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SHORT-TERM MODERATE-DOSE PELVIC RADIOTHERAPY OF ADVANCED BLADDER CARCINOMA

A questionnaire-based evaluation of its symptomatic effect

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Abstract

Thirty-nine patients with advanced bladder cancer received pelvic radiotherapy (3 Gy × 10 during 2 weeks) with palliative aim. Except for improvement of urinary incontinence, no improvement regarding urinary symptoms or general well-being could be demonstrated in 19 completely evaluable patients who were assessed by a mailed questionnaire 3 months after treatment. The median survival for all 39 patients was 7.5 months. Other forms of palliative treatment (chemotherapy combined with radiotherapy or accelerated radiotherapy, palliative surgery) should be evaluated by randomized trials in these poor-prognosis bladder cancer patients. Self-administrated questionnaires seem to be useful for assessing the subjective morbidity of such patients.

Key words: Urinary bladder cancer, palliative radiotherapy, symptoms, questionnaire evaluation.

For many years pelvic radiotherapy has been used for palliative treatment (1–5) of advanced primary bladder cancer. However, only few reports have specifically dealt with the efficacy of such therapy, which is often given with moderate target dose and short treatment period. Some authors have reported decreased hematuria after large single fractions (1, 5). Other urinary symptoms and/or the patient's overall well-being have been less often considered systematically.

In 1987 we therefore started a prospective investigation with the aim to evaluate the subjective response to palliative pelvic radiotherapy in patients who were not candidates for curative treatment.

Material and Methods

Patients. The study comprised 39 consecutive patients with advanced transitional cell carcinoma of the urinary bladder who were referred to the Norwegian Radium Hospital (NRH) from 1987 to April 1989 and not regarded as suitable for treatment with curative intent (Table 1). As a rule, in our department palliative pelvic radiotherapy was given to all symptomatic patients above the age of 80 years and to younger patients with distant metastases. Before treatment started, all patients had disturbances of the bladder function due to the primary tumour. Seven patients had received systemic chemotherapy before radiotherapy (epirubicin (6), cisplatin-based combination chemotherapy (7)). The T-category (8) as given in Table 1, is based on cystoscopy and bimanual pelvic examination under general anesthesia performed immediately before radiotherapy. In all patients, transurethral resection of the intravesical part of the tumor was done prior to radiotherapy.

Radiotherapy was given by 16 MV x-rays from linear accelerators to one anterior and one posterior pelvic field comprising the bladder and the macroscopic tumor with a 2 cm margin. A target dose of 30 Gy was given by a daily fraction of 3 Gy. Treatment was applied from Monday to Friday and each field was treated daily. All patients were hospitalized during treatment.

Evaluation of efficacy. Before treatment start the patients were asked to fill in a self-administrated questionnaire (Q1) dealing with functional status, urinary symptoms, social life and pain level. The patients indicated their answers by a Likert ('Not at all', 'A little', 'Quite a bit',

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Table 1

Patient characteristics in 39 patients with advanced bladder cancer

Demographics	Subgroup 1 (n = 19)	Subgroup 2 (n = 20)	Total (n = 39)
Age (years)	75[1] (65–87)[2]	76[1] (60–85)[2]	76[1] (60–87)[2]
Males/females	16/3	13/17	29/20
T-category			
T2	2	1	3
T3	7	6	13
T4	10	13	23
M-category			
M0	12	13	25
M > 0	7	7	14
Hgb (g%)	12.2 (9.7–14.7)	11.0 (7.9–14.8)	11.4 (7.9–14.8)
Alkaline phosph. (U/l)[3]	216 (88–597)	221 (131–1247)	218 (88–1 247)
Creatinine[4]	119 (68–438)	119 (71–258)	119 (68–438)
Interval from initial diagn. to radioth. (months)	4 (1–147)	2 (0–109)	3 (0–147)
Perf. status (WHO)			
0/1	13	9	22
2	6	8	14
3		3	3
Other chronic diseases			
No	5	11	16
Cardiovasc.	9	5	14
Other	5	4	9
Pain level			
No analgesics	12	8	20
Non narcotics irr.	2	4	6
Non narcotics reg.	3	4	7
Narcotics irr.	2	2	
Narcotics reg.	2	2	4
Previous chemotherapy	4	3	7
Median obs. time (months)	13 (4–21)	4 (9–21)	7 (1–21)

[1]Median, [2]Range, [3]Upper normal limit: < 270 U/l, [4]Normal range: < 125 μmol/l.

'Very much') except for functional state impairment where answers were given as 'Yes' = (1) or 'No' = (0). A similar questionnaire (Q2) was applied at the end of radiotherapy and was also mailed to the patients 3 months after completion of treatment (Q3). Thereafter no further evaluation of subjective symptoms was attempted, but all patients were followed up for survival by the Norwegian Cancer Registry until death or until October 1990.

Statistics. The PC program 'Medlog' was used for calculation of means, median ranges and for application of the Wilcoxon's rank-test. Survival was assessed by the Kaplan-Meier method. A p-value <0.05 was regarded as statistically significant.

Results

Compliance. All 39 patients filled in the pretreatment questionnaire and 35 of these answered Q2. Nineteen patients returned the completed Q3 (subgroup 1), whereas this questionnaire was not filled in by 20 patients (subgroup 2). Eleven patients from subgroup 2 were dead before 3 months from radiotherapy had elapsed. Based on the information from the general practitioner/local hospital, 5 of the surviving 9 patients without Q3 were in very poor general condition when they received the Q3 and were not able to complete it. The reasons for non-compliance by the remaining 4 patients are not known. No major difference of the pretreatment patient characteristics was observed between subgroups 1 and 2, except for a higher percentage of performance status 2 and 3 in subgroup 2.

Morbidity. In the 39 patients, moderate to severe polakisuria and pronounced fatigue were the most frequent subjective symptoms before treatment, and reduced social activity was equally common (Table 2). Among the 19 patients from subgroup 1 urinary symptoms were slightly less frequent than in the whole group, though the differences were not significant.

Except for hematuria there was no reduction of the

Table 2

Pre- and posttreatment subjective morbidity in patients with advanced bladder cancer, scored as 'quite a bit' or 'very much'

Morbidity	No. of patients	
	All patients (n = 39)	Subgroup 1 (n = 19)
Polakisuria	24	13 (2)[1]
Incontinence	10	5 (3)
Hematuria (macroscopic)	11	4 (3)
Dysuria	11	3 (1)
Sleeping disturbances	13	6 (1)
Pain	15	5 (1)
Fatigue	18	8 (2)
Reduced social activity	21	9 (5)
Functional status*	12	4 (3)

[1]Number of patients with 3 months' posttreatment improvement by ⩾ 1 score.
*Mean score > 0.5.

Table 3

Percentage of patients with pronounced morbidity in subgroup 1 ('quite a bit' 'very much')

	No. of patients (%)		
	Pretreatment	2 weeks	3 months
Polakisuria	67	67	68
Incontinence	28	28	26
Hematuria	29	31	21
Sleeping disturbance	34	35	32
Fatigue	46	41	42
Reduced social activity	55	56	47
Decreased functional status	31	25	26

percentage of patients with pronounced urinary symptoms if all patients are considered who answered the questionnaires at each assessment (Table 3). Nor was there a significant improvement of the general symptoms, such as decreased performance status, reduced social activity, and/or fatigue. If patients from subgroup 1 were analysed separately, some improvement of incontinence and hematuria was seen in 3 and 4 patients respectively, who had pronounced symptoms of these kinds before radiotherapy (Table 2). Also in subgroup 1, performance status and social activity had improved at the assessment after 3 months.

The one-year survival for all patients was 36%, and only 20% of the patients were alive at 18 months. The one-year survival for M0 and M+ patients was 44% and 14% respectively. Fifty percent of the patients from subgroup 1 were alive at 1 year, as compared to 19% from subgroup 2. Four patients were alive at the end of the observation period.

Discussion

The primary goal of any palliative treatment is not prolongation of life, but reduction of morbidity and improvement of quality of life (QL). Though these endpoints of palliative care are generally well recognized, most reports about pelvic palliative radiotherapy deal with survival of the patients, as for example Mameghan & Fisher's retrospective study (9). In the present prospective investigation we did not aim at doing a complete QL assessment, but analysed the most dominant symptoms of somatic morbidity, which contribute to decreased QL: disturbed bladder function, decreased functional state and reduced social activity (10). The hope was that pelvic palliative radiotherapy would improve some of these pretreatment disturbances, especially micturition problems. For evaluation of the treatment effect, we used a questionnaire which was slightly modified from that designed by the EORTC GU Group (10). This questionnaire has been found feasible in clinical routine for patients with urologic cancer.

Only 19 patients could be evaluated completely. The results would, however, not have been improved if all patients could have been included: most of the patients who did not answer the Q3 questionnaire did not survive for 3 months or were in a very poor state at that time. This suggests that the results would have been even poorer if patients from subgroup 2 could have been included in the final analysis.

The median survival time of the patients with advanced bladder cancer is only 6 months and even shorter if distant metastases are present (9, 11). It is therefore important that any palliative treatment should not necessitate long-lasting hospitalization at radiotherapy centres, often far away from the patient's home. This consideration, together with limited radiotherapy resources, led to the decision to treat our patients with a target dose of 30 Gy during 2 weeks.

Despite the limited number of patients in the present study, the results clearly suggest that the selected radiotherapy schedule often achieves only quite moderate symptomatic relief or none at all. Significant improvement was recorded only for urinary incontinence and hematuria. The poor results might partly be related to a negative selection of patients, many of them having a very short life expectancy. Also, some other authors have found radiotherapy ineffective as palliative treatment (2, 3, 9), though the radiotherapy details have only rarely been presented in these reports. Bladder cancer is only moderately radiosensitive and high radiation doses are required to sterilize a large primary tumor (12). A target dose of 30 Gy given over 10 days is most probably too low to achieve essential tumor reduction and symptomatic relief. If palliative radiotherapy is to be given, other treatment schedules should be applied which yield a better biologic effect and better palliative results. Accelerated radiotherapy may be a

promising option, especially as it can be given over short periods (13). The combination of chemotherapy with radiotherapy is also worth exploring. Cisplatin-based chemotherapy thus seems to give both an objective response of the primary tumor, and a reduction of the micturition problems in patients with muscle invasive bladder cancer (7). Urinary diversion and palliative cystectomy are other means which are claimed to lead to satisfactory palliation during the life time of patients with advanced bladder cancer (3, 9). Another important aspect is the selection of patients: Palliative radiotherapy for advanced bladder cancer should preferably be offered only to patients with a life expectancy of $\geqslant 6$ months, which means M0 patients with a reasonable performance status.

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