

Radiation Treatment of Urinary Bladder Carcinoma

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Summary. A series of 602 patients with verified urinary bladder cancer have been treated with full irradiation in the period 1957-1970. As expected, the survival rate decreased with increasing stage of the tumour. Another group was randomized and treated according to either of two fractionation schemes. This trial started in 1971 and shows that there is increased survival and tumour clearance rate with superfractionation.

Key words: Irradiation - Bladder carcinoma - Superfractionation.

Because of disappointing results from surgery in the treatment of poorly differentiated bladder carcinomas, radiation therapy was introduced in Stockholm in 1957. The 5-year survival rate for patients treated by surgery was 22 % for T2-tumours and 3 % for T3-tumours. Two studies are presented in this paper, in which the patients have been given irradiation therapy alone with different fractionation schemes as a curative therapy.

I. The first series covers all patients, a total number of 602, given full irradiation between 1957 and 1970 and followed for at least 5 years.

II. The second series involves two different fractionation schemes in a randomized clinical trial begun in 1971.

The following criteria were used in both. Patients were selected after transurethral biopsy and/or other surgical procedures, known to have removed only part of the tumour. The patients were free from metastases detectable on clinical investigation. There was no age-limited selection.

The clinical staging followed UICC recommendation for stages T2-T4. In practice it is difficult to distinguish between T1 and T2 tumours and they were grouped together as T2.

The histopathological grading followed WHO recommendation and graded 1-3. All the whole material was analysed by one histopathologist. Normal diagnostic procedures were followed with cystoscopy bimanual palpation under anaesthesia, biopsy, intravenous urography etc.

First Series 1957-1970

602 patients were included in the first series. The mean age was 65 years and the mean interval from onset of symptoms to irradiation was 12 months for all stages. All patients with stages T3 and T4 tumours were selected together with the poorly differentiated and more differentiated tumours of more extensive size in T2.

METHOD

Radiotherapy consisted of external irradiation with cobalt-60 gamma rays. The calculated mean tumour dose was 6400 rad given in 7 weeks with a three-field technique, two wedge-filter beams in front and one open back beam. Weekly doses of 900 rad, 5 days a week, once a day were given with individual irradiation plans based on the anatomical outlines of the patient. One beam was used each day.

RESULTS

From Table 1 it is evident that the survival following radiotherapy decreased with higher stage or grade or both in combination. In stage T2 tumours, 17 % of the patients died within one year diagnosis. For T3 and T4 tumours the figures were 28 % and 55 %, respectively. In the first ten years a number of patients with ureteric obstruction due to tumour, had either a

Table 1. First series 1957-1970 - results

Stage	Year	All cases	Survival rate in %		
			Grade 2	Grade 3	Grade 2-3
T2	5	186	38	29	32
	10	111	25	18	22
T3	5	285	26	20	22
	10	158	13	12	12
T4	5	131	9	11	10
	10	95	5	3	3

nephrostomy or an ureterostomy performed prior to irradiation. The average survival time was 15 months, which was shorter than in those patients irradiated without previous urinary diversion.

Miller (6) pointed out that 5-year all-stage survival rate following radiotherapy alone has only limited prognostic value, because the loss rate between the 5th and the 10th postradiation years was high - more than 50% - and largely due to cancer. Our results indicate the same situation for stages T2 and T3. The cause of death between 5 and 10 years after irradiation was cancer - T2 67%, T3 50% and T4 0%.

Special Research Projects

1. In a series of 16 patients the clinical TNM staging was compared with a diagnostic surgical staging, including lymphography, aortography, cavography and laparotomy including biopsies from suspicious lymph nodes in the surrounding area (Table 2).

2. Investigation of the upper urinary tract has been made in the cases followed over a long period. The appearance of upper urinary tract obstruction clearly indicates recurrence of the tumour (2).

3. Investigation for vesico-ureteric reflux showed that irradiation itself does not give rise to reflux (3).

4. A spectrophotometric investigation was made to determine the amount of bone mineral content in the femoral region before, during and after radiotherapy. The results were normal throughout (1).

Quality of Life

The general condition of the patients including the ability to work and enjoy a normal social life and the bladder capacity have been assessed. The results were satisfactory 5 and 10 years after irradiation (Table 3).

Cytology

Amongst asymptomatic patients 5 and 10 years after irradiation, there were some who had positive cytology with malignant cells in bladder washings. In most of them bladder biopsies became positive and cystoscopy revealed tumour recurrences (Table 4).

Bowel complications

130 patients were followed with special reference to bowel complications over a 10 year period following radiotherapy. Barium enemas were performed at regular intervals (Table 5). The 7 cases requiring surgery, were operated upon within three years of the irradiation.

In an effort to improve upon the results of this first series the irradiation schemes were altered.

Second Series 1971

The lack of homogeneity of the tumour cell population regarding oxygenation and hence radiation sensitivity constitutes a major problem in radiation therapy.

There is experimental evidence (4, 5) that the radiosensitivity of cells increases with increasing access to oxygen. With the aim of distributing a larger radiation dose to the tumour tissue without undue damage to the surrounding normal tissues irradiation was given to a high total dose but divided into a larger number of small individual doses. Since 1971 over 200 patients have been randomized to either of two fractionation schemes, one of them using a superfractionation technique.

A total of 77 are included in this analysis to provide a preliminary indication of tumour clearance rate and complication risks. There were no significant differences between the two groups in the distribution of clinical stages, malignancy grading or mean age.

METHOD

The treatments were given by 6 MV X-rays using a three-field technique as in the first series. All fields were irradiated at each treatment session.

Table 2. First series 1957-1970 - comparative staging

Clinical stage	Surgical stage		
	T2	T3	T4
T2	3 ^a	2 ^a	-
T3	2	6 ^a	2
T4	-	-	1

^a lymph node metastasis in one patient.

Table 3. First series 1957-1970 - Quality of life

Years	General condition unaffected	Normal bladder capacity
5	78 %	88 %
10	89 %	93 %

Table 4. First series 1957-1970 - Positive cytology

Stage	At 5 years	At 10 years
T2	21 %	9 %
T3	9 %	11 %
T4	7 %	-
T2-T4	14 %	8 %

Table 5. First series 1957-1970 - Bowel complications

Reduced capability of the distension	10/130
Proctitis	3/130
Diverticulitis	3/130
Strictures not requiring surgery	3/130
Strictures requiring surgical correction	7/602

Scheme 1: 100 rad given 3 times daily at 4 hour intervals, 5 days per week to a total dose of 8400 rad; the patients were given 2 weeks' rest in the middle of the treatment period.

Scheme 2: 200 rad given once daily, 5 days per week to a total dose of 6400 rad; the patients had a rest of 2 weeks in the middle of the treatment period.

RESULTS

In the group treated according to scheme 1 (36 patients), tumour regression after 6 months was observed in 64 %; in group 2 (41 patients) in 44 %.

The survival rate 20 months after irradiation was 58 % and 41 % respectively.

Complications

Severe bowel complications necessitating surgery were observed in one patient in each group. Diarrhoea and/or frequency of micturition was only transitory with no difference was observed between the two groups.

DISCUSSION

The preliminary results indicate better tumour sterilisation and increased survival rate following high dose irradiation with a superfractionation technique. There appears to be no undue damage to the surrounding tissues and no enhancement of complications. Some of these patients have not yet been observed for 5 years but these results indicate that further study is worthwhile.

REFERENCES

1. Dalén, N., Edsmyr, F.: Bone mineral contents of the femoral neck after irradiation. *Acta Radiologica (Therapy Physics Biology)* 13, 97 (1974)
2. Edsmyr, F., Giertz, G., Nilsson, A.-E.: Effect of supervoltage therapy for carcinoma of the bladder on the outflow from upper urinary tract to bladder. *Scandinavian Journal of Urology and Nephrology* 1, 247 (1967)
3. Edsmyr, F., Nilsson, A.-E.: Vesico-ureteric reflux in connection with supervoltage therapy for bladder carcinoma. *Acta Radiologica (Therapy Physics Biology)* 3, 449 (1965)
4. Littbrand, B., Edsmyr, F., Revesz, L.:

- A low-dose-fractionation scheme for the radiotherapy of carcinoma of the bladder. Bulletin du Cancer 62, 241 (1975)
5. Littbrand, B., Edsmyr, F.: Preliminary results of bladder carcinoma irradiated with low individual doses and a high total dose. International Journal of Radiation Oncology Biology Physics 1, 1059 (1976)
6. Miller, L.S.: Bladder Cancer: Superiority of preoperative irradiation and cystectomy in clinical stages B₂ and C. Cancer 39, 973 (1977)

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