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Thirty-day Morbidity and Mortality after Radical Cystectomy in Carcinoma Urinary Bladder; A Single Centre Experience

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ABSTRACT

Objective: To determine the 30-day morbidity and mortality after radical cystectomy in carcinoma urinary bladder using a validated system.

Study Design: Retrospective longitudinal study.

Place and Duration of study: Armed Forces Institute of Urology, Rawalpindi Pakistan, from Jun 2016 to Jul 2021.

Methodology: After Institutional Ethical Review Board approval, data of all patients of carcinoma urinary bladder who underwent radical cystectomy during five years at Armed Forces Institute of Urology, was collected. Data was retrieved retrospectively from the hospital operative database, indoor patient records and by contacting the patients on their given telephone numbers.

Results: In the study population (n=39), a male preponderance was found (36,92.3%). Mean age was 56.7±8.96 years (range 32-72). 26(66.7%) patients were smokers and 16(41%) received neoadjuvant chemotherapy. 9(23.7%) patients had Clavien-Dindo Grade-I complications, 6(15.38%) had Grade-II, 2(5.12%) had Grade- IIIA, 2(5.12%) Grade IIIB, 1(2.56%) Grade-IVA, 1(2.56%) had Grade IVB, 2(5.12%) had Grade V complications. The total complications were 23(58.97%), and 16(41.03%) patients had no post-operative complications. 21(53.85%) patients had less than 14 days post-op operative hospital stay, and 18(46.15%) had more than 14 days post-op operative hospital stay.

Conclusion: Radical cystectomy is still associated with high early post-op mortality and morbidity. Careful patient selection and thorough counselling before the procedure are very important.

Keywords: Clavien-dindo grading system, Carcinoma urinary bladder, Radical cystectomy.

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INTRODUCTION

Carcinoma urinary bladder is the 9th most commonly diagnosed cancer in the overall population worldwide, with more than 30,000 deaths per year.[1] It is one of the most costly cancers from the time of diagnosis to death.[2] In the United States, it is the 4th most common cancer and the eighth leading cause of cancer deaths.[3] Approximately 30% of newly diagnosed cases of bladder cancer present as muscle-invasive bladder carcinoma (MIBC).[4] MIBC has aggressive behaviour and the worst prognosis if left untreated.[5]

Radical Cystectomy (RC) with Pelvic Lymph Node Dissection (PLND) and urinary diversion remains the mainstay of treatment for localised MIBC and high-risk non-muscle invasive bladder cancer (NMIBC).[6] Complications after radical cystectomy can be as high as 50-69%, even in the high volume centres.[7] The mean length of hospital stay after radical cystectomy ranges between 9-11 days, with a re-admission rate of approximately 27% due to infections and electrolyte imbalance.[8] Despite radical cystectomy, approximately 50% of MIBC patients develop metastasis in 2-3 years after diagnosis.[8,9] The role of neo-adjuvant chemotherapy before radical cystectomy, which leads to improved overall survival-ABC Meta-analysis, has also been studied. Adjuvant chemotherapy in high-risk cases has also reduced the local as well as distant relapse rates.[10]

Radical cystectomy with pelvic lymph node dissection and urinary diversion is a comprehensive surgical procedure and is associated with high post-operative morbidity and mortality. The measures of morbidity are complication rate, re-operation rate, length of hospital stay, re-admission rate and early mortality. Radical cystectomy with pelvic lymph node dissection is a major undertaking with the need for lifelong stoma application plus high morbidity and mortality. We studied the early morbidity and mortality of this procedure in our centre.

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METHODOLOGY

After Institutional Ethical Review Board (Uro-Adm-Trg-1/IRB/2021/125 dated 02 Sep 2021) approval, data of all the patients of carcinoma urinary bladder who underwent radical cystectomy between June 2016 to July 2021 at Armed Forces Institute of Urology Rawalpindi Pakistan, was collected. The sample size was calculated using the WHO sample size calculator, keeping the prevalence of carcinoma urinary bladder at 3 %.[11]

Inclusion Criteria: Patients with carcinoma urinary bladder who underwent Radical Cystectomy and pelvic lymph node dissection with curative intent after a decision by the hospital multidisciplinary meeting (MDM), were included.

Exclusion Criteria: Patients with incomplete data, unresectable disease and those who underwent palliative cystectomies were excluded.

Data was retrieved retrospectively from the hospital operative database, indoor patient records and by contacting the patients on their given telephone numbers. A total of 43 patients of carcinoma urinary bladder who underwent radical cystectomy and pelvic lymph node dissection with curative intent were found in the study period. Four patients were excluded from the study due to incomplete data or unresectable disease. After the exclusion of four patients, the study was performed on 39 patients with carcinoma urinary bladder who underwent radical cystectomies with pelvic lymph node dissection with curative intent.

We analysed the patients' demographic profile, modality of treatment and smoking status. We also studied neo-adjuvant chemotherapy status, TNM stage of the disease, duration of surgery and type of urinary diversion. Complications were studied within the first 30 days of surgery using the Clavien-Dindo grading system. Early post-op patients' activity levels and early mortality status after radical cystectomy were also analysed. Thirty days' follow-up was the primary endpoint of the study.

All patients who underwent radical cystectomy and PLND were discussed in the Hospital Multidisciplinary Meeting (MDM) before surgery. Hospital MDM comprised Urologist, Oncologist, Histopathologist, Radiologist, Nephrologist and Anaesthetist, and Urology, Oncology and Nephrology Residents. Only after a decision by MDM did patients undergo RC and PLND. Patients and their families were counselled in detail about the nature of the disease, other available treatment options, post-operative complications and the need for lifelong stoma application. Patients were given an opportunity and time to consult with their families and decide before surgery. Neoadjuvant chemotherapy regimens used by oncology colleagues were Gemcitabine and Cisplatin for 4-6 cycles or Mitomycin and 5- Fluorouracil for 4-6 cycles.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages.

RESULTS

Thirty-nine patients were included in the study with the male preponderance. The mean age was 56.7±8.96 years (range 32-72 years). 26(66.7%) patients were smokers. Sixteen patients (41%) received neoadjuvant chemotherapy (NAC), and 23(59 %) underwent upfront radical cystectomy with pelvic lymph node dissection.

Thirty-five (89.7%) patients underwent standard radical cystectomy with pelvic lymph node dissection and ileal conduit urinary diversion, 2(5.12%) had orthotropic neobladder formation after RC and PLND, 2(5.12%) had cutaneous ureterostomies after RC and PLND.

The mean duration of surgery was 6.88±1.24 hours (Range 4-10hours). TNM staging of patients undergoing radical cystectomy is shown in Table-I.

Table-I: Tumour, node and metastasis (TNM) staging of patients undergoing radical cystectomy (n=39)

TNM Staging	n/%
T4AN0M0	8/20.5%
T4AN1M0	12/30.8%
T3BN1M0	5/12.8%
T4BN1M0	2/5.1%
T4AN2M0	3/7.7%
T3BN0M0	6/15.4%
High Risk NMIBC	3/7.7%
Total	39/100%

Nine (23.07%) had Clavien-Dindo Grade-I complica-tions, 6(15.38%) had Grade-II, 2(5.12%) Grade- IIIA, 2(5.12%) Grade IIIB, 1(2.56 %) Grade-IVA, 1(2.56%) had Grade-IVB, 2(5.12%) had Grade-V Clavien-Dindo complications and died within 30 days after surgery (Table-II). 18(46.15%) patients had good post-op acti-vity levels, 11(28.20%) had limited activity/self-care, and 10(25.64%) had poor activity

levels (wheelchair or bed bound); out of these ten patients, 2 died within the first one month after surgery. 21(53.84%) patients had less than 14 days post-op hospital stay and 18(46.16%) had more than 14 days post-op hospital stay. 7(17.95%) patients got re-admitted within the first month; the main causes were surgical site infections/sepsis, fever, renal impairment or electrolyte imbalance (Table-III).

Table-II: Complications according to clavien-dindo classification (n=39)

Grade- I	**Superficial Wound Infections and Fever n=5, Prolonged Ileus n=1, Transient rise in S. Creatinine n=1, Increase drain output n=1, Bil Epididymo orchitis n=1**	**9(23.07%)**
Grade- II	Deep Wound Infections n=3, Pneumonia n=1, DVT n=1, Transfusion due to excessive per- op bleeding n=1	6(15.38%)
Grade- IIIA	Percutaneous drain placement for leak n=1, Percutaneous nephrostomy (PCN) Placement n=1	2(5.12%)
Grade- IIIB	Re-exploration for anastomotic leakage n=1, Intestinal obstruction n=1	2(5.12%)
Grade- IVA	Acute renal failure	1(2.56%)
Grade-IVB	Urosepsis and renal failure	1(2.56%)
Grade V	Death due to sepsis n=1, death due to multi organ failure n=1	2(5.12%)
	Total	23(58.98%)

Table-III: Causes of re-admission in early post-operative period (n=39)

Wound Infections/Sepsis	**3/7.69%**
Renal Impairment	2/5.13%
Fever	1/2.56%
Electrolyte Imbalance	1/2.56%
Total	7/17.95%

DISCUSSION

Radical cystectomy with pelvic lymph node dissection (RC with PLND) is the mainstay of treatment for non-metastatic muscle-invasive bladder cancer (MIBC) and high-risk non-muscle invasive bladder cancer (NMIBC). If MIBC is left untreated, then less than 15% of patients will survive for two years.[11] RC with PLND is associated with high post-op morbidity and mortality, especially in the early post-op period.[12] There are different measures to reduce post-op mortality and morbidity, for example, surgical complication reporting system, identification of modifiable risk factors, pre-op optimisation of patients, and post-op care plans.[13,14] The accurate reporting system for post-op complications is important for counselling patients and families, treatment planning, clinical trial design and assessment of surgical success.[15,16] Donat and colleagues highlighted the importance of complications in the grading system.[15] A literature review found that only one-third of uro-oncology literature used some form of grading system to report surgical complications, and only 6% used a numerical grading system .[16,17,18]

Early Mortality after RC with PLND in our study is 5.7%, which is slightly higher than the study by Johar *et al*.[14] and Sophia et al.[13] who had 4.5 % and 4.7% early mortality, respectively but it is less than the results by Ahmed et al. and Todd *et al*. who had 7.45% and 12.7% early mortality respectively (Table-IV).[12,19] Early complications (less than 30 days) in our study were 58.98%, higher than the results of Johar *et al*.[14] i.e. 43.8%, but comparable with 55.4% by Sophia *et al*.[13] and 58% by Shabsigh *et al*.[16] 41.02% showed no post-op complications, slightly lower than the results of Johar *et al*. i.e 56.2% but comparable with the results of Sophia *et al*. and Shabsigh *et al*. i.e 44.6% and 42% respectively.[13,16]

Table-IV: Comparison of literature (early mortality rates after radical cystectomy and PLND)

Todd et al. 12	**12.7%**
Sophia *et al*.[13]	4.5%
Johar *et al*.[14]	4.7%
Shabsigh *et al*.[16]	2%
Ahmad *et al*.[19]	7.45%
Our Study	5.7%

Grade-I and grade-II complications were the most common, i.e. 23.08% (n=9) and 15.38% (n=6), respectively. Grade-IV and V complications were lesser, i.e. 5.12% (n=2) each. Wound infections were the most common post-operative complications, consistent with Johar and colleagues results. 7(17.95%) patients got re-admitted within the first 30 days, consistent with 20.3% by Ian *et al*. and 19.7% by Stimson *et al*. respectively.[17,18] Sepsis due to infections was the most common complication requiring re-admission.[19]

This study helped us know about early post-op complications and mortality after RC and PLND using a validated system in our centre that was not previously available. This knowledge is helpful for appropriate patient selection and adequate future planning. This study confirmed that RC and PLND are major surgical undertakings. Careful patient selection, thorough pre-op planning, meticulous surgical techniques and appropriate follow-up may help reduce early morbidity and mortality.

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CONCLUSION

Our study concludes that radical cystectomy with pelvic lymph node dissection is associated with high early post-op morbidity and mortality. The patient and his family should have thorough and detailed counselling before undertaking this major surgical procedure.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & MRZ: Data acquisition, data analysis, critical review, approval of the final version to be published.

AA & OR: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AJA & AS: Concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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