the follow-up period transitional cell carcinoma of urethra appeared in 8 out of 63 men who had not undergone urethrectomy in association with cysto-prostatectomy comprising a frequency of 12.7%. This agrees with the findings of Hickey et al. (18) who found carcinoma in 7 out of 72 urethras. This frequency probably indicates not routine urethrectomy but close follow-up.

It is not possible to draw any firm conclusions from this retrospective non-randomized study. However, the study suggests that some patients with invasive bladder carcinoma gain advantage from preoperative radiotherapy and that this group is mainly constituted by patients in whom a pronounced effect of the irradiation is obvious in the operative specimen ('down-staging').

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