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Research article

Perioperative factors and 30-day major complications following radical cystectomy: A single-center study in Thailand

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ABSTRACT

Objective: This study aims to evaluate the prevalence of early postoperative complications of radical cystectomy, using standardized reporting methodology to assess perioperative characteristics and determine risk factors for major complications.

Materials and methods: A retrospective study included 254 consecutive bladder cancer patients undergoing RC between 2012 and 2020 at a urological cancer referral center. Postoperative complications within 30 days were recorded and graded according to the Clavien–Dindo classification (CDC). The study examined risk factors, including novel inflammatory-nutrition biomarkers and perioperative serum chloride.

Results: Total complications were observed in 135 (53 %). Of these, 47 (18.5 %) were high grade (CDC $\geq$ 3). Wound dehiscence was the most common complication, occurring in 14 (5.5 %) patients. Independent risk factors for major complications included an age-adjusted Charlson comorbidity index (ACCI) > 4 and thrombocytopenia (odds ratio [OR] 3.67 and OR 8.69). Preoperative platelet counts < 220,000/μL and albumin < 3 mg/dL were independent risk factors for wound dehiscence (OR 3.91 and OR 4.72). Additionally, postoperative hypochloremia was a risk factor for major complications (OR 13.71), while novel serum biomarkers such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic inflammatory response index (SIRI), and prognostic nutritional index (PNI) were not associated with early major complications.

Conclusion: Patients who have multiple comorbidities are at a greater risk of developing major complications after undergoing RC. Our result suggests that preoperative platelet counts and serum albumin levels are associated with wound dehiscence.

1. Introduction

Bladder cancer (BC) is a globally prevalent malignancy, ranking 10th in incidence and 13th in fatality [1]. Incidence rates vary by region, with Thailand reporting an estimated incidence of 4.5 cases per 100,000 individuals and a mortality incidence of 2.2 cases per 100,000, alongside 5-year prevalence of 5.7 % [2]. Projections indicate a significant increase in BC cases by 2030, with anticipate rises in Japan (30 %), France (19 %), and Thailand (22 %) [3]. While most patients initially present with non-muscle invasive bladder

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cancer (NMIBC), approximately 30 % eventually progress to muscle invasive bladder cancer (MIBC).

Radical cystectomy (RC) stands as the standard treatment of various bladder cancer scenarios, including MIBC, bacillus Calmette-Guérin refractory cases, and high-risk NMIBC. This procedure, coupled with urinary diversion, is complex, involving both gastrointestinal and urinary systems, and it is associated with a spectrum of potential complications [4,5]. Given the advanced age and comorbidity burden of BC patients, clinicians must carefully balance treatment benefits against surgical risks and competing mortality factors. Notably, RC carries a perioperative mortality rate from 2 % to 13 % [6].

This study seeks to delineate the pre- and perioperative risk factors linked to early major complications within 30 days post-RC and to ascertain the prevalence of associated early postoperative complications.

2. Materials and Methods

2.1. Population

A retrospective study was conducted at Siriraj hospital, a referral center and academic institution in Thailand, focusing on 254 consecutive patients diagnosed with BC who underwent RC between 2012 and 2020. All patients underwent standard RC, or anterior pelvic exenteration, along with pelvic node dissection. The type of urinary diversion was determined through mutual decision making between the patient and surgeon after thorough discussion. Patients eligible for neoadjuvant chemotherapy (neoadj CMT) were evaluated by a medical oncologist and included in the analysis.

The surgeries were performed by consultant urologists or residents under close supervision, using either an open or minimally invasive approach, including laparoscopic and robotic-assisted techniques. For ileal conduit diversion, a 10–15 cm segment of ileum was isolated and anastomosed to the ureters using either Bricker's end-to-side technique or Wallace's end-to-end technique. The left ureter was tunneled under the sigmoid colon for anastomosis in the right lower abdomen. Neobladder reconstruction techniques varied in our institute according to the surgeon's preference and included the W, Studer and Florin pouch. Typically, around 45–60 cm of distal ileum was used for reconstruction. Ureteral stents were placed bilaterally before completing the enteroureterostomy or cutaneous ureterostomy and were intentionally left in place for at least two weeks.

Mechanical bowel preparation was conducted the day before surgery, and prophylactic antibiotics were administered intravenously perioperatively at the discretion of the attending physician. Sequential compression devices were applied to both legs until satisfactory mobilization was achieved. Routine prophylaxis with low-molecular-weight heparin prophylaxis was not administered unless there was a pre-existing condition predisposing to thromboembolic events. Admission to the intensive care unit (ICU) was based on interoperative findings. The Enhanced Recovery After Surgery (ERAS) protocol was not routinely implemented during the study period. Patients typically fasted for three days, with introduction of food gradually initiated upon the detection of bowel sounds. Metoclopramide was administered to enhance bowel motility as deemed necessary, while μ-opioid receptor antagonists were not available at our institution. All patients were followed up for at least 30 days or until death within the 30-day.

2.2. Data acquisition

All available data pertaining to patient demographics, intraoperative details, and postoperative complications and treatments were recorded. Comorbidities were assessed using the age-adjusted Charlson comorbidity index (ACCI) and adjusted ACCI (AACCI) [7,8]. Complications were categorized according to the Clavien-Dindo classification (CDC), with major complication defined as CDC grade III, IV, and V (CDC3-5). Serum chloride levels were documented both preoperatively and immediately postoperatively to reflect intraoperative chloride load. Pathological staging was reassigned based on the 2010 American Joint Committee on Cancer TNM staging system. Additionally, the following reported inflammatory-nutrition biomarkers were calculated based on the preoperative blood tests:

1 Neutrophil-to-lymphocyte ratio (NLR) [9–11].
2 Platelet-to-lymphocyte ratio (PLR) [9,10,12,13].
3. Systemic inflammation response index (SIRI) [13], and
4. Prognostic nutritional index (PNI) [13–15].

2.3. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA) with statistical significance set at a two-sided p-value of < 0.05. Descriptive analysis utilized the independent *t*-test for continuous variables and the $\chi 2$ test for categorical variables. A univariate logistic analysis was conducted for all clinical variables to determine eligibility for multivariate logistic regression. Variables with clinical significance and a univariate p-value < 0.05 were entered simultaneously into the multivariate analysis. Individual variables that lost statistical significance were subsequently removed, and model comparisons were conducted.

The following variables were categorized as dichotomous based on previously published data: ACCI, AACCI, NLR, PLR, SIRI, and PNI (> 4, > 4, ≥ 4.1, ≥ 164.7, ≥ 2.35, and ≤ 45 respectively) [7–9,13]. Cutoff values for anemia, thrombocytopenia, hypochloremia, hyperchloremia, chronic kidney disease (CKD), and hypoalbuminemia were defined as follows: hemoglobin (Hb) < 12 g/dL, Platelet count (Plt) $< 150{,}000/\mu$L, chloride (Cl) < 98 mmol/L, Cl > 107 mmol/L, GFR < 60 mL/min/1.73 m^2, and albumin (Alb) < 3.0 g/dL

[16,17].

3. Result

Preoperative demographic factors, pre- and perioperative laboratories, and medical conditions of the 254 patients, of whom major complications (CDC3-5) occurred in 47 patients (18.5 %) within 30 days of surgery, are presented in Table 1. Among these complications, 78.7 % were observed in male patients. ACCI > 4 was more prevalent among CDC3-5 complications (80.9 % versus 50.7 %), as were higher American Society of Anesthesiologists (ASA) classification; specifically, ASA 3 (40.4 % versus 27.1 %), and body mass index (BMI) (24.8 ± 4.8 vs 23.3 ± 4.3). A majority of patients (65.4 %) were de novo cases, and 20.1 % underwent neoadj CMT prior to surgery. Patients experiencing CDC3-5 complications tended to have CKD staged ≥3 (61.7 % vs 56 %), hypoalbuminemia (19.1 % vs 8.9 %), thrombocytopenia (14.9 % vs 1.9 %), and postoperative hypochloremia (6.4 % vs 0.5 %). Novel serum biomarkers did not show significant differences between the groups.

Minimally invasive approaches were conducted in 11.8 % of patients. The majority of patients underwent ileal conduit as a urinary diversion (82.3 %). There was no significant difference in surgical approach, diversion types, estimated blood loss (EBL), and operative time between the CDC0-2 and CDC3-5 groups. However, notable disparities were noted in the length of stay (LOS), significantly in the

Table 1
Summary of demographic factors, preoperative laboratories and medical conditions.

		Total N (% of 254)	CDC 0-2 N (% of 207)	CDC 3-5 N (% of 47)	P value
Demographic factors					
Gender	male	201 (79.1)	164 (79.2)	37 (78.7)	0.939
Age (years) [i]		67.6 ± 10.2	66.9 ± 0.3	70.7 ± 9.5	0.019
ACCI	ACCI > 4	143 (50.7)	105 (50.7)	38 (80.9)	< 0.001
AACCI	AACCI > 4	70 (27.6)	50 (24.2)	20 (42.6)	0.011
BMI (kg/m^2) [i]		23.6 ± 4.4	23.3 ± 4.3	24.8 ± 4.8	0.048
ASA	ASA 1	40 (15.7)	38 (18.4)	2 (4.3)	0.028
	ASA 2	139 (54.7)	113 (54.6)	26 (55.3)	
	ASA 3	75 (29.5)	56 (27.1)	19 (40.4)	
Diabetes mellitus		57 (22.4)	44 (21.3)	13 (27.7)	0.342
Disease	de novo	166 (65.4)	136 (65.7)	30 (63.8)	0.808
	progression	88 (34.6)	71 (34.3)	17 (36.2)	
Neoadjuvant CMT		51 (20.1)	41 (19.8)	10 (21.3)	0.820
Pre-op hydronephrosis		124 (48.8)	102 (49.3)	22 (46.8)	0.760
	no diversion	80 (31.4)			
	stent	5 (2.0)			
	nephrostomy	39 (15.3)			
Laboratory results					
Anemia [a]		156 (61.4)	128 (61.8)	28 (59.6)	0.774
CKD stage ≥3 [b]		145 (57.1)	116 (56.0)	29 (61.7)	0.479
Albumin (g/dL) [i]		3.8 ± 0.6	3.9 ± 0.6	3.7 ± 0.8	0.067
Hypoalbuminemia [c]		27 (10.8)	18 (8.9) [h]	9 (19.1)	0.042
NLR [j]		2.7 (1.9, 4.0)	2.7 (1.9, 3.9)	2.8 (2.0, 4.9)	0.262
PLR [j]		153.2 (116.3, 212.4)	153.2 (117.2, 210.9)	156.7 (103.1, 248.7)	0.992
SIRI [j]		1.3 (0.8, 2.5)	1.3 (0.8, 2.5)	1.3 (0.9, 2.7)	0.289
PNI [j]		40.0 (35.0, 42.0)	40.0 (35.0, 42.0)	39.0 (33.0, 42.0)	0.160
Thrombocytopenia [d]		11 (4.3)	4 (1.9)	7 (14.9)	< 0.001
Coagulopathy [e]		55 (21.7)	38 (18.4)	17 (36.2)	0.363
Pre-op serum chloride (mmol/L) [i]		101.2 ± 3.8	101.1 ± 3.9	101.5 ± 4.2	0.550
Pre-op hypoCl [f]		45 (17.7)	37 (17.9)	8 (17.0)	0.890
Post-op hypoCl [f]		4 (1.6)	1 (0.5)	3 (6.4)	0.022
Post-op hyperCl [g]		27 (10.8)	25 (12.4)	2 (4.3)	0.107

ACCI, age-adjusted Charlson comorbidity index; AACCI, adjusted age-adjusted Charlson comorbidity index; BMI, body mass index; ASA, American Society of Anesthesiologists; CMT, chemotherapy; CKD, chronic kidney disease; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SIRI, systemic inflammation response index; PNI, prognostic nutritional index; Pre-op, pre-operative; Post-op, post-operative; HypoCl, hypochloremia; HyperCl, hyperchloremia.

[a] Anemia indicates Hb < 12 g/dl
[b] CKD stage ≥3 is GFR < 60 mL/min/1.73 m^2
[c] Hypoalbuminemia is serum albumin < 3.0 g/dL.
[d] Thrombocytopenia is platelet count < 150,000/μL.
[e] Coagulopathies are PT > 11.7 s or APTT > 29 s.
[f] Hypochloremia is indicating Cl < 98 mmol/L.
[g] Hyperchloremia is indicates Cl > 107 mmol/L.
[h] Missing data.
[i] Data present as mean ± SD.
[j] Data present as median (interquartile range).

CDC3-5 group (23 days; [interquartile range (IQR) 15, 38] vs 16 days; [IQR12, 19]; p-value < 0.001). Similarly, the length of ICU stay was higher in CDC3-5 group (1 day; [IQR 0, 3] vs 0 day; [IQR 0, 1]). Positive surgical margins were identified in 56 cases (22.0 %) following RC. Pure urothelial carcinoma was the most prevalent histology reported in 139 patients (54.7 %). Additionally, the authors found incidental prostate cancer in 44 cases (17.3 %), of which 40.9 % were classified as clinically significant (Gleason scores > 6). Table 2 contains a comprehensive summary of operative characteristics, pathology and histology.

To identify factors associated with early major complications, the exploratory univariate analysis identified six factors eligible for inclusion in the multivariate model: hypoalbuminemia (odds ratio [OR] 2.24, 95 % confidence interval [CI] 1.01–5.80), NLR >4.1 (OR 1.91, 95 % CI 0.96–3.81), thrombocytopenia (OR 8.88, 95 % CI 2.48–31.76), postoperative hypochloremia (OR 13.71, 95 % CI 1.39–134.87), ACCI >4 (OR 4.10, 95 % CI 1.89–8.91), and type of diversion; neobladder (OR 2.40, 95 % CI 1.04–5.56). The analysis demonstrated thrombocytopenia and ACCI >4 as significant risks of 30-day CDC3-5 (adjusted OR 8.69, 95 % CI 2.17–34.90 and adjusted OR 3.67, 95 % CI 1.60–8.42, respectively). Table 3 provides the final model factors with their adjusted ORs and 95 % CIs.

The overall occurrence of postoperative complications, classified according to the CDC, is summarized in Table 4. The most frequently encountered early complication was anemia requiring transfusion (CDC 2), with 54 events (27.8 %). Additionally, the most common early major complication was wound dehiscence (CDC 3), with 14 events (7.2 %). Unfortunately, seven patients (2.8 %) experienced mortality (CDC 5), with causes including gastrointestinal bleed (1), sepsis (4), ischemic stroke (1), and gut obstruction (1).

For wound dehiscence, the most prevalent major complication observed, receiver operating characteristic (ROC) curve analyses were conducted to assess the true-positive (sensitivity) and false-positive rates (1- specificity) of Plt in relation to the binary outcome of early major complications. The areas under the curve (AUC) were calculated, and the cutoff value with the highest sensitivity and specificity was determined to be 220,000/μL (refer to Fig. 1). The exploratory univariate analysis identified four factors eligible for inclusion into the multivariate model: ACCI >4 (OR 4.99, 95 % CI 1.09–22.79), hypoalbuminemia (OR 3.69, 95 % CI 1.07–12.70), Plt

Table 2
Summary of operative characteristics and pathological findings.

		CDC 0-2 N (% of 207)	CDC 3–5 N (% of 47)	P value
Operative characteristics				
Surgical approach	open	179 (86.5)	43 (91.5)	0.585
	laparoscopic	17 (8.2)	2 (4.3)	
	robotic	11 (5.3)	2 (4.3)	
Type of diversion	ileal conduit	173 (83.6)	36 (76.6)	0.061
	neobladder	18 (8.7)	9 (19.1)	
	ureterostomy	16 (7.7)	2 (4.3)	
Operative time (minutes) [a]		361.0 ± 130.0	349.0 ± 151.0	0.583
EBL[b]		900 (550, 1500)	1200 (700, 2000)	0.143
ICU stay [b]		0 (0, 1)	1 (0, 3)	< 0.001
LOS [b]		16 (12, 19)	23 (15, 38)	< 0.001
Pathology				
Presence of LVI		96 (46.4)	26 (55.3)	0.263
Positive surgical margin		46 (22.2)	10 (21.3)	0.880
Number of obtained lymph node [a]		15.0 ± 9.0	13.1 ± 9.1	0.208
Histology				
Pure UC		111 (53.6)	28 (59.6)	0.651
UC with CIS		34 (16.4)	6 (12.8)	
UC with variant [c]		51 (24.6)	10 (21.3)	
	micropapillary (7) glandular (12) squamous differentiation (40) sarcomatoid (13) nested (9) plasmacytoid (9)			
Non-UC		10 (4.8)	3 (6.4)	
	SCC	1 (0.5)	2 (4.3)	
	adenocarcinoma	5 (2.4)	1 (2.1)	
	neuroendocrine	2 (1)	0	
	clear cell	1 (0.5)	0	
	leiomyosarcoma	1 (0.5)	0	
Stage	1	17 (8.2)	3 (6.4)	0.574
2	59 (28.5)	12 (25.5)		
3	123 (59.4)	28 (59.6)		
4	8 (3.9)	4 (8.5)		
Prostate cancer	non-CS	21 (10.2)	5 (10.9)	0.084
	CS	14 (6.8)	4 (8.5)	

EBL, estimated blood loss (mL); ICU stay, Intensive care unit stay (days); LOS, length of stay (days); LVI, lymphovascular invasion; UC, urothelial carcinoma; CIS, carcinoma in situ; SCC, squamous cell carcinoma; CS, clinically significant.

[a] Data present as mean ± SD.

[b] Data present as median (interquartile range).

[c] More than 1 variant may present in single patient.

Table 3
Preoperative clinical parameters associated with major complications (CDC3-5) following radical cystectomy.

Variable	OR	Univariate 95 % CI	P value	Adjusted OR	Multivariate 95 % CI	P value
BMI ≥25 kg/m^2	1.65	0.87–3.14	0.125			
Hypoalbuminemia [a]	2.24	1.01–5.80	0.042	1.46	0.54–3.93	0.460
Anemia [b]	0.91	0.48–1.74	0.774			
NLR ≥4.1	1.91	0.96–3.81	0.062	1.68	0.75–3.77	0.205
PLR ≥164.7	1.23	0.65–2.33	0.523			
SIRI ≥2.35	1.01	0.50–2.04	0.986			
PNI ≤45	2.36	0.69–8.12	0.162			
Thrombocytopenia [c]	8.88	2.48–31.76	0.001	8.69	2.17–34.90	0.002
Post-op hypoCl [d]	13.71	1.39–134.87	0.022	5.51	0.49–62.05	0.167
Post-op hyperCl [e]	0.32	0.07–1.38	0.107			
ACCI >4	4.10	1.89–8.91	< 0.001	3.67	1.60–8.43	0.002
AACCI >4	2.33	1.20–4.50	0.011			
CKD stage ≥3 [f]	1.26	0.66–2.42	0.479			
Gender (female)	1.03	0.48–2.24	0.939			
Progression (vs de novo*)*	1.09	0.56–2.10	0.808			
Coagulopathy [g]	2.24	0.57–8.76	0.363			
Neoadjuvant CMT	1.09	0.50–2.38	0.820			
Type of diversion			0.062			0.681
Ileal conduit	ref			ref		
Ureterostomy	0.34	0.04–2.69	0.309	0.69	0.08–5.85	0.732
Neobladder	2.40	1.04–5.56	0.041	1.46	0.57–3.73	0.431

CDC, Clavien-Dindo classification; OR, odds ratio; BMI, body mass index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SIRI, systemic inflammation response index; PNI, prognostic nutritional index; Post-op, post-operative; HypoCl, hypochloremia; HyperCl hyperchloremia; ACCI, age-adjusted Charlson comorbidity index; AACCI, adjusted age-adjusted Charlson comorbidity index; CKD, chronic kidney disease; CMT, chemotherapy.

[a] Hypoalbuminemia is serum albumin < 3.0 g/dl.
[b] Anemia indicates Hb < 12 g/dl
[c] Thrombocytopenia is platelet count < 150,000/μL.
[d] Hypochloremia is indicating Cl < 98 mmol/L.
[e] Hyperchloremia is indicating Cl > 107 mmol/L.
[f] CKD stage ≥3 is GFR < 60 mL/min/1.73 m^2
[g] Coagulopathy are PT > 11.7 s or APTT > 29 s.

Table 4
Overall events of postoperative complications according to Clavien-Dindo classification system.

GRADE	N (total 194)	Complications (N, % of total events)
I	13	Ileus (10, 5.2 %), nausea and vomiting (2, 1.0 %), diarrhea (1, 0.5 %)
II	114	Anemia requiring transfusion (54, 27.8 %), wound infection (18, 9.3 %), ileus require treatment (13, 6.7 %), collection (7, 3.6 %), pneumonia (6, 3.1 %), DVT (5, 2.6 %), delirium (5, 2.6 %), COPD exacerbation (3. 1.5 %), arrhythmia (2, 1.0 %), seizure (1, 0.5 %)
III	31	Wound dehiscence (14, 7.2 %), small bowel obstruction/perforation (8, 4.1 %), stomal ischemia (3, 1.5 %), hydronephrosis (2, 1.0 %), urinary leakage (2, 1 %), AVF thrombosis (1, 0.5 %), pelvic hematoma (1. 0.5 %)
lV	29	Sepsis (8, 4.1 %), vascular injury (4, 2.1 %), renal failure (4, 2.1 %), hemorrhagic shock (4, 2.1 %), anastomosis leakage with sepsis (3, 1.5 %), cerebrovascular accident (2, 1.0 %), DIC (1, 0.5 %) pulmonary embolism (1, 0.5 %), liver failure (1, 0.5 %), UGIB (1, 0.5 %)
V	7	Death from gastrointestinal bleed (1, 0.5 %), death from sepsis (4, 2.1 %), death from ischemic stroke (1, 0.5 %), death from gut obstruction (1, 0.5 %)

DVT, deep vein thrombosis; COPD, chronic obstructive pulmonary disease; AVF, arteriovenous fistula; DIC, disseminated intravascular coagulation; UGIB, upper gastrointestinal bleeding.
N = number of events that occur.
Complications occurred in each patient are separately reported.

<220,000/μL (OR 3.75, 95 % CI 1.25–11.22), and thrombocytopenia (OR 13.31, 95 % CI 3.43–53.03). Multivariate logistic regression analysis yielded a final risk model for wound dehiscence comprised of three factors: ACCI >4, hypoalbuminemia, and Plt <220,000/μL. The analysis demonstrated that hypoalbuminemia and Plt <220,000/μL were independent risk factors for wound dehiscence. Additional subgroup analysis revealed no risk factor associated with thrombocytopenia. On the other hand, neoadj CMT (OR 2.77, 95 % CI 1.46–5.27) and AACCI >4 (OR 2.12, 95 % CI 1.20–3.74) were associated with Plt <220,000/μL (not showed in the table). However, both factors were not associated with wound dehiscence. Table 5 provides the final model factors with their adjusted ORs and 95 % CIs.

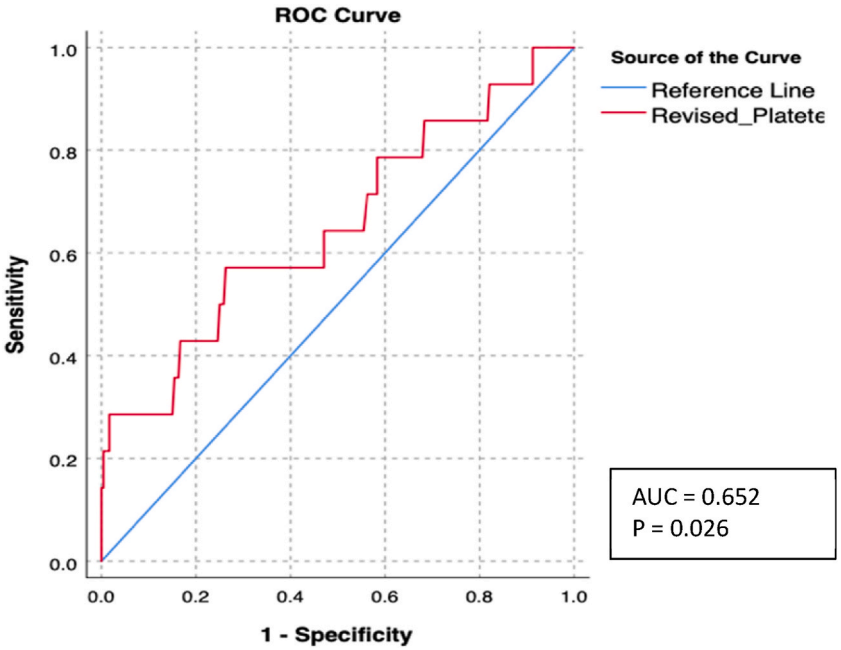

Fig. 1. ROC curves of platelet counts for early postoperative major complications (CDC 3–5).

Table 5
Univariate and multivariate analyses of factors associated with wound dehiscence.

Variable	OR	Univariate 95 % CI	P value	Adjusted OR	Multivariate 95 % CI	P value
ACCI >4	4.99	1.09–22.79	0.022	3.64	0.77–17.16	0.102
AACCI >4	1.06	0.32–3.48	1.000			
NLR ≥4.1	1.31	0.40–4.35	0.746			
PLR ≥164.7	1.11	0.37–3.29	0.857			
SIRI ≥2.35	1.06	0.32–3.48	0.931			
PNI ≤45	0.46	0.24–15.07	1.000			
Hypoalbuminemia [a]	3.69	1.07–12.70	0.052	4.72	1.23–18.19	0.024
BMI ≥25 kg/m^2	2.62	0.88–7.80	0.088			
CKD stage ≥3 [b]	1.94	0.59–6.37	0.265			
Neoadjuvant CMT	1.64	0.49–5.47	0.490			
Platelet <220,000	3.75	1.25–11.22	0.026	3.91	1.18–12.91	0.025
Thrombocytopenia [c]	13.31	3.34–53.03	0.002			
Type of diversion			0.509			
Ileal conduit	ref					
Ureterostomy	N/A	N/A	0.530			
Neobladder	0.297	0.03–3.03	0.338			

OR, odds ratio; ACCI, age-adjusted Charlson comorbidity index; AACCI, adjusted age-adjusted Charlson comorbidity index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SIRI, systemic inflammation response index μ; PNI, prognostic nutritional index; BMI, body mass index; CKD, chronic kidney disease CMT, chemotherapy; N/A, not applicable.

[a] Hypoalbuminemia is serum albumin < 3.0 g/dL.

[b] CKD staged ≥3 is GFR < 60 mL/min/1.73 m^2

[c] Thrombocytopenia is platelet count < 150,000/μL.

4. Discussion

Radical cystectomy with urinary diversion is a complex procedure often performed in patients with advanced age and multiple comorbidities. Previous studies have reported complication rate ranging from 30 to 70 % [18–21], making predicting complications challenging. In our study, we observed an overall complication rate of 53.1 %, with approximately 18.5 % of patient experienced major early complications (CDC3-5), a proportion slightly higher than that reported in other studies (11.2 %–14.2 %) [19,22,23]. Notably, wound dehiscence emerged as the most frequently encountered early major complication in our study population.

The study highlighted the importance of a high ACCI score as a predictive factor for 30-day postoperative complications. Consistent with previous research, advanced age and a high burden of comorbidity have been linked to worse outcomes following RC [13,24–29].

Studies by McFerrin et al. and Knorr et al. demonstrated that increasing Charlson score correlate with higher rate of 30-day readmission and mortality after cystectomy [22,30]. Additionally, Koppie et al. showed that patient with ACCI 3–5 and >5 were less likely to receive any adjuvant treatment post-RC and had lower overall survival rates [8]. Notably, Chang et al. proposed the adjusted-ACCI (AACCI) as a potentially more accurate predictor 90-day postoperative mortality, particularly beneficial for patient over 80 years old [7]. While the AACCI's validation in bladder cancer remains limited, our findings suggest its efficacy in predicting 30-day major complications, even among BC patient of relatively younger ages.

Previous studies have illuminated the intricate relationship between platelets, immune cells and the tumor progression [31–33]. Todenhöfer et al. reported that around 10.1 % of patients undergoing RC had elevated platelet counts, which were associated with lower 3-year cancer-specific survival rates [32]. Similarly, Jokisch et al. found that preoperative thrombocytosis was linked to advanced tumor stage and poorer oncological outcomes, as well as an increased risk of venous thromboembolism (VTE) [34]. However, our study revealed that thrombocytopenia was associated with early major complication following RC, even after controlling for ACCI and other perioperative factors. Interestingly, a Plt over 150,000/μL did not show an association with major complications, indicating that thrombocytopenia may pose a unique risk factor independent of thrombotic events. Moreover, we identified that even within the normal range, a Plt <220,000/μL independently increased the risk factor for wound dehiscence. Beyond their conventional role in hemostasis, platelets are increasingly recognized as modulators of inflammation, wound healing, and tissue regeneration [35]. Aksamija et al. reported that 7 % of adults with surgical wound dehiscence after laparotomy had thrombocytopenia [36], while Kim et al. showed an association between thrombocytopenia and surgical site infections in patients undergoing shoulder arthroplasty [37]. Notably, subgroup analysis revealed that neoadj CMT and high AACCI were associated with lower preoperative Plt. However, there is currently no evidence confirming that platelet concentrate infusion to raise Plt before surgery would decrease the risk of wound dehiscence. Additionally, neoadj CMT has not been found to increase complications related to RC [38–40], as corroborated by the finding of this study.

In addition to traditional TNM stage and histologic classification, several novel serum biomarkers, including NLR, PLR, SIRI, and PNI have been identified as potential prognostic indicators in various type of cancers, including bladder cancer [10,15,41]. Elevated level of monocytes and neutrophils typically indicate a higher tumor burden, while lymphocytes play a crucial role in anti-tumor defense through cytotoxic cell death and suppression of the tumor proliferation [42,43]. Additionally, malnutrition, as reflected by serum albumin levels, can compromise the immune system. Consequently, patients with high inflammatory-nutrition biomarkers may exhibit frailty and be more susceptible to postoperative complications. Cinar et al. reported that a SIRI >2.35 could accurately predict CDC ≥3b at 90 days postoperatively [13]. However, novel serum biomarkers were not found to be associated with early major complications in our study. It's noteworthy that both our study and that of Cinar et al. included approximately 20 % of patient received neoadj CMT. The disparity in findings regarding the predictive abilities of novel serum markers for major complications in our study could be attributed to the relatively short follow-up period of only 30 days postoperatively, unlike other studies that extended follow-up to at least 90 days [9,12]. Furthermore, the higher mean Alb observed in our study, even among patient who experienced major complication, may have influenced the predictive effect of PNI. Additionally, the cutoff points for novel serum markers derived from other studies may not be directly applicable to the Thai population, as evidenced by the NLR cutoff of 4.1. It's important to note that the mean NLR in our study was only 2.7, further highlighting potential population-specific variations in marker thresholds.

Several studies have identified BMI and smoking as independent risk factors for wound complications [44,45]. In our study, we also observed a significant higher BMI in patients with high-grade CDC. However, when using a dichotomous cutoff point of 25 kg/m^2, BMI was not associated with major complications or wound dehiscence. Previous studies have reported wound dehiscence rates post-RC ranging for 2.8–8.9 % with risk factors including, male gender, surgical site infection, chronic obstructive pulmonary disease, smoking, and morbid obesity [17,46–49]. Interestingly, our study additionally identified thrombocytopenia and hypoalbuminemia as the risk factors for this complication. Consistent with the previous findings, we observed that 10.8 % of our patient had low preoperative Alb. This nutritional deficiency has been associated with higher rates of complications and mortality within 90 days postoperatively [50]. Additionally, a prior study conducted at our center demonstrated an association between low serum prealbumin and increasing early postoperative complications, as well as prolonged recovery periods following RC [51]. These findings underscore the detrimental effects of nutritional deficiencies on bladder cancer survival after RC and highlight the importance of implementing nutritional interventions to optimize patient outcomes.

The significance of serum chloride levels and intraoperative fluid resuscitation remains a topic of debate. Our study found that immediate postoperative hypochloremia was a risk factor for major complications, while hyperchloremia tended to be a protective factor. Similarly, Kimura et al. found that hypochloremia observed within 48 hours was independently associated with increased hospital deaths following surgery in patients requiring postoperative intensive care [16]. However, these findings contradict beliefs about the effects of postoperative hyperchloremia reported in previous studies [52–54]. McCluskey et al. reported that postoperative hyperchloremia increased 30-day mortality by approximately 2-fold in a study involving 22,850 patients who underwent noncardiac surgery [55]. The study hypothesized that surgical patients are more susceptible to perioperative hyperchloremia because the frequent use of 0.9 % NaCl during the perioperative period. Additionally, Semler et al. reported a lower rate of death, new renal-replacement therapy, or persistent renal dysfunction with the use of balanced crystalloid solution compared to normal saline in critically ill adults [56]. Since almost fifty percent of complications developed during the delayed period (31–90 days) post-RC, it can be concluded that longer follow-up studies are required, intravenous fluid resuscitation must be administered carefully, and hypochloremia may warrant caution in RC.

There are several limitations to our study that warrant consideration. Firstly, the retrospective nature of our study and the reliance data from a single institution, may introduce bias in terms of patient selection and outcomes assessment. Secondly, as all patients included in our study were Thai, the generalizability of our finding to other ethnic populations may be limited. Additionally, Longer

follow-up periods may provide further insight into the significance of proposed novel serum marker and the impact of postoperative hypochloremia on complication following radical cystectomy.

5. Conclusion

This study reveals that thrombocytopenia and ACCI >4 as significant risk factors for early morbidity in RC patients. Wound dehiscence emerges as the most prevalent early major complication, associated with hypoalbuminemia and a Plt <220,000/μL. Predicting the risk of major complications following RC would allow for the improvement of preoperative counseling through addressing modifiable risk factors and the optimization of perioperative care for patients at high risk.

Ethics statement

The study was approved by the Ethics Committee of Siriraj Institutional Review Board (318/2562(IRB3)), Faculty of Medicine Siriraj Hospital, Mahidol University.

Data availability

The data from this study are not deposited in a publicly available repository. However, the data will be made available upon request for academic purposes.

CRediT authorship contribution statement

Songyot Veerakulwatana: Writing – original draft, Formal analysis, Data curation. **Chalairat Suk-ouichai:** Writing – review & editing, Conceptualization. **Tawatchai Taweemonkongsap:** Writing – review & editing, Resources. **Ekkarin Chotikawanich:** Writing – review & editing, Resources. **Siros Jitpraphai:** Resources. **Varat Woranisarakul:** Resources, Data curation. **Nattaporn Wanvimolkul:** Formal analysis, Data curation. **Thitipat Hansomwong:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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