



Contemporary Outcomes of Open Radical Cystectomy: a 5-Year Experience from a Tertiary Care Center

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Abstract

To evaluate the perioperative outcomes of patients undergoing open radical cystectomy for carcinoma bladder in a tertiary care center. A retrospective analysis of a prospectively maintained database of all patients undergoing open radical cystectomy with a urinary diversion from July 2014 to August 2019 was done. A total of 195 patients were included. A total of 172 patients (88.2%) underwent radical cystectomy with ileal or sigmoid conduit, 6 patients underwent orthotopic neobladder, and 17 patients underwent cutaneous ureterostomy. The mean American Society of Anaesthesiology (ASA) score was 1.4. On preoperative histopathology, 125 patients had the muscle-invasive disease. The mean operative time (\pm SD) was 303.6 ± 53.4 min and the operative time was significantly longer for neobladder ($p = 0.033$). The mean blood loss (\pm SD) was 977.5 ± 346.5 ml. Among the complications, a total of 350 events occurred in 96 patients (49.3%). Thirty-nine patients (20%) suffered grade I complications, 12 patients (6.2%) suffered grade II complications, 26 patients (13.3%) suffered grade III complications, and 9 patients (4.6%) suffered grade IV complications. Grade III, IV, and V complications were considered major complications and 46 patients (23.5%) had major complications. Among the grade III complications, the majority included fascial dehiscence (burst abdomen), i.e., 13.3%, and uretero-ileal leak, i.e., 2.6%. The overall 30-day mortality rate was 5.2% (10/195). On multivariate analysis, the presence of diabetes mellitus ($p = 0.047$), operative time ($p = 0.003$), and low preoperative albumin ($p = 0.009$) were significant predictors for major preoperative complications. Diabetes mellitus, serum albumin, and operative time are significant predictors of postoperative complications. The ASA score, low preoperative hemoglobin, and blood loss are significant predictors of perioperative mortality. Though radical cystectomy has been associated with significant perioperative morbidity and mortality, the advancements in surgical techniques and intensive care tools have led to a significant decrease in morbidity and mortality in the contemporary era.

Keywords Open radical cystectomy · Carcinoma bladder · Perioperative complications · Ileal conduit · Orthotopic neobladder

Introduction

Bladder cancer accounts for the second most common genitourinary malignancy and seventh most common malignancy in men. The incidence of bladder cancer is increasing in developing nations as the economic development of a nation goes along with a rise in the prevalence of smoking [1]. Bladder cancer is three times more common in men as compared with women [2]. Radical cystectomy with bilateral pelvic lymphadenectomy remains the standard of care for the management of muscle-invasive bladder cancer and high-grade superficial

bladder cancer refractory to endoscopic and intravesical treatment [3]. Radical cystectomy also provides an accurate determination of the stage and grade of the disease as well as the involvement of regional lymph nodes which could be erroneous in 30–50% cases on clinical staging. Though radical cystectomy has been associated with significant perioperative morbidity and mortality, the advancements in surgical techniques and intensive care tools have led to a significant decrease in morbidity and mortality [4]. With the advancement in minimally invasive surgery, laparoscopic and robot-assisted radical cystectomy has become popular but no definite evidence exists to prove its clinical superiority over open radical cystectomy [5]. As the chemotherapy has evolved, the outcomes of surgical management for bladder cancer have improved, and multimodal management, based on the stage of the disease, has become the standard of care.

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Various series have reported good long-term survival with radical cystectomy with 5-year overall survival ranging between 60 and 70% and recurrence-free survival ranging between 50 and 60% [2, 4, 6, 7]. Few studies have reported outcomes of radical cystectomy in Indian patients [2, 8, 9]. This study aims to study the perioperative outcomes of patients undergoing radical cystectomy and urinary diversion for carcinoma bladder at our center over the past 5 years and predict the factors determining the outcome.

Materials and Methods

A retrospective analysis of a prospectively maintained database of all patients undergoing open radical cystectomy with a urinary diversion from July 2014 to August 2019 was done. All the patients underwent standard preoperative workup including hemogram, renal and liver function tests, and chest X-ray along with cross-sectional imaging, contrast-enhanced computed tomography if the renal function was normal otherwise magnetic resonance imaging. The preoperative parameters assessed were patient age, gender, comorbidities, and the American Society of Anaesthesiologists (ASA) score. All patients undergoing open radical cystectomy were included. The decision of the type of urinary diversion was individualized according to patients' age, preferences, compliance, and extent of disease. Perioperative parameters included duration of total operative time, blood loss, hospital stay, and perioperative complications. During the initial years, we used mechanical bowel preparation with polyethylene glycol solution routinely and later conducted a randomized controlled trial between April 2017 and May 2018 for studying the enhanced recovery after surgery (ERAS) protocol in radical cystectomy [10]. Based on the result of our study, we are no longer using routinely preoperative mechanical bowel preparation since May 2018. Deep venous thrombosis prophylaxis included pneumatic compression devices and early mobilization. The standard steps of surgery were followed and bilateral pelvic lymphadenectomy was done up to bifurcation of the common iliac vessels. All uretero-ileal anastomosis were stented and the stent was removed after 2 weeks in ileal conduit and 3 weeks after neobladder. Pathological outcomes assessed were a pathological stage, margin status, number of lymph nodes removed, and number of positive lymph nodes for tumor deposits. The bladder carcinoma was classified according to the seventh American Joint Committee on Cancer [11], and the postoperative complications for a duration of 30 days were recorded and graded as per the modified Clavien-Dindo classification [12]. Among the complications, Ileus was defined as non-passage of flatus or stools with an inability to tolerate oral feeding and abdominal distension by postoperative day 5 [3].

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation (SD) or median (interquartile range [IQR]) as appropriate. Categorical variables were compared using chi-square test and continuous variables were compared using Student's *t* test, multiple ANOVA, Mann-Whitney test, or Kruskal-Wallis test as appropriate. The correlation between two variables was assessed using Spearman's rank correlation or Pearson's coefficient as appropriate. Multivariate regression analysis was used to identify the predictors of perioperative complications. The various perioperative variables were first studied for correlation with postoperative complications (graded with Clavien-Dindo scale) using univariate analysis, and stepwise multivariate regression analysis was used to identify the independent predictors of the postoperative complications and mortality. The preoperative variables included the age, gender, ASA score, comorbidities, presence of obstructive uropathy, and blood parameters including hemoglobin, total leukocyte count, platelet count, creatinine level, and albumin levels while the intraoperative blood loss, operative time, type of urinary diversion, and need of ancillary procedures along with the histopathological stage were studied as a part of intraoperative and postoperative variables. All statistical tests were two-sided. Statistical significance was taken as $p < 0.05$. Data were analyzed using IBM SPSS Statistics software (version 20.0, Chicago, IL, USA).

Results

One hundred ninety-five patients underwent open radical cystectomy between July 2014 and August 2019. The mean (\pm SD) age of the population was 57.3 ± 10.9 years. Of the 195 patients, 172 patients (88.2%) underwent radical cystectomy with ileal or sigmoid conduit (IC), 6 patients underwent orthotopic neobladder (ONB), and 17 patients underwent cutaneous ureterostomy (CU). Most of the patients were males, i.e., 178 (91.3%). The mean age and gender distribution were similar across the three groups (Table 1). Most of the patients presented with hematuria, i.e., 189 patients (96.9%). Twenty-four patients had obstructive uropathy at the time of presentation while 32 patients underwent preoperative percutaneous nephrostomy either for obstructive uropathy or for salvage of hydronephrotic kidney. Among the comorbidities, 37 patients (18.9%) had diabetes mellitus while 49 patients (25.2%) had hypertension. Sixteen patients had chronic kidney disease with eGFR < 60 ml/min at the time of surgery. Six patients had urinary bladder diverticulum with the tumor in it, and 108 patients had hydroureteronephrosis due to vesicoureteric junction involvement by the tumor. All the patients underwent at least one transurethral resection of the bladder tumor before radical cystectomy. On preoperative histopathology, 125

Table 1 Demographic details of the patients undergoing radical cystectomy with urinary diversion

Parameter	Overall	Conduit	Orthotopic neobladder	Cutaneous ureterostomy	<i>p</i> value
Number	195	172 (171, ileal; 1, sigmoid)	6	17	
Mean age (\pm SD), years	57.3 \pm 10.9	57.5 \pm 10.7	52.7 \pm 15.7	56.6 \pm 12.2	0.754
Gender, male/female, <i>n</i>	178/17	158/14	5/1	15/2	0.688
Presentation					
Hematuria, <i>n</i> (%)	183 (93.8%)	161 (93.6%)	5 (83.3%)	17 (100%)	
Acute urinary retention with hematuria, <i>n</i> (%)	6 (3.1%)	6 (3.5%)	0 (0%)	0 (0%)	
Lower urinary tract symptoms, <i>n</i> (%)	5 (2.6%)	4 (2.3%)	1 (16.7%)	0 (0%)	
Incidental, <i>n</i> (%)	1 (0.5%)	1 (0.6%)	0 (0%)	0 (0%)	
Patients having obstructive uropathy at presentation, <i>n</i> (%)	24 (12.3%)	16 (93.0%)	0 (0%)	8 (47.1%)	
Patients undergoing preoperative percutaneous nephrostomy, <i>n</i> (%)	32 (16.4%)	24 (14.0%)	0 (0%)	8 (47.1%)	
ASA score, mean (\pm SD)	1.4 \pm 0.6	1.4 \pm 0.7	1.0 \pm 0.1	1.4 \pm 0.6	0.098
Comorbidities					
Diabetes mellitus, <i>n</i> (%)	37 (18.9%)	34 (19.8%)	1 (16.7%)	2 (11.7%)	0.717
Hypertension, <i>n</i> (%)	49 (25.1%)	44 (25.6%)	3 (50%)	2 (11.7%)	0.165
COPD, <i>n</i> (%)	108 (55.4%)	94 (54.7%)	1 (16.7%)	13 (76.5%)	0.912
CKD, <i>n</i> (%)	16 (8.2%)	10 (5.8%)	0 (0%)	6 (35.3%)	0.07
Diverticular mass, <i>n</i> (%)	6 (3.1%)	6 (3.5%)	0 (0%)	0 (0%)	0.001
Presence of hydronephrosis on CT scan, <i>n</i> (%)	108 (55.4%)	95 (55.2%)	0 (0%)	13 (76.5%)	0.005
Presence of significant pelvic lymphadenopathy on CT scan, <i>n</i> (%)	60 (30.8%)	53 (30.8%)	0 (0%)	7 (41.2%)	0.975
Neoadjuvant chemotherapy, <i>n</i> (%)	17 (8.7%)	15 (8.7%)	0	2 (11.7%)	0.234

**p* < 0.05 considered as significant

ASA, American Society of Anaesthesiologist Score; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease (defined as estimated glomerular filtration rate < 60 ml/min/m²; CT scan, computed tomography scan

patients had the muscle-invasive disease and 44 patients had high-grade transitional cell carcinoma refractory to endoscopic or intravesical treatment (Table 2). Only 17 patients (8.7%) received neoadjuvant chemotherapy. Table 2 highlights the histopathological characteristics of the bladder tumor.

Most of our patients underwent radical cystectomy with an ileal conduit while only one of the patients underwent a sigmoid conduit. The mean operative time (\pm SD) was 303.6 \pm 53.4 min and the operative time was significantly longer for neobladder as compared with conduit or cutaneous ureterostomy (*p* = 0.033). Table 3 highlights the perioperative details of the patients. Since the majority of patients (13 out of 17) in the ureterostomy group underwent additional nephroureterectomy due to non-functioning kidney, the mean operative time of the ureterostomy group and conduit group was similar. Among the other ancillary procedures, 15 patients underwent urethrectomy for prostatic urethral involvement. Intraoperatively, 2 patients had rectal injuries and 2 had sigmoid injuries. The mean blood loss (\pm SD) was 977.5 \pm 346.5 ml, and the blood loss was similar between the three

groups. In the intraoperative period, 114 patients (58.5%) received a blood transfusion and the mean number of blood transfusions in the intraoperative period was 2.33 \pm 0.8 units. The mean duration (\pm SD) of hospital stay was 10.4 (\pm 5.3) days, and the hospital stay for neobladder was significantly longer than conduit or ureterostomy (*p* = 0.012). The complications were graded using the modified Clavien-Dindo classification.

Among the complications, a total of 350 events occurred in 96 patients (49.3%). The complications were studied as the highest Clavien-Dindo classification suffered by a patient and the total complications suffered by the patient. Table 4 highlights the details of the complications of the cohort included in the study. Grade III, IV, and V complications were considered major complications, and 46 patients (23.5%) had major complications. One patient underwent re-exploration for fecal fistula due to a leak following repair of rectal injury and underwent diversion colostomy. Another patient underwent re-exploration to remove the pack, kept for hemostasis due to intraoperative bleeding. The overall 30-day mortality rate

Table 2 Pathological characteristics and stage of the patients undergoing radical cystectomy with urinary diversion

Parameter	Overall	Conduit	Orthotopic neobladder	Cutaneous ureterostomy
Number	195	172	6	17
Preoperative histopathology				
T2 disease (muscle-invasive high-grade TCC), <i>n</i> (%)	125 (64.1%)	110 (63.9%)	3 (50%)	12 (70.6%)
High-grade TCC not amenable to endoscopic/intravesical treatment, <i>n</i> (%)	44 (22.6%)	39 (22.7%)	2 (33.3%)	3 (17.7%)
Micropapillary variant of TCC, <i>n</i> (%)	4 (2.1%)	4 (2.3%)	0	0
Low-grade TCC not amenable to endoscopic treatment, <i>n</i> (%)	2 (1.0%)	2 (1.2%)	0	0
High-grade TCC with squamous differentiation, <i>n</i> (%)	7 (3.6%)	6 (3.5%)	0	1 (5.9%)
High-grade TCC with sarcomatoid differentiation, <i>n</i> (%)	2 (1.0%)	1 (0.6%)	0	1 (5.9%)
Adenocarcinoma of bladder, <i>n</i> (%)	5 (2.6%)	4 (2.3%)	1 (16.7%)	0
Small cell carcinoma of bladder, <i>n</i> (%)	6 (3.0%)	6 (3.5%)	0	0
Pathological stage				
pT0, <i>n</i> (%)	5 (2.6%)	5 (2.9%)	0	0
pT1, <i>n</i> (%)	16 (8.2%)	16 (9.3%)	0	0
PT2a, <i>n</i> (%)	51 (26.2%)	46 (26.8%)	2 (33.3%)	3 (17.7%)
pT2b, <i>n</i> (%)	35 (18.0%)	27 (15.7%)	4 (66.7%)	4 (23.5%)
pT3a, <i>n</i> (%)	49 (25.2%)	43 (25.0%)	0	6 (35.3%)
pT3b, <i>n</i> (%)	5 (2.6%)	5 (2.9%)	0	0
pT4a, <i>n</i> (%)	33 (16.9%)	29 (16.8%)	0	4 (23.5%)
pT4b, <i>n</i> (%)	1 (0.5%)	1 (0.6%)	0	0
Lymph nodal disease				
pN0, <i>n</i> (%)	141 (72.3%)	123 (71.6%)	6 (100.0%)	12 (70.6%)
pN1, <i>n</i> (%)	27 (13.8%)	25 (14.5%)	0	2 (11.7%)
pN2, <i>n</i> (%)	25 (12.8%)	22 (12.8%)	0	3 (17.7%)
pN3, <i>n</i> (%)	2 (1.0%)	2 (1.2%)	0	0
Ureteric margin, <i>n</i> (%) positivity rate	6 (3.1%)	6 (3.5%)	0	0

p < 0.05 considered as significant

TCC, transitional cell carcinoma

was 5.1% (10 out of 195 patients). Among the causes of mortality, 7 patients had a septic shock with a chest infection in 6 patients, and one patient had a postoperative abdominal collection. Among these seven patients, three patients had

electrolyte disturbances associated with sepsis predominantly hyponatremia. Two patients had cardiovascular complications, i.e., myocardial infarction in postoperative period while one patient had aspiration pneumonitis.

Table 3 Perioperative parameters of the patients undergoing radical cystectomy with urinary diversion

Parameter	Overall	Conduit	Orthotopic Neobladder	Cutaneous ureterostomy	<i>p</i> value
Number	195	172	6	17	
Mean operative time, SD, minutes	303.6 ± 53.4	301.2 ± 51.7	377.2 ± 57.1	300.1 ± 63.8	0.033
Mean intraoperative blood loss, SD, ml	977.5 ± 346.5	986.7 ± 353.7	1050.2 ± 488.4	864.4 ± 183.6	0.563
Mean number of pRBC units transfused intraoperatively, SD	2.3 ± 0.8	2.2 ± 0.8	2.3 ± 1.5	2.0 ± 0.6	0.756
Ancillary procedure					< 0.001*
Nephroureterectomy, <i>n</i> (%)	28 (14.4%)	15 (8.7%)	0	13 (76.5%)	
Urethrectomy, <i>n</i> (%)	15 (7.7%)	13 (7.6%)	0	2 (11.7%)	
Ureterorenoscopy, <i>n</i> (%)	2 (1.0%)	2 (1.2%)	0	0	
Mean duration of hospital stay, SD, days	10.4 ± 5.3	10.5 ± 5.3	16.25 ± 5.3	8.5 ± 3.1	0.012*

**p* < 0.05 considered as significant

Table 4 Perioperative complications of the patients undergoing radical cystectomy with urinary diversion

Parameter	Overall	Conduit	Orthotopic neobladder	Cutaneous ureterostomy	<i>p</i> value
Number	195	172	6	17	
Highest complications (Clavien-Dindo)					
Grade I, <i>n</i> (%)	39 (20.0%)	35 (20.2%)	2 (33.3%)	2 (11.8%)	
Grade II, <i>n</i> (%)	12 (6.2%)	11 (63.9%)	1 (16.7%)	0	
Grade IIIa, <i>n</i> (%)	22 (11.3%)	19 (11.1%)	1 (16.7%)	2 (11.8%)	
Grade IIIb, <i>n</i> (%)	4 (2.1%)	4 (2.3%)	0	0	
Grade IV, <i>n</i> (%)	9 (4.6%)	8 (4.6%)	1 (16.7%)	0	
Grade V, <i>n</i> (%)	10 (5.1%)	10 (5.8%)	0	0	
Major complications (grade III, IV, and V), <i>n</i> (%)	46 (23.6%)	41 (23.8%)	3 (50%)	2 (11.8%)	
Overall complications					
Grade I					0.717
Paralytic ileus, <i>n</i> (%)	59 (30.3%)	54 (31.4%)	2 (33.3%)	3 (17.6%)	
Superficial wound infection, <i>n</i> (%)	37 (19.0%)	32 (18.6%)	2 (33.3%)	3 (17.6%)	
Diarrhea, <i>n</i> (%)	23 (11.8%)	20 (11.6%)	2 (33.3%)	1 (5.9%)	
Post-op fever due to unknown cause, <i>n</i> (%)	24 (12.4%)	18 (10.5%)	4 (66.7%)	2 (11.8%)	
Pulmonary complications- pneumonia/atelectasis, <i>n</i> (%)	17 (8.7%)	16 (9.3%)	1 (16.7%)	0	
Lymphorrhea, <i>n</i> (%)	61 (31.2%)	58 (33.7%)	2 (33.3%)	1 (5.9%)	
Grade II					0.005*
Post-op anemia requiring blood transfusion in postoperative period, <i>n</i> (%)	48 (24.6%)	44 (25.6%)	3 (50%)	1 (5.9%)	
Grade IIIa					< 0.001*
Fascial dehiscence managed with secondary suturing under local anesthesia, <i>n</i> (%)	21 (10.8%)	19 (11.1%)	0	2 (11.8%)	
Uretero-ileal leak/conduit leak, <i>n</i> (%)	5 (2.6%)	4 (2.3%)	1 (16.7%)	0	
Post-op fever with drainage of collection, <i>n</i> (%)	6 (3.1%)	5 (2.9%)	1 (16.7%)	0	
Pneumothorax, <i>n</i> (%)	2 (1.0%)	2 (1.2%)	0	0	
Grade IIIB					< 0.001*
Fascial dehiscence managed with fascial repair under general anesthesia, <i>n</i> (%)	4 (2.0%)	4 (2.3%)	0	0	
Re-exploration for rectal injury, <i>n</i> (%)	1 (0.5%)	1 (0.6%)	0	0	
Re-exploration for hemostatic pack removal, <i>n</i> (%)	1 (0.5%)	1 (0.6%)	0	0	
Grade IV					< 0.001*
Postoperative ICU stay, <i>n</i> (%)	15 (7.7%)	14 (8.1%)	1 (16.7%)	0	
Grade V					
30-day mortality, <i>n</i> (%)	10 (5.2%)	10 (5.8%)	0	0	

* $p < 0.05$ considered as significant

Using univariate analysis for predictors of major complications, the presence of diabetes mellitus ($p = 0.001$), mean ASA score ($p = 0.011$), operative time ($p = 0.001$), blood loss ($p = 0.021$), preoperative hemoglobin ($p = 0.031$), and preoperative albumin ($p = 0.04$) were found to be significant predictors while presence of diabetes mellitus ($p = 0.047$), operative time ($p = 0.003$), and preoperative albumin ($p = 0.009$) were found to be independent predictors of major postoperative complications (Table 5). On subgroup analysis, increased age ($p = 0.01$), presence of diabetes mellitus ($p = 0.03$), and prolonged operative time ($p = 0.02$) were significant predictors of paralytic ileus while prolonged operative time ($p = 0.005$) and low preoperative albumin ($p = 0.017$) were independent predictors

Table 5 Predictors of perioperative major complications (Clavien-Dindo grade III, IV, and V) in patients undergoing radical cystectomy and urinary diversion

Predictor	Univariate analysis	Multivariate analysis
Age	0.065	0.106
Diabetes mellitus	0.001	0.047
Mean ASA score	0.011	0.655
Operative procedure	0.482	0.432
Operative time	0.001	0.003
Blood loss	0.021	0.168
Preoperative hemoglobin	0.031	0.092
Preoperative albumin	0.04	0.009

$p < 0.05$ is considered as significant

of postoperative wound dehiscence. However, the ASA score ($p = 0.035$), low preoperative hemoglobin ($p = 0.039$), and blood loss ($p = 0.027$) found significant predictors of perioperative mortality.

The histopathological staging and grading of radical cystectomy and lymphadenectomy specimens have been depicted in Table 2. Of 195 patients, 88 patients (45.1%) had pT3 or higher disease, and 54 patients (27.2%) had lymph nodal positive disease. Six patients (3.1%) had a ureteric margin positivity. All patients with high-risk disease (pT3, pT4 disease, or lymph node-positive disease) or margin-positive disease received adjuvant chemotherapy. Table 2 highlights the pathological stage of various patients undergoing radical cystectomy.

Discussion

Ours is one among the few studies available on Indian population analyzing the contemporary outcomes of open radical cystectomy in the current era of minimally invasive surgery. More importantly, as the complication rate of radical cystectomy has been decreased with the advancements in surgical technique and perioperative care, this study tries to identify the predictors of perioperative complications in the Indian population. This study also highlights the under-utilization of neoadjuvant chemotherapy in Indian setting despite its strong recommendation in the literature.

The radical cystectomy with bilateral pelvic lymph node dissection has remained the gold standard treatment for muscle-invasive and non-muscle-invasive bladder cancer refractory to endoscopic and intravesical treatment. Despite the current era of minimally invasive surgery, the open radical cystectomy has stood over time with few studies only supporting the role of minimally invasive radical cystectomy. In a recent systematic review by Iwata et al. involving five randomized controlled trials and 28 non-randomized controlled trials, robotic radical cystectomy had similar oncological outcomes in terms of lymph node yield, positive margins, and short-term survival [13]. Hussein et al. also reported similar oncological outcomes at 10-year follow-up in open and robotic radical cystectomy [7]. In terms of perioperative complications, Sutkunasivam et al. reported that the only advantage of robotic cystectomy over open surgery is less blood loss at the cost of more operative time. However, there was no difference in length of hospital stay or complication rates with robotic surgery as compared with open radical cystectomy [14]. Shrivastava et al. reported outcomes of 63 patients of robotic radical cystectomy with an extracorporeal diversion from our center and reported the mean operative time of 348 min and mean hospital stay of 10.4 days. They also reported the perioperative complication rate of 38.4% [15]. Similar to the published literature, the mean operative time

in our open radical cystectomy cohort was 303 min and the mean hospital stay was 10.4 days. However, the perioperative complication rate was 49.6%. This could be because of a higher number of patients included and a more systematic assessment of complications.

In our study, the mean age of the population was 57.3 years with a mean ASA score of 1.4. Thirty-two patients underwent percutaneous nephrostomy before surgery while 16 patients had eGFR < 60 before surgery. Gupta et al. reported outcomes of radical cystectomy in 36 patients of carcinoma bladder presenting with obstructive uropathy and azotemia. The majority of these patients, i.e., 28 out of 36 patients, underwent percutaneous nephrostomy, and 32 of these patients underwent ileal conduit. They reported similar perioperative outcomes in these patients; however, they recommended optimization of renal function before surgery [16]. Similarly, El-Tabey et al. reported outcomes of 61 patients of carcinoma bladder with obstructive uropathy. However, only 38 patients were eligible for cystectomy with conduit. They reported similar perioperative outcomes but a higher stage of the disease [17]. In our study, 16 patients had eGFR < 60 ml/min before radical cystectomy and 10 out of 16 patients (62.5%) underwent ileal conduit while 6 patients underwent cutaneous ureterostomy. The perioperative outcomes in this cohort were similar to the overall cohort. The use of neoadjuvant therapy in muscle-invasive carcinoma bladder with stage \geq pT3 or higher or N1 disease has shown to have overall survival benefit of 5.8% and the improvement in absolute disease-free survival by 9% [18]. However, of the 105 patients (88.1%) who would have been the suitable candidates of neoadjuvant chemotherapy in our series, only 17 patients (8.8%) received neoadjuvant therapy. This marks the under-utilization of neoadjuvant therapy despite proven benefit in randomized controlled trials. This is not uncommon even in western countries. Cowan et al. surveyed active members of Society for Urologic Oncology to understand the contemporary use of neoadjuvant chemotherapy and observed neoadjuvant chemotherapy use in the range of 30–57%. Most uro-oncologist agreed to give neoadjuvant therapy for T3/T4 disease. However, concerns with age, comorbidities, and delay in the surgery were the primary deterrents for its use [19].

In our study, the use of neobladder was far less common as compared with contemporary practices in the Western countries. Although the continent diversion might be advocated by various bladder cancer experts, Farber et al. analyzed the Nationwide/National Inpatient Sample (NIS) database of the USA between 2001 and 2012 and reported 90.8% of ileal conduit and only 9.8% of continent diversion in 76,040 patients undergoing radical cystectomy [20]. They observed a steady rise continent diversion till 2008 while a gradual decline in the use of neobladders after 2008. They also observed a higher number of patients undergoing ileal conduit irrespective of age or comorbidities. The continent diversion was

common in only urban teaching hospitals and large volume centers. Moreover, an analysis of the British Association of Urological Surgeons (BAUS) registry also showed 86% use of ileal conduit and only 5% use of neobladders [20]. In our study, only 3% of patients underwent continent diversion. The advanced disease of presentation, i.e., 45.1% patients presenting with \geq pT3 disease, 24.2% patients presenting with obstructive uremia, and 7.7% patients undergoing urethrectomy for urethral involvement, might preclude the use of continent diversion in these patients.

The radical cystectomy is a morbid procedure associated with minor and major complications. Overall, the complication rate was 49.3%, and major complications (grade III/IV/V) were 23.5%. The 30-day mortality was 5.1%. Rossanese et al. reported an overall complication rate of 32.8% in an analysis of the British Association of Urological Surgeons (BAUS) registry involving 710 cases of open radical cystectomy. They reported major complications in 10% cases and 30-day mortality of 1.6% [21]. Stein et al. reported the outcomes of radical cystectomy in 1054 patients with the median to follow-up of 10 years and observed 28% perioperative complication rate with 2.5% perioperative mortality [4]. Abe et al. compared the 90-day complication rate between 175 patients undergoing neobladder and 493 patients undergoing ileal conduit in a retrospective study of Japanese patients and found no difference in overall complication rate. The neobladder was found to be associated with more infectious complications while conduit was associated with higher wound-related complications [22]. Our study does not report this variation owing to a small number of patients undergoing neobladder formation.

Our overall complication rate was higher than those reported in western literature. The reason for the higher rate of complications could be probably the presentation of advanced disease in a nutritionally challenged population with low hemoglobin and albumin levels. However, studies from the Indian subcontinent have reported similar results. Patidar et al. [9] reported complications of radical cystectomy in 212 patients with 88 patients undergoing ileal conduit, 113 patients undergoing neobladder, and 11 patients undergoing cutaneous ureterostomy. They reported an overall complication rate of 64% with a mortality rate of 3.7%. The most common complications were hematological (21.6%) followed by gastrointestinal or infectious complications (18% each). Twenty-eight percent of the patients had major complications (grade III or more). Gupta et al. [8] also analyzed outcomes of open radical cystectomy and reported the complication rate of 25.7% and perioperative mortality of 6.9%.

Among the predictors of complications, we found the presence of diabetes mellitus, operative time, and preoperative albumin as significant predictors of perioperative major complications while the ASA score, blood loss, and low preoperative hemoglobin were independent predictors of mortality.

Similar results have been reported in the literature. Johnson et al. reported albumin < 3.5 g/dl as an independent predictor of perioperative complications [23], while Bostrom et al. reported age, higher ASA score, higher blood loss, and need of blood transfusion as independent predictors of perioperative mortality and morbidity [24]. Takada et al. reported a 68% complication rate in patients undergoing open radical cystectomy and reported the presence of previous cardiovascular morbidity and type of urinary diversion as predictors of complications [25]. Abe et al. also reported age and volume of the center as an important parameter governing perioperative outcomes [22]. The hospital volume has also been studied to play a role in perioperative outcomes. In a study involving 196 hospitals in Spain performing radical cystectomy for carcinoma bladder, hospital volume with 38 cases/year or greater were found to have lowest mortality (3.8%) and morbidity as compared to overall mortality of 6.5% [26]. Being a tertiary care center, our center performs about 39 radical cystectomies/year. Though some authors suggest 50cases/year as a desirable rate for an experienced center, the International Consultation on bladder cancer has lowered the threshold to 10 cases/year per hospital as an adequate rate. With increase in experience and advancement in intensive care during perioperative period, the complication rates are likely to decrease.

This study has several strengths. The study demonstrates the contemporary outcomes of open radical cystectomy, which is still the most common procedure performed for the management of muscle-invasive bladder cancer. This study is among the few studies analyzing the perioperative complications, using systematic Clavien-Dindo classification, of open radical cystectomy in the Indian subcontinent, and provides an insight into the use of neobladder and cutaneous ureterostomy as well as contemporary use of neoadjuvant chemotherapy in the Indian context compared with western population. This study for the first time tried to address the predictors of perioperative complications following radical cystectomy among Indian patients.

However, the study has several limitations. Being a retrospective study adds an inherent bias. Certain variables such as performance status, Charlson comorbidity index, and body mass index were not available for all the patients. The histopathology was not studied by a single pathologist, though, the reporting was done by experienced genitor-urinary pathologists. The study does not involve any comparison with the perioperative outcomes of minimally invasive radical cystectomy.

Conclusion

Diabetes mellitus, serum albumin, and operative time are significant predictors of postoperative complications. The ASA score, low preoperative hemoglobin, and blood loss are significant predictors of perioperative mortality. Though radical

cystectomy has been associated with significant perioperative morbidity and mortality, the advancements in surgical techniques and intensive care tools have led to a significant decrease in morbidity and mortality in the contemporary era.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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