

# Patient's Outcome of Bladder Cancer managed by radical Cystectomy with lymphadenectomy at a University Hospital

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## Abstract

**Objective:** To study the impact of tumour staging and nodal metastases in predicting 5- year's survival after radical cystectomy and bilateral pelvic lymphadenectomy for primary bladder cancer.

**Methods:** During the period 1995 to 2005, 58 patients underwent radical cystectomy and bilateral pelvic lymphadenectomy and urinary diversion at a University hospital. Patients were identified using medical indexing coding system (ICD 9CM) using standard key words. The patient records were analyzed and follow up data updated. Disease specific survival, death or recurrence was taken as end point.

**Results:** Out of 58 patients, 50 (86%) were males and 8 (14%) females with a mean age of  $61 \pm 13.1$  years (range from 27 to 87 years). Of 58 patients, 11 (23%) were excluded from the study because of inadequate follow up. The mean follow up was 5.7 years (range, 7 months to 11 years). The overall 5 years survival was 55% with disease specific survival being 66%. Patients with pathological stage T0 at cystectomy have 87% 5 years disease specific survival compared to 60%, in patients with pT4 ( $p=0.705$ ) The 5-year survival for node positive patients was 16%, compared to 60% for node negative patients ( $p<0.01$ )

**Conclusions:** Radical cystectomy and bilateral pelvic lymphadenectomy is the standard treatment for muscle invasive and high grade T1 cancers, and as salvage for recurrent cancers. Lymphadenectomy has a potential therapeutic benefit. The pathological stage at cystectomy and nodal status are predictors of 5 years survival (JPMA 57:536:2007).

## Introduction

Bladder cancer is the second most common genitourinary malignancy, with transitional carcinoma (TCC) comprising nearly 90% of all primary bladder tumors. It represents a significant worldwide health problem. In the United States its current prevalence is approximately 500,000.<sup>1</sup> Though majority of newly diagnosed bladder tumors are superficial cancers, approximately one fourth of patients either present with or subsequently develop invasive cancers that will require aggressive management.

Radical cystectomy, along with extended pelvic lymphadenectomy, is considered as gold standard treatment for invasive bladder cancer.<sup>2</sup> Improved perioperative care and technique of anaesthesia have reduced the morbidity and mortality. Furthermore, ability to offer orthotopic reconstruction has improved the quality of life and patient's acceptance for the extirpative surgery.

Radical cystectomy cures half of the patients, while the remainder suffer from loco-regional and distant metastasis within 2-3 years. A more aggressive approach is warranted for some patients. This involves the use of adjuvant chemotherapy with surgery.<sup>3-5</sup>

Predicting outcomes (survival and risk of disease recurrence) after radical cystectomy has been most

commonly based on pathological staging of primary tumour and regional lymph node status. Several large, contemporary radical cystectomy series have documented risks of recurrence and death based on either TNM staging or pathological groupings that separate organ confined, extra vesical, or node-positive tumors.<sup>6-12</sup>

Alternative prognostic models capable of simultaneous evaluation of multiple relevant variables have been shown to provide improved estimates of outcome that more accurately can be applied to an individual patient.<sup>13,14</sup> Providing accurate estimate for the risk of disease progression after radical cystectomy is critical for improved patient/clinician decision making with regards to the need of adjuvant therapy. In addition, accurate prognostic tools will enhance the ability to interpret and compare clinical trials of bladder cancer treatments by assigning risk estimate for the patient populations studied.

The current work is conducted to study the impact of tumour staging and nodal metastasis as the predictors of 5-year survival following radical cystectomy and bilateral pelvic lymphadenectomy in patients at a university hospital.

## Patients and Methods

Between the year 1995 and 2005, 58 patients underwent radical cystectomy for primary carcinoma of bladder. Bladder cancer was diagnosed by cystoscopy and

transurethral resection of bladder tumour was done. Preoperative staging work-up involved complete history and physical examination, complete laboratory work-up, chest radiography, CT scan, MRI or ultrasound of abdomen and pelvis. Radio isotopic bone scan was done for patients in whom the clinical symptoms or laboratory finding suggested bone metastases.

Indications of radical cystectomy were based on clinical and pathological staging of the disease. This included muscle invasive bladder cancer, high grade tumour, high volume superficial cancer, invasive tumor refractory to radiotherapy and/or systemic chemotherapy, or highly recurrent superficial cancer following endoscopic resection and intra vesical treatment.

All patients underwent bilateral pelvic lymphadenectomy with radical cystectomy and urinary diversion. Concomitant urethrectomy was performed only in patient, with concomitant urethral cancer or bladder cancer involving bladder neck and prostatic urethra. The tumors were staged according to TNM 1997 classification.

Following cystectomy, patients were initially seen one month after surgery and then after every 3 months for 1 year and every 6 months until disease progression or death. Patients were followed-up by complete physical examination, complete renal profile and blood picture and electrolytes, chest X-ray, CT abdomen and pelvis and radioisotope bone scan whenever indicated.

Survival estimate were constructed using the Kaplan-Meier product limit methods. The variables evaluated were, age gender, tumour cell type, pathological stage and nodal involvement.

## Results

The mean patient's age was  $61 \pm 13.1$  (range 28-87 years) for 50 (86%) men and 8 (14%) women. Follow up ranged from 7 months to 11 years (mean 5.7 years). All patients were subjected to cystectomy, bilateral pelvic lymphadenectomy and urinary diversion in the form of ileal conduit in 43 (74%) patients, orthotopic ileal neo bladder replacement in 12 (21%) patients, Mainz 2 pouch (modified uretero-sigmoidostomy) in 1 (2%) patients, Indiana pouch (cutaneous continent diversion) in 2 (3%) patients.

Histopathologically, TCC was the most common tumour cell type diagnosed in 55 (95%) patients, followed by squamous cell carcinoma in 2 (3%) patients and adenocarcinoma in 1 (2%) patient. The pathological tumour stage at cystectomy was pT0 in 10 (17%) patients, pT1 in 3 (5%) patients, pT2 in 21 (36%) patients, pT3 in 7 (12%) patients, pT4 in 14 (24%) patients, adenocarcinoma in 1 (2%), and squamous cell carcinoma in 2 (3%) patients.

Out of 58 patients 5 (9%) had preoperative radiotherapy and systemic chemotherapy and 2 (3%) received only systemic chemotherapy. Out of 5 patients, who received both systemic chemotherapy and radiotherapy, 1 (20%) belonged to pT1 group; and 2 patients receiving only systemic chemotherapy belonged to pT0 group. The most common systemic chemotherapy given was MVAC (3 patients), Cisplatin was given to 2 patients, and 2 patients received TAXOl. Fourteen (24%) patients received intra vesical chemo or immuno-therapy. Mitomycin was given to 10 patients while 4 patients received intravesical BCG. Out of 58 patients, 11 (23%) were excluded from study due to inadequate follow up.

Kaplan Meier estimate of the 5-year disease free survival for the entire group was 66 % (Figure). Survival was directly related to final pathological stage and as the tumor stage progressed from superficial bladder cancer through pT4, survival significantly decreased ( $p=0.71$ ). In pT0 the 5 year survival was 87%, 33 % in pT1, 44 % in pT2, 40% in pT3, and 60% in pT4. The 5-year survival dropped sharply from 60% in node negative to 16 % in node positive patient ( $p<0.01$ ). The recurrence rate for pT0 was 0%, 33% for pT1, 4% for pT2, 60% for pT3, 20% for pT4, 0% for patient with squamous cell carcinoma and adenocarcinoma ( $p=0.450$ ). The recurrence increase sharply from 19 % in node negative to 33 % in node positive patients ( $p<0.138$ ).

## Discussion

Radical cystectomy and bilateral lymphadenectomy is a standard treatment for muscle invasive bladder cancer. It effectively removes the primary tumour and the regional lymph nodes that contain metastases in about 25% of patients undergoing this procedure.<sup>15-17</sup> However, even if muscle invasive bladder cancer was shown to be organ confined at radical cystectomy, up to half of patients ultimately die of disease in spite of apparently complete surgical removal.

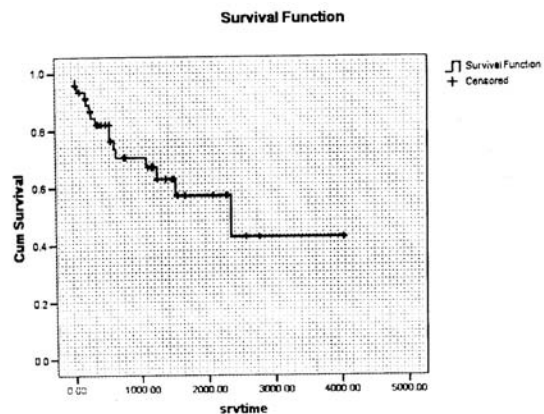


Figure. The 5-year survival. Kaplan-Myer survival curve.

In the current work pathological staging and lymph node status were the main prognostic factors that influenced the survival and recurrence of disease. But the results relating to the tumour staging were not significant.

Over all survival of patients was 66%, which is comparable with most published reports.<sup>17-19</sup> The final pathological stage of tumour is a powerful prognostic indicator after radical cystectomy.<sup>15,17</sup> In pT0, the overall survival was 87%; 60% of the patients in the pT3 group had metastases at a mean follow up of 5.7 years.

Pelvic lymph node involvement has been demonstrated to be a highly ominous factor in most reported contemporary series.<sup>19-24</sup> The reported incidence of regional involvement varied between 14 and 27% and this correlated with the pathologic stage of the primary tumors. In the present series, 12% of the patients had metastatic lymph node involvement. Survival in lymph node negative group was 60% while it was only 16% in the lymph node positive group. Recurrence in lymph node positive group was 33% while in lymph node negative group was 19%.

Early detection, proper patient selection and improved surgical techniques all have been reported to significantly decrease the chance of local pelvic recurrence following radical cystectomy. In the recent years most contemporary series with extended lymph node dissection reports an average of 10 % local recurrence (range, 4% to 8%).<sup>25</sup>

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