

Bladder Cancer

Survival after Bladder-Preservation with Brachytherapy versus Radical Cystectomy; A Single Institution ExperienceJ.A. Nieuwenhuijzen^{a,1}, F. Pos^{b,1,*}, L.M.F. Moonen^b, A.A.M. Hart^b, S. Horenblas^a^aDepartment of Urology, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands^bDepartment of Radiation Oncology, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

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Abstract

Objective: To evaluate the long-term survival following brachytherapy and following cystectomy of patients with invasive bladder cancer treated in our institution.

Patients and methods: Between 1988 and 2000 108 patients with solitary, organ confined T1–T2 invasive bladder cancer of ≤ 5 cm were treated with a transurethral resection, and a course of external beam radiotherapy (30 Gy) followed by 40 Gy brachytherapy. The overall and disease specific survival rates of these patients are compared with those of 77 patients with T1–T2 invasive bladder cancer treated with cystectomy between 1988–2003.

Results: The 5/10 year overall survival rates were 62%/50% after brachytherapy and 67%/58% after cystectomy ($p = 0.67$). The 5/10 year disease specific survival rates were 73%/67% after brachytherapy and 72%/72% after cystectomy ($p = 0.28$). When adjusted for age, multiplicity, T-stage, N-stage and grade, the 5/10 year overall survival rates were 65%/53% after brachytherapy and 62%/51% after cystectomy, respectively. The adjusted disease specific survival rates were 75%/70% after brachytherapy and 66%/66% after cystectomy.

Conclusions: This study does not provide evidence regarding survival against the use of bladder preservation with brachytherapy for patients with solitary, T1–T2 invasive bladder cancer of ≤ 5 cm diameter, seeking bladder-sparing alternatives to radical cystectomy.

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1. Introduction

Conservative treatment is now standard care for numerous malignancies including breast cancer, laryngeal cancer, anal cancer and soft-tissue sarcomas. For patients with invasive bladder cancer radical surgery is still considered standard treatment. Nonetheless, there are bladder-preserving alternatives for these patients, such as treatment with brachytherapy after transurethral resection (TUR) and external beam radiotherapy (EBRT). This treatment strategy has proven to

be effective for patients with solitary, organ confined, invasive bladder cancer (tumour category T1–T2) with a diameter of less than 5 cm. Reports mention high local control rates of 70–90% and excellent maintenance of bladder function [1–10]. Despite these results there remains a reluctance to accept brachytherapy as a reasonable alternative to radical cystectomy. An important reason for this could be the commonly held belief that bladder-sparing strategies lead to inferior survival. To become a reasonable alternative to cystectomy, a bladder-sparing approach should not compromise survival. Additionally, the bladder-sparing alternative should have excellent bladder sparing capacities.

For many years it has been the policy at our institute to offer patients with solitary, T1–T2 invasive bladder

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cancer smaller than 5 cm the option of bladder preservation with brachytherapy. We recently published our updated results [10]. Based on local control rates brachytherapy appears to be a reasonable alternative to cystectomy. The purpose of this study was to establish whether this could be sustained in the light of evidence from our own patients regarding survival as well. The following analysis reports on the survival rates after brachytherapy and cystectomy in our institution. Furthermore we describe the chance of bladder preservation after brachytherapy, based on our previously published results [10].

2. Patients and methods

2.1. Tumour staging

This is a retrospective review over patients treated between 1988–2003. In that time period the UICC TNM-staging changed. One of the inclusion criteria for brachytherapy is organ confined disease. Up to 1997 that included stage T3a (tumour invades in deep muscle). From 1997 onwards, T3a became T2b. We converted all stages to the 2002 TNM-system of the International Union Against Cancer [11], so a T3a tumour before 1997 is included in the analysis as T2 tumour. As no resected specimens are present for brachytherapy patients, pathological classification is not available for these patients. In order to be able to compare tumour classifications between brachytherapy and cystectomy, for both only clinical staging was used.

2.2. Brachytherapy

Patients with histologically confirmed bladder cancer with the following criteria were offered brachytherapy: solitary lesion with a diameter ≤ 5 cm; clinical T1G3 and T2 stages; fit for surgery; and adequate bladder capacity (estimated subjectively by patient-interviews). Before referral all patients had undergone TUR of the tumour. Evaluation of clinical tumour classification was determined by pelvic-abdominal CT, chest X-ray, TUR, and physical examination. Between 1987–2000 108 patients were treated with brachytherapy.

2.3. Cystectomy

Between 1988–2003 246 patients were treated with cystectomy. Evaluation before cystectomy did not differ from evaluation before brachytherapy. From these 246 patients, patients with clinical stage T1G3 and T2 tumours with a diameter ≤ 5 cm were selected. Patients who had previous irradiation for bladder cancer or neoadjuvant chemotherapy were excluded from analysis. If the diameter was unknown, patients were not excluded from the analysis. Also patients with multiple bladder tumours were not excluded. The inclusion of multiple tumours and tumours of unknown diameter will be addressed in the discussion. In total 77 cystectomy patients were selected. They were no candidates for brachytherapy for the following reasons; multiple bladder tumours (60), previous irradiation (3), patients' choice (2), tumour location not suitable (3), inadequate bladder capacity (2), unknown (7).

2.4. Treatment, brachytherapy

108 patients underwent brachytherapy. They received pelvic EBRT (30 Gy in 2 Gy fractions) to prevent scar metastases caused by tumour manipulation [12]. Within two weeks following com-

pletion of EBRT a suprapubic cystostomy was performed. Hollow nylon tubes for afterloading with $^{192}\text{Iridium}$ were then inserted into the tumour area parallel and halfway through the bladder wall. To aid recognition of the target area on treatment planning, 4–5 small silver seeds were inserted at the boundaries of the tumour area with a 0.5–1 cm margin. Usually three tubes in a single plane were adequate to encompass the target area. Subsequently the tubes were brought to the abdominal wall. A suprapubic or transurethral catheter allowed bladder drainage.

In 24 patients tube insertion was combined with a partial resection limited to the macroscopic lesion (pathologically staged pT0 in 5, pT1 in 3, pT2 in 12, and pT3 in 4 patients). Reasons for tumour resection were: location in the bladder dome and/or evidence of residual tumour at surgery not amenable to brachytherapy only on the basis of the volume of tissue palpated at surgery. Lymph node dissection as a staging procedure was not performed routinely. Only in case of suspected nodes on CT-scan or suspicion during the surgical procedure a modified lymph node dissection was done. Of the 11 lymph node dissections, three were tumour positive.

Treatment planning was performed a week post-surgery. Iso-dose curves were generated and the iso-dose encompassing the tumour area as marked with the silver seeds was selected as a reference. A dose of 40 Gy was delivered by the implant with $^{192}\text{Iridium}$. The mean application time was 71 h ranging from 36–102 h and the mean dose rate was 59 cGy/h ranging from 40–110 cGy/h. Immediately after completion of treatment the tubes were removed percutaneously without need of anaesthesia or analgesics. The urinary catheter was removed 3 weeks post-operatively after cystographic confirmation of absence of urinary leakage.

2.5. Treatment, cystectomy

77 patients underwent a pelvic iliac lymphadenectomy with a radical cystectomy and urinary diversion. The neighbouring organs, (prostate and seminal vesicles in males, uterus and adnexa in females) were also removed in most cases. The type of urinary diversion, either incontinent/continent with/without an orthotopic reconstruction depended primarily on the time period in which the cystectomy was performed. From 1995 onwards, a sexuality preserving cystectomy was performed in suitable patients, with preservation of the vasa deferentia, prostate and seminal vesicles in males, and all internal genitalia in females [13].

2.6. Follow-up

Patients were followed by regular CT-scan of the abdomen and chest X-ray. For patients treated with brachytherapy the follow-up included cystoscopy with urine cytology every three months the first three years, hereafter two times a year. Transurethral resection or biopsies were performed when in doubt of tumour recurrence. Superficial bladder recurrences were treated by TUR with/without additional intravesical chemo- or immunotherapy. Invasive recurrences were treated by salvage cystectomy, provided that no systemic disease was apparent and general condition was sufficient. The median follow-up for the patients treated with brachytherapy was 54 months (range 1–178 months); 44% has been followed up 5 years or more, and 17% 10 years or more. The median follow-up for the patients treated with cystectomy was 24 months (range 1–174 months). For patients still alive, median follow-up was 30 months for the cystectomy group and 68 months for the brachytherapy group.

2.7. Statistical analysis

The distribution of potential prognostic factors between both treatment-groups was compared using the two-sided Student *t*-test or Chi-square test. The Kaplan–Meier method was used to estimate

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