Original Article

Assessing neoadjuvant chemotherapy's impact on complications following radical cystectomy

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ABSTRACT

Introduction: Despite level 1 evidence supporting neoadjuvant chemotherapy (NACT) followed by radical cystectomy (RC) for muscle-invasive bladder cancer (MIBC), its adoption is hindered by concerns about toxicity and detrimental impact on post-RC complications. We retrospectively reviewed post-RC complications at a tertiary care hospital, particularly assessing impact of NACT.

Methods: Data from the institutional bladder cancer database were retrieved for patients aged ≥18 with MIBC (≥American Joint Committee on Cancer Clinical Stage T2), treated with RC between May 2013 and July 2023. Exclusions were nonurothelial histology, salvage cystectomy, and palliative intent. Data abstracted included patient characteristics, NACT administration, surgery, and outcomes. Patients were divided into two groups based on NACT and compared. Complications were categorized as early (≤30 days) or late (31–90 days) and graded. Statistical analysis set significance at $P < 0.05$.

Results: Of 154 patients who underwent RC, 33 were excluded due to non-MIBC, nonurothelial histology, or salvage cystectomy. The 121 patients analyzed had a mean age of 64 years and a Charlson Comorbidity Index (CCI) of 4.9. Among them, 61 received NACT and 60 did not. There was no significant difference between the NACT+RC and RC-only groups in overall complication rates (85.3% vs. 75.0%, $P = 0.16$) or in major complications (50.8% vs. 58.3%, $P = 0.41$). CCI >5 predicted major complications, while NACT did not.

Conclusion: In our study of MIBC patients managed at a tertiary care institute in India, NACT administration did not increase postoperative complications.

INTRODUCTION

Bladder cancer (BC) is the 17th most common cancer in India.[1] Thirty percent present with muscle-invasive disease.[2] Neoadjuvant chemotherapy (NACT) followed by radical cystectomy (RC) with pelvic lymph node dissection and urinary diversion is the standard of care for muscle-invasive bladder cancer (MIBC).[3] Depsite level 1 evidence for NACT, adoption remains poor, in part due to the concerns of chemotherapy-related toxicity and its potential adverse consequences on physiologic reserves in a precystectomy patient.

Despite advancements in surgical techniques, technology, and perioperative care, RC remains a challenging procedure

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/iju.iju_217_24

Received: 01.06.2024, **Revised:** 14.09.2024,

Accepted: 16.09.2024, **Published:** 01.01.2025

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

with a substantial rate of complications. Morbidity and mortality following RC vary, with rates ranging from 30% to 70% and 0.3% to 5.7%, respectively.[4]

Retrospective data from RC series from high-income countries have reported that the outcomes of RC after NACT are not worse compared to RC alone.[5-7] The average BC patient in India is likely to be malnourished and have higher comorbidity.[8,9] In addition, presentation with advanced disease is common.[2] Concern remains regarding the use of NACT in an already physiologically compromised patient, which may make the patient unfit for surgery, or increase complications after surgery, with increased morbidity and mortality.

The primary aim of our study was to determine complication rates after RC, among patients who received NACT in comparison to those that did not. The secondary aim was to determine the preoperative factors predicting complications after RC.

PATIENTS AND METHODS

After approval from the Institutional Ethics Committee, a retrospective observational study was performed by reviewing the prospectively maintained institutional BC database for all patients aged ≥18 years with MIBC (≥ American Joint Committee on Cancer Clinical Stage T2) who underwent RC between May 2013 and July 2023.

Patients who underwent RC for nonurothelial histology, salvage cystectomy after bladder preservation, palliative intent, and intraoperative procedure termination due to inoperability or other factors were excluded from the analysis.

Data analysed included patient and tumor characteristics, whether NACT was received or not, operative data including approach (robot-assisted, laparoscopic, or open) and urinary diversion performed (neobladder, ileal conduit, or cutaneous ureterostomy), pathologic data, and postoperative outcomes.

Complications were classified as early, occurring ≤30 days of surgery, and late, occurring after 30 days and before 90 days postsurgery. Grading was per the modified Clavien–Dindo scoring system.[10] Grades 1 and 2 were categorized as minor and Grades 3, 4, and 5 as major complications.

Statistical analysis was performed using the IBM SPSS version 20.0 software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA: IBM Corp). The results are given as mean, median, and interquartile range (IQR), for all the continuous variables and in frequency (percentage) for categorical variables. The normality of the data was checked by Kolmogorov–Smirnov *Z*-test. The Pearson Chi-Square test was used to assess the association between NACT groups with other categorical factors. Mann–Whitney U test and independent sample *t*-test were used to assess the median and mean level of parameters between both groups. $P < 0.05$ was considered statistically significant. All tests of statistical significance were two-tailed. Logistic regression was used to determine the effect of NACT on the occurrence of early or late complications following RC.

All the authors confirm the availability of and access to all original data reported in this study.

RESULTS

A total of 154 patients underwent RC at our institute between May 2013 and July 2023. Of these 33 patients were excluded as RC was performed for non-MIBC (6), non-urothelial histology (17), and salvage cystectomy after chemoradiation for bladder preservation (10) [Figure 1].

Of 121 patients included for analysis, 104 (86.0%) were male with a median (IQR) age of 66 (59–72) years. The median (IQR) Charlson Comorbidity Index (CCI) was 5 (4–6). The American Society of Anaesthesiology (ASA) category was ≥2 in 113 (93.4%) and ≥3 in 30 (24.8%) patients. Of all patients, 101 (83.5%) had at least 1 comorbidity, with type-2 diabetes mellitus in 71 (58.7%), hypertension in 68 (56.2%), and ischemic heart disease in 21 patients (17.4%) [Table 1].

Sixty-one (50.4%) patients received NACT, of which 47 (77.0%) received gemcitabine with cisplatin, 8 (13.1%) received gemcitabine and carboplatin, and 6 (9.8%) received methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy. Forty-six

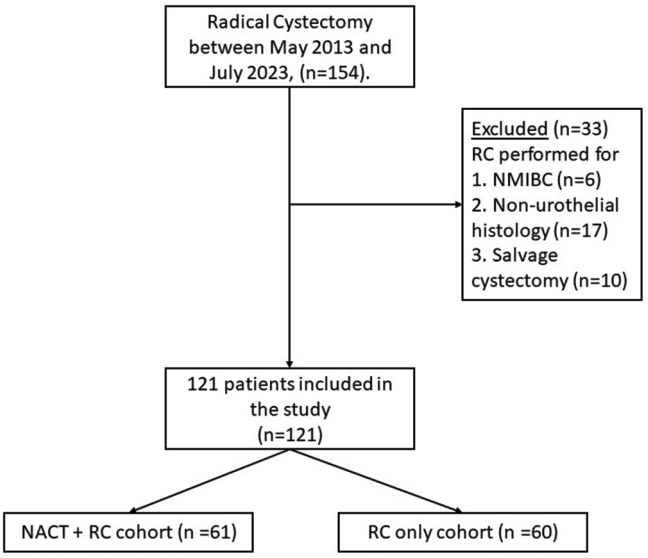

Figure 1: STROBE flowchart. Flowchart of patient inclusion, exclusion and study design

patients (75.4%) completed the prescribed NACT, while 15 (24.6%) did not. Among those who did not complete NACT, the reasons included disease progression in 6 patients (40.0%), intolerability in 4 (26.7%), complications from NACT in 1 (6.7%), and other causes in 4 (26.7%) [Supplementary Table 1]. However, despite NACT cessation, all patients did undergo RC.

In comparison to patients that received NACT + RC, the RC-only patients were older (mean age = 66.0 vs. 62.1 years,

Table 1: Patient, operative and tumor characteristics

Variable	Total (*n*=121), *n* (%)	NACT + RC (*n*=61), *n* (%)	RC only (*n*=60), *n* (%)	*P*
Gender				
Male	104 (86.0)	55 (90.2)	49 (81.7)	0.18
Female	17 (14.0)	6 (9.8)	11 (18.3)	
Age, years; median (mean, IQR)	66.0 (64.0, 59.0–72.0)	63.5 (62.1, 58.0–70.3)	69.0 (66.0, 60.5–74.0)	0.04
Comorbid conditions				
DM	71 (58.7)	36 (59.0)	35 (58.3)	0.94
HTN	68 (56.2)	32 (52.5)	36 (60.0)	0.40
CAD	21 (17.4)	14 (23.0)	7 (11.7)	0.10
DLP	25 (20.7)	13 (21.3)	12 (20.0)	0.86
CKD	12 (9.9)	2 (3.3)	10 (16.7)	0.01
COPD	5 (4.1)	2 (3.3)	3 (5.0)	0.63
CCI, median (mean, IQR)	5 (4.9, 4–6)	5 (5.0, 4–6)	5 (4.8, 4–6)	0.51
ASA category				
1	8 (6.6)	4 (6.6)	4 (6.7)	
2	83 (68.6)	43 (70.5)	40 (66.7)	
3	29 (24.0)	14 (23.0)	15 (25.0)	
4	1 (0.8)	0	1 (1.7)	
Median (mean, IQR)	2 (2.19, 2–2)	2 (2.16, 2–2)	2 (2.22, 2–3)	0.64
Preoperative investigations; median (mean, IQR)				
Hb (g dL^{-1})	11.4 (11.6, 9.8–13.3)	11.0 (11.3, 9.8–12.9)	12.1 (11.9, 9.8–14.0)	0.19
Albumin (g dL^{-1})	3.9 (3.9, 3.5–4.3)	4.0 (3.9, 3.5–4.3)	3.8 (3.8, 3.4–4.3)	0.25
Serum creatinine (mg dL^{-1})	1.1 (1.2, 0.9–1.3)	1.1 (1.1, 0.9–1.3)	1.1 (1.3, 1.0–1.3)	0.08
eGFR (mL/min/1.73 m^2)	66.3 (66.3, 53.2–79.5)	67.7 (70.1, 55.7–82.5)	63.2 (62.4, 48.8–76.3)	0.04
Chemotherapy received				
Gemcitabine + cisplatin	47 (38.8)	47 (77.0)	NA	
Gemcitabine + carboplatin	8 (6.6)	8 (13.1)	NA	
MVAC	6 (5.0)	6 (9.8)	NA	
NACT completion status				
Completed	46 (38.0)	46 (75.4)	NA	
Did not complete	15 (12.4)	15 (24.6)	NA	
Surgical approach				
Open	76 (62.8)	41 (67.2)	35 (58.3)	0.19
Laparoscopic	9 (7.4)	2 (3.3)	7 (11.7)	
Robot-assisted	36 (29.8)	18 (29.5)	18 (30.0)	
Urinary diversion				
IC	75 (62.0)	42 (68.9)	33 (55.0)	0.12
ONB	24 (19.8)	6 (9.8)	15 (25.0)	
CU	21 (17.4)	12 (19.7)	12 (20.0)	
Continent pouch	1 (0.8)	1 (1.6)	0	
DOS, min; median (mean, IQR)	540 (521, 440–610)	460 (410, 430–600)	625 (627, 585–667)	0.95
Blood loss, mL; median (mean, IQR)	600 (545.2, 300–800)	600 (569.0, 300–800)	500 (521.4, 300–700)	0.57
Length of hospital stay, days; median (mean, IQR)	11 (14.0, 9–18)	11 (13.6, 8–18)	11 (14.3, 9–17)	0.69
Pathologic stage				
pTis/Ta	8 (6.6)	3 (4.9)	5 (8.3)	0.03
pT0	37 (30.6)	26 (42.6)	11 (18.3)	
pT1	5 (4.1)	4 (6.6)	1 (1.7)	
pT2	31 (25.6)	11 (18.0)	20 (33.3)	
pT3	25 (20.7)	9 (14.8)	16 (26.7)	
pT4	15 (12.4)	8 (13.1)	7 (11.7)	
pN0	97 (80.2)	51 (83.6)	46 (76.7)	0.82
pN1	14 (11.6)	6 (9.8)	8 (13.3)	
pN2	5 (4.1)	2 (3.3)	3 (5.0)	
pNx	5 (4.1)	2 (3.3)	3 (5.0)	
PSM	12 (9.9)	6 (9.8)	6 (10.0)	0.97

NACT=Neoadjuvant chemotherapy, RC=Radical cystectomy, IQR=Interquartile range, DM=Diabetes mellitus, HTN=Hypertension, CAD=Coronary artery disease, DLP=Dyslipidaemia, CKD=Chronic kidney disease, COPD=Chronic obstructive pulmonary disease, CCI=Charlson comorbidity index, ASA=American Society of Anaesthesiology, eGFR=Estimated glomerular filtration rate, MVAC=Methotrexate, vinblastine, doxorubicin, and cisplatin, IC=Ileal conduit, ONB=Orthotopic neobladder, CU=Cutaneous ureterostomy, DOS=Duration of surgery, PSM=Positive surgical margin, NA=Not available, Hb=Hemoglobin

$P = 0.04$), and had a significantly lower GFR (mean = 62.4 vs. 70.1 ml/min/1.73 m^2, $P = 0.04$). Both groups were comparable with respect to CCI and ASA scores.

We recorded 220 complications with 97 (80.2%) patients developing at least one complication. Sixty-six patients (54.6%) had major complications. Comparing complication rates among the NACT + RC group to the RC-only group, there was no significant difference in overall complication rates, 85.3% versus 75%, $P = 0.16$, or major complication rates 50.8% versus 58.3%, $P = 0.41$ respectively [Table 2].

One hundred nine (49.5%) complication events occurred ≤30 days of surgery (early), and 111 (50.5%) occurred between 30 and 90 days (late). Among early complications, infection-related complications were most common (8.6%), followed by urinary diversion-related complications (7.7%) and gastrointestinal complications (5.5%). In the early postoperative period, six patients required re-exploration. The reasons included intestinal obstruction due to inter-bowel adhesions in two, hypotensive shock resulting from bleeding in the dorsal venous plexus in one, and urine leakage from the ureteroileal anastomosis site in three patients. Wound-related complications (24.5%) accounted for most of the late complications, followed by infection-related complications (6.8%). However, there was no significant difference in the severity or type of complications between the NACT + RC group and the RC-only group.

On univariate analysis, urinary diversion by orthotopic neobladder (OR 4.35, 95% CI 1.36–13.91, $P = 0.01$) or cutaneous ureterostomy (OR 3.53, 95% CI 1.08–11.47, $P = 0.04$) was predictive of "any complication," and CCI >5

Table 2: Postoperative complications following radical cystectomy*

Variable	Total (*n*=121)		NACT + RC (*n*=61)		RC only (*n*=60)		*P*	
Any complication	97 (80.2)		52 (85.3)		45 (75.0)		0.16	
Major complication	66 (54.6)		31 (50.8)		35 (58.3)		0.41	
Early	16 (13.2)		8 (13.1)		8 (13.3)		0.97	
Late	57 (47.1)		28 (45.9)		29 (48.3)		0.79	
Minor complication	86 (71.1)		46 (75.4)		40 (66.7)		0.29	
Early	67 (55.4)		35 (57.4)		32 (53.3)		0.66	
Late	45 (37.2)		24 (39.3)		21 (35.0)		0.57	
Deaths								
Early	5 (4.1)		2 (3.3)		3 (5.0)		0.63	
Late	7 (5.8)		3 (4.9)		4 (6.7)		0.68	
Complication event	**Total (*n*=220)**		**NACT + RC (*n*=108)**		**RC only (*n*=112)**		***P***	
	Early	**Late**	**Early**	**Late**	**Early**	**Late**	**Early**	**Late**
Infectious	19 (8.6)	15 (6.8)	7 (6.5)	6 (5.6)	12 (10.7)	9 (8.1)	0.26	0.47
Major: Urosepsis	2 (0.9)	4 (1.8)	1 (0.9)	1 (0.9)	1 (0.9)	3 (2.7)		
Minor: UTI	17 (7.7)	11 (5.0)	6 (5.6)	5 (4.6)	11 (9.8)	6 (5.4)		
GI	12 (5.5)	7 (3.2)	7 (6.5)	4 (3.7)	5 (4.5)	3 (2.7)	0.51	0.66
Major: IO requiring surgery	1 (0.5)	2 (0.9)	0	0	1 (0.9)	2 (1.8)		
Minor: Paralytic ileus	11 (5.0)	5 (2.3)	7 (6.5)	4 (3.7)	4 (3.6)	1 (0.9)		
UD related	17 (7.7)	11 (5.0)	11 (10.2)	5 (4.6)	6 (5.4)	6 (5.4)	0.18	0.88
Major: Urine leak requiring re-exploration/PCN/ureteric stricture requiring stenting	6 (2.7)	8 (3.6)	4 (3.7)	4 (3.7)	2 (1.8)	4 (3.6)		
Minor: Peristomal dermatitis	11 (5.0)	3 (1.4)	7 (6.5)	1 (0.9)	4 (3.6)	2 (1.8)		
Wound related	6 (2.7)	54 (24.5)	3 (2.8)	27 (25.0)	3 (2.7)	27 (24.1)	0.96	0.88
Major: Wound dehiscence, SSI deep/organ space, incisional hernia	3 (1.4)	32 (14.6)	1 (0.9)	15 (13.9)	2 (1.8)	17 (15.2)		
Minor: SSI superficial	3 (1.4)	22 (10.0)	2 (1.8)	12 (11.1)	1 (0.9)	10 (8.9)		
Cardio- and cerebrovascular	11 (5)	8 (3.6)	6 (5.6)	2 (1.9)	5 (4.5)	2 (1.8)	0.73	0.98
Major: MI/CVA/PE	7 (3.2)	6 (2.7)	3 (2.7)	2 (1.8)	4 (3.6)	0		
Minor: DVT	4 (1.8)	2 (0.9)	3 (2.7)	0	1 (0.9)	2 (1.8)		
Hematologic (BT requirement)	34 (15.5)	3 (1.4)	15 (13.8)	1 (0.9)	19 (16.9)	2 (1.8)	0.53	0.58
Others	10 (4.5)	13 (5.9)	5 (4.6)	9 (8.3)	5 (4.5)	8 (7.2)	0.98	0.76
Major: Renal dysfunction requiring HD, Vaginal vault prolapse	0	4 (1.8)	0	4 (3.7)	0	4 (3.6)		
Minor: Delerium, dyselectrolytemia	10 (4.5)	9 (4.1)	5 (4.6)	5 (4.6)	5 (4.5)	4 (3.6)		
Total events	109 (49.5)	111 (50.5)	54 (50)	54 (50)	55 (49.1)	57 (50.9)	0.90	0.90
Death	5 (2.3)	7 (3.2)	2 (1.9)	3 (2.8)	3 (2.6)	4 (3.6)	0.63	0.68
MI	2 (0.9)	1 (0.5)	2 (1.9)	1 (0.9)	0	0		
Metastatic disease, cachexia	0	2 (0.9)	0	0	0	2 (1.8)		
CVA	2 (0.9)	1 (0.5)	0	1 (0.9)	2 (1.8)	0		
Aneurysm rupture	0	2 (0.9)	0	0	0	2 (1.8)		
Urosepsis	1 (0.5)	1 (0.5)	0	1 (0.9)	1 (0.9)	0		

*All values in *n* (%). GI=Gastro-intestinal, UD related=Urinary diversion related, UTI=Urinary tract infection, ICU=Intensive care unit, DVT=Deep venous thrombosis, HD=Hemodialysis, MI=Myocardial infarction, CVA=Cerebrovascular accidents, BT=Blood transfusion NACT=Neoadjuvant chemotherapy, RC=Radical cystectomy, IO=Intestinal obstruction, PCN=Percutaneous nephrostomy, SSI=Surgical site infection

Table 3: Univariate analysis of factors predicting complications after radical cystectomy

Variable	Any complication			Major complications		
	OR	95% CI	*P*	OR	95% CI	*P*
Age >65 years	1.45	0.68–3.09	0.33	1.86	0.85–4.06	0.12
DM (yes)	0.60	0.27–1.30	0.19	1.40	0.64–3.07	0.40
CCI >5	1.04	0.48–2.28	0.91	2.17	0.99–4.75	0.05
ASA category >2	0.51	0.22–1.18	0.11	1.36	0.55–3.10	0.55
Hb ≤11.5 g dL^{-1}	0.89	0.37–2.12	0.79	1.11	0.52–2.39	0.78
Albumin <4 g dL^{-1}	0.66	0.29–1.52	0.33	1.26	0.53–2.98	0.60
Creatinine >1.5 mg dL^{-1}	1.29	0.46–3.65	0.63	0.66	0.22–1.96	0.45
NACT (yes)	1.37	0.65–2.91	0.41	0.9	0.42–1.94	0.79
DOS >540 min	1.95	0.50–7.60	0.38	1.86	0.57–6.03	0.29
Urinary diversion						
IC (reference)	1	-	-	1	-	-
ONB	4.35	1.36–13.91	0.01	0.63	0.22–1.77	0.38
CU	3.53	1.08–11.47	0.04	1.23	0.45–3.36	0.69

OR=Odds ratio, CI=Confidence interval, DM=Diabetes mellitus, CCI=Charlson comorbidity index, ASA=American Society of Anaesthesiology, NACT=Neoadjuvant chemotherapy, DOS=Duration of surgery, IC=Ileal conduit, ONB=Orthotopic neobladder, CU=Cutaneous ureterostomy, Hb=Hemoglobin

was found to be predictive of "major complications" (OR 2.17, 95% CI 0.99–4.75, $P = 0.05$) [Table 3]. NACT was not associated with an increased risk of complications.

DISCUSSION

Our study evaluated postoperative complications after RC at a tertiary care center and assessed the impact of NACT. We recorded complications in 80.2% of patients, with 54.6% having Clavien–Dindo Grade ≥3 complications. There was no significant difference in complication rates, type, or severity among patients who had NACT + RC compared to patients who had RC alone. In addition, our analysis did not show NACT to be a predictive factor of postoperative complications.

Disease recurrence after RC is more commonly due to metastasis rather than local recurrence.[11] This is attributed to micrometastasis already present at the time of cystectomy and forms the basis for the addition of systemic chemotherapy, which has been shown to improve 5-year overall survival by 5%–9%.[12] The advantages of administering neoadjuvant systemic chemotherapy include better tolerability compared to the post-operative preiod, decrease in tumor burden, potentially increasing resectability, timely treatment of micrometastatic disease, and providing an *in vivo* assessment of tumor response to chemotherapy that can guide further systemic therapy and prognosticate the patient.

The Society of Urologic-Oncology/American Urologic Association guidelines, and the European Association of Urology guidelines advocate NACT.[3,13] Despite this, adoption of NACT remains low, with reported utilization rates of 15%–40% in contemporary Western series.[5,6,14]

An open RC series from All India Institute of Medical Sciences, New Delhi reported NACT usage in 8.7% (17/195) patients between July 2014 and August 2019.[8] In our series, 50% of patients with ≥ cT2 urothelial carcinoma were initiated on NACT. Cisplatin ineligibility has been reported in 30%–40% of RC patients.[7,15] Therefore, reasons other than cisplatin ineligibility must account for avoidance of NACT in a significant proportion of patients.

The primary concern with NACT is toxicity of chemotherapy. Patients with MIBC usually have comorbid conditions and are physiologically compromised at diagnosis. Chemotherapy draws on the limited physical reserves of the patient and may potentially convert a surgically fit to an unfit candidate, who then becomes ineligible for cystectomy. In our series, 25% had to stop NACT due to disease progression noted on interval imaging, or intolerance to chemotherapy, however, no patient became ineligible for surgery. In a study by Johnson *et al*., that evaluated the toxicity of NACT with MVAC, despite a hematologic or gastrointestinal complication rate of 30%, all patients recovered, and the possibility of undergoing cystectomy was not adversely impacted.[7]

Delay in cystectomy due to time spent on administering chemotherapy is yet another concern. Chemotherapy regimens take 2–3 months to complete, and this delay can compromise oncologic outcomes, especially in nonresponders. A delay of >12 weeks from diagnosis to cystectomy has been reported to adversely impact outcomes.[16] However, this is applicable to the prechemotherapy era. On the contrary, Audenet *et al*. reported no change in outcomes when surgery was performed within 8 months if NACT was administered, provided it was initiated within 8 weeks of diagnosis.[17]

Finally, concerns exist regarding increased complications and resulting perioperative morbidity and mortality in patients who receive NACT. Complications following cystectomy are common, with reported rates of 51%–68% in Western

series, with Clavien–Dindo Grade ≥3 complications in 13%–25%, and mortality after cystectomy in 4%–8%.[5-7,18-21] In two Indian series, complication rates were 49.3%–64.1%, with one study reporting major complications in 23.5% and mortality in 5.2%.[8,9]

Previous retrospective studies have reported no difference in postoperative complications or mortality among NACT + RC compared to RC-only patients.[5-7,20] In a population-based study from Finland, that included 1385 patients, Salminen *et al*. reported no significant increase in complication rates or mortality among RC patients after NACT, however, the NACT usage in the study was only 16%.[6] In a large multicenter retrospective study of 3113 RC patients, treated across 13 tertiary care centers from 2007 to 2019, with NACT usage in 31.1%, Arora *et al*. reported NACT usage did not lead to a higher complication rate.[5] However, these were North American and European high-volume centers, and their data are not necessarily extrapolatable to the Indian healthcare scenario. Our study included real-world data from a tertiary care center and is representative of MIBC patients in India.

The limitations of our study include its retrospective nature, although complications and outcome data are rigorously captured by our BC database, not all variables, such as socio-economic status, performance score, smoking history, criteria for cisplatin ineligibility, inflammatory markers, among others were available for all patients. Since this was a single institutional study, the number of cases was relatively small. Multicentric studies with larger populations are required to validate the results. Although other standardized systems for reporting complications after RC exist, such as the Martin criteria,[22] and the EAU guideline recommendation,[23] our database recorded complications based on the Clavien-Dindo scoring system, as it is relatively simple and easy to follow, and is applicable for recording complications following treatment of other Urologic cancers.

CONCLUSION

In our study of MIBC patients managed at a tertiary care institute in India, the administration of NACT did not increase complication rates after RC.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al.* Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-49.
2. Prakash G, Pal M, Odaiyappan K, Shinde R, Mishra J, Jalde D, *et al*. Bladder cancer demographics and outcome data from 2013 at a tertiary cancer hospital in India. Indian J Cancer 2019;56:54-8.
3. Witjes JA, Bruins HM, Cathomas R, Compérat EM, Cowan NC, Gakis G, *et al.* European association of urology guidelines on muscle-invasive and metastatic bladder cancer: Summary of the 2020 guidelines. Eur Urol 2021;79:82-104.
4. Razdan S, Sljivich M, Pfail J, Wiklund PK, Sfakianos JP, Waingankar N. Predicting morbidity and mortality after radical cystectomy using risk calculators: A comprehensive review of the literature. Urol Oncol 2021;39:109-20.
5. Arora A, Zugail AS, Pugliesi F, Cathelineau X, Macek P, Barbé Y, *et al.* Neoadjuvant chemotherapy does not increase peri-operative morbidity following radical cystectomy. World J Urol 2022;40:1697-705.
6. Salminen AP, Koskinen I, Perez IM, Hurme S, Murtola TJ, Vaarala MH, *et al.* Neoadjuvant chemotherapy does not increase the morbidity of radical cystectomy: A 10-year retrospective nationwide study. Eur Urol Oncol 2018;1:525-30.
7. Johnson DC, Nielsen ME, Matthews J, Woods ME, Wallen EM, Pruthi RS, *et al.* Neoadjuvant chemotherapy for bladder cancer does not increase risk of perioperative morbidity. BJU Int 2014;114:221-8.
8. Patidar N, Yadav P, Sureka SK, Mittal V, Kapoor R, Mandhani A. An audit of early complications of radical cystectomy using Clavien-Dindo classification. Indian J Urol 2016;32:282-7.
9. Nayak B, Garg H, Goel R, Singh P, Nayyar R, Kumar R, *et al.* Contemporary outcomes of open radical cystectomy: A 5-year experience from a tertiary care center. Indian J Surg Oncol 2021;12:86-93.
10. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, *et al.* The Clavien-Dindo classification of surgical complications: Five-year experience. Ann Surg 2009;250:187-96.
11. von Deimling M, Furrer M, Mertens LS, Mari A, van Ginkel N, Bacchiani M, *et al.* Impact of the extent of lymph node dissection on survival outcomes in clinically lymph node-positive bladder cancer. BJU Int 2024;133:341-50.
12. Advanced Bladder Cancer (ABC) Meta-Analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: Update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. Eur Urol 2005;48:202-5.
13. Chang SS, Bochner BH, Chou R, Dreicer R, Kamat AM, Lerner SP, *et al.* Treatment of non-metastatic muscle-invasive bladder cancer: AUA/ASCO/ASTRO/SUO guideline. J Urol 2017;198:552-9.
14. Gopalakrishnan D, Elsayed AS, Hussein AA, Jing Z, Li Q, Wagner AA, *et al.* Impact of neoadjuvant chemotherapy on survival and recurrence patterns after robot-assisted radical cystectomy for muscle-invasive bladder cancer: Results from the International Robotic Cystectomy Consortium. Int J Urol 2022;29:197-205.
15. Dash A, Galsky MD, Vickers AJ, Serio AM, Koppie TM, Dalbagni G, *et al.* Impact of renal impairment on eligibility for adjuvant cisplatin-based chemotherapy in patients with urothelial carcinoma of the bladder. Cancer 2006;107:506-13.
16. Gore JL, Lai J, Setodji CM, Litwin MS, Saigal CS, Urologic Diseases in America Project. Mortality increases when radical cystectomy is delayed more than 12 weeks: Results from a surveillance, epidemiology, and end results-Medicare analysis. Cancer 2009;115:988-96.
17. Audenet F, Sfakianos JP, Waingankar N, Ruel NH, Galsky MD, Yuh BE, *et al*. A delay≥8 weeks to neoadjuvant chemotherapy before radical cystectomy increases the risk of upstaging. Urol Oncol 2019;37:116-22.
18. Proietti F, Flammia RS, Licari LC, Bologna E, Bove AM, Brassetti A, *et al.* Impacts of neoadjuvant chemotherapy on perioperative outcomes in patients with bladder cancer treated with radical cystectomy: A single high-volume center experience. J Pers Med 2024;14:212.
19. Gandaglia G, Popa I, Abdollah F, Schiffmann J, Shariat SF, Briganti A, *et al.* The effect of neoadjuvant chemotherapy on perioperative outcomes in patients who have bladder cancer treated with radical cystectomy: A population-based study. Eur Urol 2014;66:561-8.
20. Hoeh B, Flammia RS, Hohenhorst L, Sorce G, Chierigo F, Panunzio A, *et al*. Effect of neoadjuvant chemotherapy on

complications, in-hospital mortality, length of stay and total hospital costs in bladder cancer patients undergoing radical cystectomy. Cancers (Basel) 2022;14:1222.
21. Cinar NB, Yilmaz H, Avci IE, Cakmak K, Teke K, Dillioglugil O. Reporting perioperative complications of radical cystectomy: The influence of using standard methodology based on ICARUS and EAU quality criteria. World J Surg Oncol 2023;21:58.
22. Martin RC 2nd, Brennan MF, Jaques DP. Quality of complication reporting in the surgical literature. Ann Surg 2002;235:803-13.
23. Mitropoulos D, Artibani W, Graefen M, Remzi M, Rouprêt M, Truss M, *et al*. Reporting and grading of complications after urologic surgical procedures: An ad hoc EAU guidelines panel assessment and recommendations. Eur Urol 2012;61:341-9.

How to cite this article: Nuthalapati M, Menon AR, Patil VD, Sukumaran SV, Yensani PR, Agrawal S, *et al*. Assessing neoadjuvant chemotherapy's impact on complications following radical cystectomy. Indian J Urol 2025;41:28-34.

Supplementary Table 1: Causes of premature neoadjuvant chemotherapy cessation

Cause of NACT cessation	*n*=15, *n* (%)
Disease progression	6 (40.0)
Intolerability	4 (26.7)
Complications from NACT	1 (6.7)
Other (COVID-19, DVT, CVA, defaulted)	4 (26.7)

NACT=Neoadjuvant chemotherapy, DVT=Deep vein thrombosis, CVA=Cerebral vascular accident