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Radical Cystectomy with or without Planned Preoperative Irradiation in the Treatment of Bladder Cancer

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Summary. A retrospective analysis of 342 patients with carcinoma of the bladder treated by radical cystectomy at Memorial Sloan Kettering Cancer Center with or without planned preoperative irradiation revealed that preoperative irradiation significantly improved survival of patients with deeply infiltrating tumours (pathological Stage B2 and C), and reduced the prognostic importance of distinctions between pathological B1 and B2 neoplasms. Preoperative irradiation had no discernible effect on the survival of patients with superficially infiltrating neoplasms.

Key words: Bladder cancer - Preoperative irradiation - Radical cystectomy.

Salient features of the use of radical cystectomy with or without planned irradiation in the treatment of bladder cancer at the Memorial Sloan Kettering Cancer Center (MSKCC) are presented.

PATIENTS AND METHODS

Between 1949 and 1971 342 patients with carcinoma of the bladder were treated by radical cystectomy *with or without planned prior irradiation at MSKCC. Excluded are 109 patients who received irradiation as definitive treatment and who were subsequently subjected to salvage cystectomy. The indications for cystectomy have been discussed elsewhere (3-8).

The methods of clinical and pathological staging and of tumour grading have not changed over the past 20 years, and there were no significant differences amongst the various treatment groups with regard to age and sex of the patients and histological type, grade, and clinical or pathological stage of the tumour.

The 342 patients may be divided into three groups:

Group 1 - (1949-1958): 137 patients who had radical cystectomy alone.

Group II - (1966-1971): 86 patients who ceived 4000 r to the bladder and true pelvis in four weeks with megavoltage as deliberate preoperative irradiation and subjected to radical cystectomy 6 weeks later.

Group III - (1966-1971): 89 patients who received 2000 r to the bladder and true pelvis in one week with megavoltage as deliberate preoperative irradiation and subjected to radical cystectomy within one week of completion of the radiation therapy.

Clinical staging, based on bimanual examination under anaesthesia, cystourethroscopy and transurethral biopsy, was recorded immediately prior to cystectomy in Group I and immediately prior to irradiation in Groups II and III.

RESULTS

Analysis of the clinical versus pathological stage revealed that clinical staging is inaccurate in distinguishing pathological Stage B1 from B2,

*Radical cystectomy involves bilateral pelvic lymphadenectomy, and en bloc removal of the bladder, perivesical fat, peritoneal covering, seminal vesicles, prostate, and, in selected cases, urethrectomy in continuity. The plane of dissection follows the muscular and bony pelvic walls.

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Table 1. Five year survival according to pathological stage

Pathological Stage	5 year survival alive/total (%)		
	Group I	Group II	Group III
Superficial (O, A, B1)	33/52 (63%)	38/65 (58%)	17/32 (53%)
Deep (B2, C)	10/50 (20%)	10/26 (38%)	15/26 (58%)
Metastatic (D)	2/34 (6%)	3/28 (11%)	4/28 (14%)
Overall	45/136 (33%)	51/119 (43%)	36/86 (42%)
Survival B1/B2 %(ratio)	60%/26% (2.3)	44%/44% (1.0)	50%/64% (0.8)

Table 2. Five year survival according to pathological stage and grade

Pathological stage and Grade[a]	5 Year survival (%)		
	Group I	Group II	Group III
Low grade, superficial	50%	56%	57%
Low grade, deep	33%	46%	63%
High grade, superficial	37%	37%	33%
High grade, deep	16%	28%	37%

[a] Superficial = O, A, B1
Deep = B2, C

and pathological Stages B2 and C from D1. Its accuracy in distinguishing superficially infiltrating tumours (O, A, B1), from deeply infiltrating or metastatic t nours (B2, C, D) was 79% for Group I, 76% fc Group II, and 62% for Group III (7, 8).

Table 1 illustrates 5 ar survival rates relative to pathologica ge. A source of potential bias is the fact that in Group II, tumour downstaging as a consequence of preoperative irradiation shifts some originally deeply infiltrating tumours to the superficially infiltrating category, adversely affecting the survival rates in the former category. Preoperative irradiation appears to add no survival benefit to patients in the superficially infiltrating categories, appears to double the survival of patients in the deeply infiltrating category, and obliterates the survival advantage of patients in the B1 as opposed to the B2 categories.

Table 2 illustrates 5 year survival according to the pathological stage and grade. In Group I both high grade and deep infiltration have an adverse effect on survival while in Groups II and III only high grade carries an adverse effect on survival.

The incidence of treatment failure due to local pelvic recurrence was 28% for Group I, 16% for Group II, and 14% for Group III.

DISCUSSION

In this retrospective analysis patients were not randomised into the various treatment groups, nor was treatment administered contemporaneously; however the uniformity in the clinical material, pathological staging, surgical therapy, and responsible surgeons, lends a "qualified" validity to intergroup comparisons.

The multiple clinical-pathological staging discrepancies limit the usefulness of clinical staging to distinguishing the very favourable from the very unfavourable lesions (7, 8).

Circumstantial evidence indicating the value of preoperative irradiation includes: (1) a doubling in 5 year survival of patients with deeply infiltrating (pathological B2-C) lesions (Table 1), which is reflected in a failure of high stage lesions to adversely effect survival in the irradiated group (Table 2); (2) a similar or identical 5 year survival in patients with pathological stage B1 and B2 lesions receiving preoperative irradiation (Table 1); and (3) a 50% decrease in the incidence of pelvic recurrences in the irradiated group.

While well oxygenated cancer cells, occupying the microscopic peripheral extensions of a central tumour are most sensitive to irradiation and least amenable to radical surgery, relatively hypoxic tumour cells occupying the central tumour mass are relatively radioresistant but are easily controllable with radical surgery (1, 2). On theoretical grounds, the failure of radical surgery alone may be related to easily overlooked microscopic extensions of regional neoplasm, or to local, vascular, and/or lymphatic dissemination of tumour cells during surgical manipulation. The effectiveness of preoperative irradiation and radical surgery in regionally controlling cancer is thus synergistic when considering bulky and/or regionally extended tumour. The failure of tumour stage alone (Table 2) to affect survival in preoperatively irradiated patients, may be explained on that basis. The failure to demonstrate a survival advantage with preoperative irradiation in patients with high grade cancers, may either be due to a relative radioresistance of high grade neoplasms or to a propensity of the latter for early vascular and/or lymphatic dissemination.

It seems reasonable to state that with the advent of preoperative irradiation** and cystectomy, the major influence on survival of patients with non-metastatic bladder cancer appears to be tumour grade. The stage seems set for adjunctive chemotherapy, especially since preliminary observations at MSKCC have suggested that high grade tumours are more responsive to this form of therapy.

**Considering the similarity in results with the two preoperative irradiation protocols (7, 8), 2000 r in one week is preferable because of the convenience in time and economy to the patient.

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