

Postoperative Radiotherapy in Bladder Cancer Patients in Presence of Neobladder: Safety and Morbidity

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Abstract

Objectives: To assess the safety of postoperative radiotherapy in bladder cancer patients, in presence of neobladder, in patients treated by radical cystectomy with positive surgical margin.

Methods: Out of 98 patients only 10 patients with bladder cancer treated by radical cystectomy with neobladder inserted after R1 resection. This was an indication for postoperative radiotherapy. Examined parameters included: patients' demographics, surgical data, pathology data, radiotherapy details, length of follow-up, recurrence events.

Results: Between 2007 and 2013, 10/98 patients, met the inclusion criteria. Three females and seven males. Radical cystectomy with pelvic lymphadenectomy was done in six patients with 4 patients didn't have lymph node dissection. Dose prescribed to the isocenter was 45-50Gy in 5 weeks. Late complication included thickened wall of the neobladder in all patients reported in CT scans with hydroureter and hydronephrosis in 3/10 (30%) patients with no deterioration in renal function. Disease free survival and overall survival were 50% and 58% respectively at three years, Local tumor control was 75%, and almost all patients except two had distant metastasis. No patients had re-surgery for local recurrence or a complication related to the neobladder.

Conclusion: Postoperative radiotherapy post radical cystectomy and orthotopic neobladder is safe and didn't increase morbidity. However, the number of patients is still small for this conclusion and more patients is still needed.

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Introduction

Role of postoperative radiotherapy (RT) in locally advanced bladder cancer remains an object of controversy and debate. Although many non-randomized clinical trials and retrospective series showed that it improves local tumor control and disease free survival [1][2, 3], it did not gain widespread use and adoption because of the associated toxicity [4]. The published Egyptian series may represent the largest series in this field mainly in Bilharziasis induced carcinoma [5], hence postoperative radiotherapy is integrated in our routine practice protocols for all T3, T4 disease. However, in patients with neobladder, radiotherapy is usually not administered for fear of irradiating the neobladder small bowel segment. In this study we aim to challenge this theory based on the hypothesis that the neobladder is not anymore part of the gastrointestinal tract once it is incorporated into the urinary tract, and it may be irradiated if indicated.

Methods

We searched in our records for bladder cancer patients referred for postoperative adjuvant radiation therapy from 2007 through 2013. Out of 98 patients only 10 patients met our inclusion criteria which are basically bladder cancer patients treated by radical cystectomy with neobladder insertion and positive margin that necessitate postoperative radiotherapy. Examined parameters included: patients' demographics, surgical data, pathology data, radiotherapy details, length of follow-up, recurrence events, (Table 1 shows patients characteristics). Radiotherapy included CT planning or

conventional simulator in supine position with knee support. Routinely, 4 fields box technique was used with the upper border at L5/S1 space, lower border below the obturator foramen and the lateral border 2cm outside the pelvic brim. The anterior border of the lateral field was anterior to symphysis pubis and the posterior border at S2/S3.

Patients were followed up by clinical examination and CT of abdomen ad pelvis every three months for the first year, every four months for the second year and every six months thereafter, according to our follow-up protocols. Overall survival, progression free survival and local recurrence free survival were calculated from the date of diagnosis to the date of the reported event.

Statistical analysis was performed with the SPSS 16 package.

Results

Between 2007 and 2013, 10/98 patients, met the inclusion criteria for our analysis. Three of our patients were females and seven were males. Six patients were below 65 years (mean age 59 year (range 45-71). Radical cystectomy with pelvic lymphadenectomy was done in six patients with 4 patients didn't have lymph node dissection. Renal profile was adequate in 6 patients to receive postoperative chemotherapy in addition to radiotherapy. Reported toxicity included: Diarrhea GII-III in 5 patients (50%) with two patients requiring radiotherapy treatment interruption for 1 week. Dermatitis GI occurred in all patients (100%). Dose prescribed to the isocenter was 45-50 Gy in 5 weeks. Late complication included thickened wall of the neobladder in all patients reported in CT scans with hydronephrosis and hydroureter in 3/10 (30%) patients with no deterioration in renal function. Disease free survival and overall survival were 50% and 58% respectively at three years, Local tumor control was 75%, and almost all patients except two had distant metastasis; to the lung in six patients, para-aortic lymph nodes in two, and bone in three patients (one patient had both lung and bone metastasis). No patients had re-surgery for local recurrence or a complication related to the neobladder.

Treatment received after failure: Cisplatin/Gemcitabine was given for 4 patients the remaining didn't receive chemotherapy due to poor general condition and were referred for the palliative care unit.

Discussion

Radical cystectomy and pelvic lymphadenectomy is considered the main line of treatment for muscle invasive bladder cancer with neoadjuvant chemotherapy for locally advanced disease (>T2c disease) with a reported survival advantage [6, 7, 8]. However in patients with poor performance status or inadequate renal profile chemotherapy may not be given. Additionally, local recurrence in bladder cancer correlates to tumor stage and margin status [4, 9]. Radiotherapy may potentially reduce the risk of local recurrence thus improving local-regional control that might enhance survival [5]. Whole

pelvic irradiation is associated with potential gastrointestinal toxicity as the intestine usually fill the true pelvis and this precluded the routine use of postoperative radiotherapy in bladder cancer [3]. There has been contradicting reports regarding surgery following pelvic radiotherapy and the associated toxicity on irradiated bowel [10-12], [13, 14]. Nieuwenhuijzen published a series of 27 patients who underwent salvage cystectomy following interstitial or pelvic radiation for TCC of bladder with acceptable complication rates [15]. This report included patients who underwent orthotopic neobladder following salvage cystectomy, but, no reports found regarding the effect of radiotherapy following the insertion of neobladder. Vascular changes are one of the effects of radiotherapy on the intestinal loop that have been demonstrated in experimental studies [16]. Biel and his colleagues studied the effect of radiotherapy on a free jejunal autograft in dogs. They demonstrated fibrous replacement of lymphatics with microvasculature in the intra-villous space and focal destruction and replacement of muscle layers with fibrosis [17]. However, the clinical impact of these changes is yet to be determined. Wei et al in an elegant way studied the effect of radiotherapy in a transposed jejunal loop [18] and pathological changes on the mucosa, but again they didn't report any clinically significant problem in swallowing or phonation or any re-surgical interference up to two years post radiation treatment. Putting in mind that in neobladder the effect of acidic urine on the intestinal mucosa may be more pronounced, however we didn't report any clinical problem and no patients developed urinary diversion related complications requiring re-operation. The cumulative radiotherapy dose in the Wei study was between the 50 and the 70Gy which is even more than the dose routinely used in the postoperative bladder radiotherapy. Complications of neobladder may include hydronephrosis which depends mainly on the type of surgery whether it's a direct or anti-reflux technique also it may be related to the previous effect of the tumor. In our patients hydronephrosis reported in 3 patients however, it didn't affect the initial renal profile of the patients. Still the number of patients is very small to conclude or exclude a direct effect of pelvic radiotherapy on the neobladder, but it warrant further investigation. Also, the effect may be didn't appear because of the lack of long term survival in our patients although survival and local control for our patients seems to be reasonably good, when compared to the literature [1, 19] however this may be due to selection bias being a retrospective analysis'.

To our knowledge this is the first report for radiotherapy given in presence of neobladder. Number patients still small to make a final conclusion, but it seems that whole pelvic irradiation in presence of neobladder is safe, at least when high risk for local recurrence do exist and radiotherapy is essential.

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