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Risk factors and outcomes of myocardial injury after non-cardiac surgery in high-risk patients who underwent radical cystectomy

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Abstract

Radical cystectomy is considered the standard treatment for patients with muscle-invasive bladder tumors and has high postoperative complication rates among urological surgeries. High-risk patients, defined as those ≥45 years of age with history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age, can have a higher incidence of cardiac complications. Therefore, we evaluated the incidence, risk factors, and outcomes of myocardial injury after non-cardiac surgery (MINS) in high-risk patients who underwent radical cystectomy.

This retrospective observational study analyzed 248 high-risk patients who underwent radical cystectomy. MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days. The risk factors for MINS were evaluated by multivariate logistic regression analysis. Postoperative outcomes were evaluated. The 1-year survival after radical cystectomy was also compared between patients who developed MINS (MINS group) and those who did not (non-MINS group) by Kaplan–Meier analysis.

MINS occurred in 35 patients (14.1%). Multivariate logistic regression analysis showed that early diastolic transmitral filling velocity (E)/ early diastolic septal mitral annular velocity (E') ratio (odds ratio = 1.102, 95% confidence interval [1.009–1.203], $P = .031$) and large volume blood transfusion (odds ratio = 2.745, 95% confidence interval [1.131–6.664], $P = .026$) were significantly associated with MINS in high-risk patients who underwent radical cystectomy. Major adverse cardiac events and 1-year mortality were significantly higher in the MINS group than in the non-MINS group (17.1% vs 6.1%, $P = .035$; 28.6% vs 12.7%, $P = .021$, respectively). Kaplan–Meier analysis showed significantly lower 1-year survival in the MINS group than in the non-MINS group ($P = .010$).

MINS occurred in 14.1% of patients. High E/E' ratio and large volume blood transfusion were risk factors for MINS in high-risk patients who underwent radical cystectomy. Postoperative major adverse cardiac events and 1-year mortality were significantly higher in the MINS group than in the non-MINS group. Preoperative evaluation of risk factors for MINS may provide useful information to detect cardiovascular complications after radical cystectomy in high-risk patients.

Abbreviations: A' = late diastolic septal mitral annular velocity, A = late diastolic transmitral filling velocity, AKI = acute kidney injury, E' = early diastolic septal mitral annular velocity, E = early diastolic transmitral filling velocity, ICU = intensive care unit, MACE = major adverse cardiac event, MINS = myocardial injury after non-cardiac surgery, RBC = red blood cell, S' = systolic septal mitral annular velocity.

Keywords: high-risk patients, myocardial injury after non-cardiac surgery, radical cystectomy

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Radical cystectomy is considered the standard treatment for patients with muscle-invasive bladder tumors.[1] This major abdominal surgery has high postoperative complication rates in the range of 28% to 64% among urological surgeries.[2] Due to the nature of bladder cancer, radical cystectomy is usually performed in elderly patients who have multiple comorbidities.[3,4] Older patients with multiple comorbidities have a significantly higher incidence of complications after radical cystectomy.[3] Importantly, high-risk patients such as those ≥45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age are associated with short- and long-term mortality in non-cardiac surgery.[5] Therefore, meticulous care and attention should be given during anesthesia and surgical procedures to such high-risk patients during the perioperative period of radical cystectomy.

Myocardial injury after non-cardiac surgery (MINS) is an emerging issue that results in increased morbidity, mortality, and hospital costs.[5] Cardiac complication is a common postoperative complication after radical cystectomy.[6,7] However, typical cardiac ischemic symptoms such as chest pain or discomfort may be obscured in the postoperative period due to postoperative pain management. MINS, defined as a serum troponin I concentration ≥0.04 mg/L within postoperative 3 days,[8] can be easily diagnosed based on elevated troponin level. The reported incidence of MINS after major abdominal surgery is around 10%.[9,10] The incidence of MINS is higher in older patients (over 70 years of age) or those with a history of cardiovascular disease than in the general population in cases of open major vascular surgery.[11] Therefore, it is important to detect MINS early to reduce morbidity and mortality in high-risk patients. However, to the best of our knowledge, no previous studies have investigated MINS in high-risk cystectomy patients.

We hypothesized that perioperative factors might affect MINS in radical cystectomy. Therefore, we assessed the incidence and risk factors of MINS in high-risk patients who underwent radical cystectomy. We also compared postoperative outcomes between high-risk patients who developed MINS (MINS group) and those who did not (non-MINS group).

2. Methods

2.1. Patients

We retrospectively reviewed consecutive patients who underwent open radical cystectomy due to bladder cancer at Asan Medical Center in Seoul, Republic of Korea, between January 2007 and February 2019. We included high-risk patients, defined as those ≥45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age.[5] We excluded patients without troponin I measurements and those who underwent radical cystectomy combined with other surgeries. The study was approved by the Institutional Review Board of Asan Medical Center (approval no. 2020-0410), which waived the requirement for written informed consent.

2.2. Perioperative protocol

No patients were administered premedication. Anticoagulant agents were discontinued according to the standard protocol before radical cystectomy.[12,13] General anesthesia was performed according to our institutional standards for radical cystectomy.[14–16] Anesthesia was induced with propofol or thiopental sodium and rocuronium and was maintained with sevoflurane. The concentration of sevoflurane was set to maintain a bispectral index of 40 to 60. The administration of fluids and vasopressors or inotropic agents was performed to maintain a mean arterial blood pressure of above 65 mm Hg. The heart rate was maintained at 60 to 100 beats/min. Hemodynamic changes in high-risk patients were minimized by close perioperative monitoring. Crystalloids such as lactated Ringer's solution or plasma solution A (CJ Pharmaceutical, Seoul, Korea) and colloids such as 6% hydroxyethyl starch or 5% albumin were used for fluid administration. Ephedrine, phenylephrine, or norepinephrine were used as vasopressors or inotropic agents. Red blood cells (RBCs) were transfused when the hemoglobin concentration was <8 g/dL. A neostigmine-glycopyrrolate mixture or sugammadex was used to reverse neuromuscular blockade at the discretion of the anesthesiologist. Patient-controlled intravenous analgesia based on fentanyl was used to manage postoperative pain. Based on anesthesiologist and urologist determination, the evaluation of coronary artery disease-related symptoms, troponin I measurement, and electrocardiogram monitoring were performed after radical cystectomy.

Radical cystectomy with standard or extended pelvic lymphadenectomy was performed according to our institutional management protocol.[17,18] Standard pelvic lymph node dissection included the distal common iliac, external iliac, internal iliac, obturator, and perivesical lymph nodes. Extended lymph node dissection included the lymph nodes extending to the proximal common iliac artery, distal aorta, and inferior vena cava. Urinary diversion (ileal neobladder or ileal conduit) was subsequently performed according to the urologist's judgment. Ileal neobladder reconstruction was performed as follows: Depending on the type of neobladder, a specific length of the distal ileum (15–20 cm from the ileocecal valve) was harvested to create an orthotopic continent diversion (ileal neobladder). Continuity of the remnant bowel was re-established by ileo-ileostomy. Ileal conduit reconstruction was performed as follows: An ileal segment 20 cm in length was harvested, sparing the distal 15 cm of the ileum, and the remaining ileal segment was re-anastomosed. Both ureters were implanted in the conduit. The stoma was formed at the selected site on the surface of the abdomen. Five highly experienced surgeons performed all the surgeries.

2.3. Definition of MINS and measurement of troponin I

MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days.[8] Postoperative troponin I measurement was planned before surgery according to patient characteristics or was determined during surgery in case of the occurrence of specific events such as electrocardiogram change, hemodynamic instability, and a large volume of blood loss. Serum troponin was measured daily on postoperative days 0 and 1 for all high-risk patients and repeatedly from postoperative day 2 for patients with abnormal serum troponin levels.

2.4. Data collection and definitions

Data on patient demographics and clinical characteristics were collected, including sex; age; body mass index; American Society of Anesthesiologists Physical Status; comorbidities (diabetes mellitus, hypertension, atrial fibrillation, coronary artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, end-stage renal disease, and number of associated comorbidities); tumor T, N, and M stages; tumor grade; tumor pathology; neoadjuvant chemotherapy; preoperative laboratory tests (white blood cell count, hemoglobin concentration, platelet count, and serum albumin, creatinine, sodium, potassium, chloride, uric acid, and glucose levels); preoperative transthoracic echocardiography parameters (left ventricular end-diastolic volume; left ventricular ejection fraction; mitral deceleration time; early diastolic septal mitral annular velocity (E'); late diastolic septal mitral annular velocity (A'); systolic septal mitral annular velocity (S'); early diastolic transmitral filling velocity (E); late diastolic transmitral filling velocity (A); E/A ratio, E/E' ratio; valvulopathies including aortic regurgitation, aortic stenosis, mitral regurgitation, and tricuspid regurgitation; and study period.

Tumor stage was defined according to the 2010 American Joint Committee on Cancer tumor-node-metastasis staging system.[19] Tumor grade was defined according to the 2016 World Health Organization grading system.[20] Neoadjuvant chemotherapy was applied with one of the following combinations: gemcitabine and carboplatin; gemcitabine and cisplatin; methotrexate and vinblastine; or sulfate, cisplatin, and doxorubicin. The study duration was divided into period 1 (January 2007 to December 2012) and period 2 (January 2013 to February 2019).

Intraoperative and postoperative data included anesthesia and operation durations, crystalloid and colloid amounts, RBC transfusion rate, RBC transfusion amount, large volume blood transfusion, intraoperative hypotension, agent used to reverse neuromuscular blockade, urethrectomy, urinary diversion type, and adjuvant chemotherapy. Large volume blood transfusion was defined as an intraoperative transfusion of four or more units of RBCs.[21] Intraoperative hypotension was defined as a mean arterial blood pressure <65 mm Hg for >5 minutes noted in the intraoperative anesthesia records.[23] Postoperative outcomes included acute kidney injury (AKI), hospital stay duration (from surgery to discharge), intensive care unit (ICU) admission rate, ICU stay duration, major adverse cardiac events (MACEs), and 1-year mortality. AKI was defined by applying the Kidney Disease: Improving Global Outcomes criteria.[22] Postoperative MACEs were defined according to the European Perioperative Clinical Outcome definitions[24] and were recorded if a patient had one or more of the following complications within 6 months after radical cystectomy: arrhythmia, nonfatal cardiac arrest, acute myocardial infarction, heart failure, or cerebrovascular accident.

2.5. Statistical analysis

Categorical variables were examined by chi-square or Fisher exact tests, and continuous variables were examined by Student *t*- or Mann–Whitney *U*-test between the MINS and non-MINS groups. Categorical variables are expressed as number (percentage), and continuous variables as mean ± standard deviation. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors for MINS in high-risk patients who underwent radical cystectomy. The most relevant factors associated with MINS in radical cystectomy were included in the univariate logistic regression analysis. Multivariate logistic regression analysis using the backward conditional method was performed for all factors with $P<.05$ in the univariate logistic regression analyses. To estimate multicollinearity, the variance inflation factor was calculated before performing multivariate logistic regression analyses. Multicollinearity was considered to be present if the variance inflation factor was above 10. To measure the calibration and discrimination of the logistic regression model, the Hosmer–Lemeshow goodness-of-fit statistic and C-statistic were performed.

Kaplan–Meier analysis was performed to estimate the distribution of survival time within 1 year after radical cystectomy. Log-rank test was performed to assess the differences in survival rates between the MINS and non-MINS groups. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY), with $P<.05$ considered statistically significant.

3. Results

Between January 2007 and February 2019, 455 high-risk patients underwent radical cystectomy. A total of 207 patients were excluded (195 patients due to lack of troponin I data and 12 patients due to having other surgeries combined with radical cystectomy). Thus, 248 patients were finally analyzed, of whom 35 (14.1%) experienced MINS (Fig. 1).

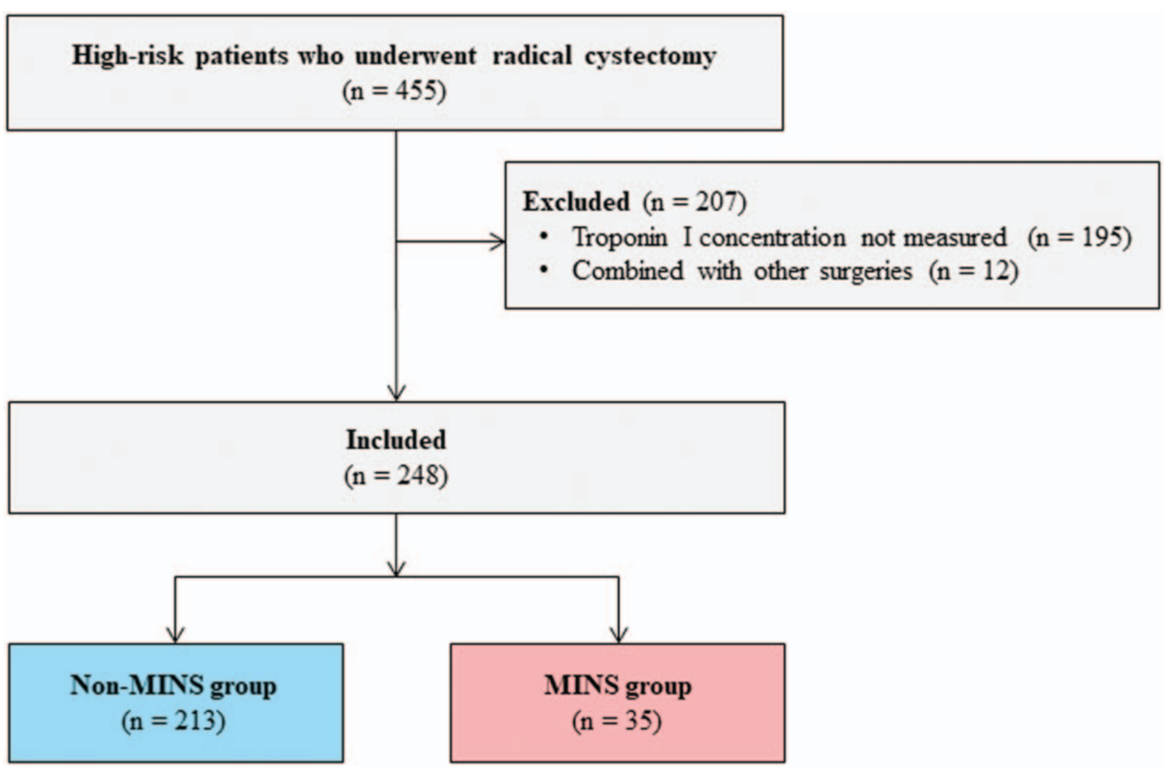

Figure 1. Flowchart of the study patients. High-risk patients were defined as those ≥45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age. MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days. MINS = myocardial injury after non-cardiac surgery.

Table 1

Patient demographics and clinical characteristics.

Variables	All patients (n=248)	Non-MINS group (n=213)	MINS group (n=35)	*P* value*
Sex (male)	209 (84.3)	183 (85.9)	26 (74.3)	.219
Age (yrs)	72±5	72±5	73±7	.219
Body mass index (kg/m^2)	24.0±3.2	23.8±3.1	24.8±3.4	.089
ASA Physical Status				.202
2	187 (75.4)	164 (77.0)	23 (65.7)	
3	61 (24.6)	49 (23.0)	12 (34.3)	
Diabetes mellitus	53 (21.4)	43 (20.2)	10 (28.6)	.270
Hypertension	126 (50.8)	106 (49.8)	20 (57.1)	.468
Atrial fibrillation	10 (4.0)	8 (3.8)	2 (5.7)	.637
Coronary artery disease	32 (12.9)	25 (11.7)	7 (20.0)	.274
Cerebrovascular disease	15 (6.0)	12 (5.6)	3 (8.6)	.452
COPD	14 (5.6)	12 (5.6)	2 (5.7)	>.999
ESRD	1 (0.4)	0 (0.0)	1 (2.9)	.141
Number of associated comorbidities				.116
0	86 (34.7)	76 (35.7)	10 (28.6)	
1	89 (35.9)	78 (36.6)	11 (31.4)	
2	60 (24.2)	51 (23.9)	9 (25.7)	
3	10 (4.0)	6 (2.8)	4 (11.4)	
4	3 (1.2)	2 (0.9)	1 (2.9)	
Tumor T stage				.974
1	105 (42.3)	90 (42.3)	15 (42.9)	
2	40 (16.1)	35 (16.4)	5 (14.3)	
3	38 (15.3)	33 (15.5)	5 (14.3)	
4	65 (26.2)	55 (25.8)	10 (28.6)	
Tumor N stage				.810
0	206 (83.1)	176 (82.6)	30 (85.7)	
1	42 (16.9)	37 (17.4)	5 (14.3)	
Tumor M stage				.038
0	242 (97.6)	210 (98.6)	32 (91.4)	
1	6 (2.4)	3 (1.4)	3 (8.6)	
Tumor grade				.367
2	9 (3.6)	9 (4.2)	0 (0.0)	
3	239 (96.4)	204 (95.8)	35 (100.0)	
Tumor pathology				.430
Transitional cell carcinoma	178 (71.8)	149 (70.0)	29 (82.9)	
Squamous cell carcinoma	14 (5.6)	13 (6.1)	1 (2.9)	
Micropapillary carcinoma	5 (2.0)	5 (2.3)	0 (0.0)	
Others†	51 (20.6)	46 (21.6)	5 (14.3)	
Neoadjuvant chemotherapy	54 (21.8)	42 (19.7)	12 (34.3)	.075
Preoperative laboratory tests				
White blood cells (/μL)	6796±2890	6783±2777	6877±3548	.858
Hemoglobin (g/dL)	12.0±1.9	12.1±1.8	11.3±1.9	.017
Platelets (10^3/μL)	241.9±81.2	243.5±80.5	232.5±85.4	.481
Albumin (g/dL)	3.6±0.5	3.6±0.5	3.5±0.4	.135
Creatinine (mg/dL)	1.0±0.6	1.0±0.3	1.3±1.3	.012
Sodium (mmol/L)	140±3	140±3	139±3	.135
Potassium (mmol/L)	4.4±0.4	4.4±0.4	4.4±0.5	.609
Chloride (mmol/L)	105±3	105±3	104±4	.094
Uric acid (mg/dL)	5.1±1.5	5.2±1.6	4.8±1.3	.219
Glucose (mg/dL)	125±45	123±44	135±50	.149
Preoperative TTE parameters				
LV end-diastolic volume (mL)	90.6±26.1	89.3±23.6	98.4±37.3	.054
LV ejection fraction (%)	61.1±6.8	61.3±6.9	59.9±6.1	.256
Mitral deceleration time (ms)	222.8±51.9	223.6±52.5	218.0±49.0	.557
E' (cm/s)	5.6±1.4	5.7±1.4	5.1±1.4	.027
A' (cm/s)	9.3±1.7	9.3±1.7	9.2±1.9	.687
S' (cm/s)	7.1±1.3	7.1±1.2	7.4±1.3	.837
E (cm/s)	59.9±18.1	59.4±17.8	63.1±19.7	.257
A (cm/s)	76.0±20.0	75.8±19.9	76.9±20.8	.759
E/A ratio	0.8±0.2	0.8±0.2	0.8±0.2	.727
E/E' ratio	10.8±3.8	10.6±3.3	12.6±5.9	.053
AR	51 (20.6)	43 (20.2)	8 (22.9)	.821

(*continued*)

Table 1

(continued).

Variables	All patients (n=248)	Non-MINS group (n=213)	MINS group (n=35)	*P* value*
AS	4 (1.6)	2 (0.9)	2 (5.7)	.097
MR	20 (8.1)	16 (7.5)	4 (11.4)	.498
TR	47 (19.0)	39 (18.3)	8 (22.9)	.641
Study period‡				.848
1	85 (34.3)	74 (34.7)	11 (31.4)	
2	163 (65.7)	139 (65.3)	24 (68.6)	

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as number (percentage). MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days.

A' = late diastolic septal mitral annular velocity, A = late diastolic transmitral filling velocity, AR = aortic regurgitation, AS = aortic stenosis, ASA = American Society of Anesthesiologists, COPD = chronic obstructive pulmonary disease, E' = early diastolic septal mitral annular velocity, E = early diastolic transmitral filling velocity, ESRD = end-stage renal disease, LV = left ventricular, MINS = myocardial injury after non-cardiac surgery, MR = mitral regurgitation, S' = systolic septal mitral annular velocity, TR = tricuspid regurgitation, TTE = transthoracic echocardiography.

* For comparisons between the MINS and non-MINS groups.

† Others included adenocarcinoma, sarcomatoid carcinoma, plasmacytoid carcinoma, giant cell carcinoma, and syncytiotrophoblastic cell carcinoma.

‡ Study period 1 was defined as January 2007 to December 2012, and study period 2 was defined as January 2013 to February 2019.

Patient demographics, clinical characteristics, and intraoperative and postoperative data are shown in Tables 1 and 2. Tumor M stage, preoperative hemoglobin concentration, serum creatinine level, E', RBC transfusion amount, and large volume blood transfusion differed significantly between the MINS and non-MINS groups. In multivariate logistic regression analysis, E/E' ratio (odds ratio = 1.102, 95% confidence interval [1.009–1.203], *P* = .031), and large volume blood transfusion (odds ratio = 2.745, 95% confidence interval [1.131–6.664], *P* = .026) were significantly associated with MINS in high-risk patients who underwent radical cystectomy (Table 3). All variance inflation factors were <10, indicating a lack of multicollinearity. The Hosmer–Lemeshow goodness-of-fit probability was 0.104 and the C-statistic value for the model was 0.827, demonstrating good calibration and discrimination. In addition, the occurrence of MINS was significantly higher in patients who received large blood transfusion than in those who did not (10/33 patients [30.3%] patients vs 25/215 patients [11.6%], *P* = .008).

No significant difference in AKI incidence was observed between the MINS and non-MINS groups (14/35 patients [40.0%] vs 71/213 patients [33.3%], *P* = .448) (Table 4). ICU admission rate, ICU stay duration, postoperative MACEs, and 1-year mortality were significantly higher in the MINS group than in the non-MINS group (Table 4). Kaplan–Meier analysis demonstrated a significantly lower 1-year survival in the MINS group than in the non-MINS group (*P* = .010) (Fig. 2).

4. Discussion

The results of the present study showed a 14.1% incidence rate of MINS in high-risk patients who underwent radical cystectomy. E/E' ratio and large volume blood transfusion were independent risk factors associated with MINS in high-risk cystectomy patients. Moreover, ICU admission rate, ICU stay duration, postoperative MACEs, and 1-year mortality were significantly higher in the MINS group than in the non-MINS group.

Table 2

Intraoperative and postoperative data.

Variables	All patients (n=248)	Non-MINS group (n=213)	MINS group (n=35)	*P* value*
Anesthesia duration (min)	435 ± 98	431 ± 97	455 ± 102	.203
Operation duration (min)	413 ± 101	410 ± 100	436 ± 106	.173
Crystalloid amount (mL)	3093 ± 1312	3135 ± 1274	2839 ± 1522	.217
Colloid amount (mL)	483 ± 416	479 ± 418	517 ± 433	.560
RBC transfusion rate	136 (54.8)	113 (53.1)	23 (65.7)	.200
RBC transfusion amount	1.5 ± 1.8	1.4 ± 1.7	2.2 ± 2.2	.019
Large volume blood transfusion	33 (13.3)	23 (10.8)	10 (28.6)	.008
Intraoperative hypotension	74 (29.8)	64 (30.0)	10 (28.6)	>.999
NMB reversal agent				.099
Neostigmine-glycopyrrolate	226 (91.1)	197 (92.5)	29 (82.9)	
Sugammadex	22 (8.9)	16 (7.5)	6 (17.1)	
Urethrectomy	125 (50.4)	103 (48.4)	22 (62.9)	.144
Urinary diversion type				.201
Ileal conduit	127 (51.2)	113 (53.1)	14 (40.0)	
Ileal neobladder	121 (48.8)	100 (46.9)	21 (60.0)	
Adjuvant chemotherapy	14 (5.6)	13 (6.1)	1 (2.9)	.699

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as number (percentage). MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days. Large volume blood transfusion was defined as an intraoperative transfusion of four or more units of RBCs.

MINS = myocardial injury after non-cardiac surgery, NMB = neuromuscular blockade, RBC = red blood cell.

* For comparisons between the MINS and non-MINS groups.

Table 3

Univariate and multivariate logistic regression analyses of risk factors for MINS in high-risk patients who underwent radical cystectomy.

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Sex (male)	2.112 (0.902–4.944)	.085		
Age	1.053 (0.984–1.126)	.132		
Body mass index	1.099 (0.985–1.226)	.091		
ASA Physical Status		.155		
2	1			
3	1.746 (0.811–3.762)			
Diabetes mellitus	1.581 (0.706–3.541)	.265		
Hypertension	1.346 (0.654–2.769)	.420		
Coronary artery disease	1.880 (0.744–4.752)	.182		
Cerebrovascular accident	1.570 (0.420–5.872)	.502		
Number of associated comorbidities				
0	1			
1	1.072 (0.430–2.670)	.882		
2	1.341 (0.509–3.531)	.552		
3	5.067 (1.217–21.101)	.026		
4	3.800 (0.315–45.803)	.293		
Tumor T stage				
1	1			
2	0.857 (0.290–2.536)	.781		
3	0.909 (0.306–2.698)	.864		
4	1.091 (0.458–2.598)	.844		
Tumor N stage				
0	1			
1	0.793 (0.288–2.179)	.653		
Tumor M stage				
0	1			
1	6.562 (1.269–33.931)	.025		
Neoadjuvant chemotherapy	2.124 (0.978–4.612)	.057		
White blood cells	1.011 (0.896–1.141)	.857		
Hemoglobin	0.784 (0.640–0.960)	.019		
Platelets	0.998 (0.993–1.003)	.458		
Albumin	0.569 (0.271–1.194)	.136		
Creatinine	1.805 (0.873–3.733)	.111		
Uric acid	0.858 (0.672–1.095)	.219		
LV end-diastolic volume	1.013 (1.000–1.026)	.057		
E/E' ratio	1.128 (1.037–1.228)	.005	1.102 (1.009–1.203)	.031
AR	1.171 (0.497–2.760)	.717		
AS	6.394 (0.871–46.963)	.068		
MR	1.589 (0.498–5.064)	.434		
TR	1.322 (0.558–3.130)	.526		
Study period				
1	1			
2	1.162 (0.539–2.502)	.702		
Operation duration	1.003 (0.999–1.006)	.151		
Crystalloid amount	1.000 (1.000–1.000)	.216		
Colloid amount	1.000 (0.999–1.001)	.559		
RBC transfusion	1.696 (0.803–3.584)	.166		
Large volume blood transfusion	3.304 (1.410–7.743)	.006	2.745 (1.131–6.664)	.026
Intraoperative hypotension	0.931 (0.423–2.051)	.860		
Reversal agent of NMB				
Neostigmine-glycopyrrolate	1			
Sugammadex	2.547 (0.922–7.036)	.071		
Urethrectomy	1.807 (0.865–3.775)	.115		
Urinary diversion type				
Ileal conduit	1			
Ileal neobladder	1.695 (0.819–3.510)	.155		

MINS was defined as serum troponin I concentration $\geq$0.04 mg/L within postoperative 3 days. High-risk patients were defined as those $\geq$45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those $\geq$65 years of age. Study period 1 was defined as January 2007 to December 2012, and study period 2 was defined as January 2013 to February 2019. Large volume blood transfusion was defined as an intraoperative transfusion of four or more units of RBCs.

Multivariate logistic regression analysis by using the backward conditional method was performed for all factors (ie, number of associated comorbidities, tumor M stage, hemoglobin, E/E' ratio, and large volume blood transfusion) with $P < .05$ in univariate logistic regression analyses.

AR = aortic regurgitation, AS = aortic stenosis, ASA = American Society of Anesthesiologists, CI = confidence interval, E/E' ratio = early diastolic transmitral filling velocity/early diastolic septal mitral annular velocity ratio, LV = left ventricular, MINS = myocardial injury after non-cardiac surgery, MR = mitral regurgitation, NMB = neuromuscular blockade, OR = odds ratio, RBC = red blood cell, TR = tricuspid regurgitation.

Table 4

Postoperative outcomes.

Variables	Non-MINS group (n=213)	MINS group (n=35)	*P* value
Acute kidney injury	71 (33.3)	14 (40.0)	.448
Hospital stay duration (d)	24.8±14.2	30.2±33.8	.362
ICU admission rate	62 (29.1)	17 (48.6)	.030
ICU stay duration (d)*	1.1±0.3	1.5±0.7	.001
MACEs within 6 mo	13 (6.1)	6 (17.1)	.035
1-yr mortality	27 (12.7)	10 (28.6)	.021

Continuous variables are presented as mean±standard deviation, and categorical variables are presented as number (percentage). MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days. MACEs were determined based on the diagnosis of one of the following complications within 6 months after radical cystectomy: arrhythmia, nonfatal cardiac arrest, acute myocardial infarction, heart failure, or cerebrovascular accident.

ICU=intensive care unit, MACEs=major adverse cardiac events, MINS=myocardial injury after non-cardiac surgery.

* ICU stay duration was evaluated in 79 patients who were admitted to the ICU.

Myocardial injury is the most common cardiovascular complication after non-cardiac surgery and is around 30 times more common than postoperative myocardial infarction in patients with increased cardiovascular risk.[25] Many patients with myocardial injury do not satisfy the diagnostic criteria for myocardial infarction.[26] However, as myocardial injury has a poor prognosis, timely diagnosis and treatment are important.[27] MINS can be detected based on increased perioperative levels of cardiac troponin I,[8] which is a myocardial regulatory protein that is a highly sensitive and specific biomarker for myocardial damage. The incidence of MINS is approximately 8% in the general population after major non-cardiac surgery.[28] However, the present study included only high-risk patients, defined as those ≥45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age.[5] In this study, the incidence of MINS in high-risk patients who underwent radical cystectomy was 14.1%, which was higher than that in the general population after major non-cardiac surgery. These findings are consistent with those of a previous study by Puelacher et al, who reported an incidence of MINS in high-risk patients of 16% after non-cardiac surgery such as visceral, orthopedic, traumatic, vascular, and thoracic surgeries.[5] Therefore, preoperative evaluation of independent risk factors for MINS and postoperative monitoring of serum troponin I may be needed for the early detection of MINS in high-risk patients undergoing radical cystectomy.

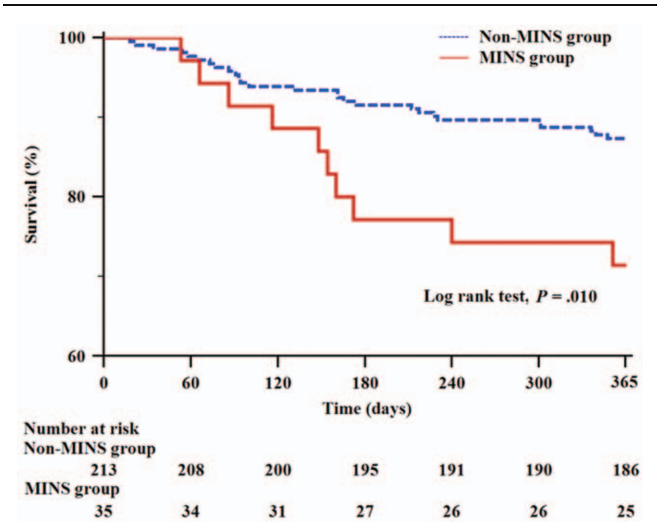

Figure 2. Kaplan–Meier curves of 1-year survival in the non-MINS (blue dashed line) and MINS (red solid line) groups comprising high-risk patients who underwent radical cystectomy. MINS was defined as serum troponin I concentration ≥0.04 mg/L within postoperative 3 days. High-risk patients were defined as those ≥45 years of age with a history of coronary artery disease, stroke, or peripheral artery disease or those ≥65 years of age. MINS=myocardial injury after non-cardiac surgery.

In the present study, E/E' ratio was a risk factor for MINS in high-risk cystectomy patients. The tissue Doppler-derived parameter (E/E' ratio) indicates left ventricular filling pressure[29] and is used to predict cardiovascular events and assess the prognosis of patients with cardiac disease.[30,31] Preoperative diastolic dysfunction, which is assessed using E/E' ratio, is also reportedly associated with cardiac complications after non-cardiac surgery.[6,32] Coronary blood flow predominantly occurs during the diastole period. Diastolic dysfunction (impairment of left ventricle relaxation) reduces early diastolic coronary flow and could provoke myocardial injury in the perioperative period.[33] Therefore, the preoperative evaluation of E/E' ratio by transthoracic echocardiography may be important for the prediction of MINS in high-risk cystectomy patients. Meticulous anesthetic management, especially preventing fluid volume overload, should be performed during radical cystectomy in high-risk patients.

We found that large volume blood transfusion, defined as four or more units of RBC transfusion during radical cystectomy,[21] to be significantly associated with MINS in high-risk cystectomy patients. Four units of RBCs is around 1000 mL; this volume of RBC transfusion may be associated with severe blood loss and significant increases in perioperative morbidity and mortality.[21,34] Large volume blood transfusion has been linked to poor outcomes with increased overall morbidity including cardiovascular complications in large retrospective studies of non-cardiac surgery.[35,36] The mechanisms by which large volume blood transfusion increases the risk of cardiovascular complications have not been well elucidated. However, circulatory derangement and metabolic, inflammatory, and coagulopathic complications caused by the transfusion of large volumes of RBCs could be involved. Moreover, these events may aggravate pre-existing medical conditions such as cardiovascular disease. Therefore, careful anesthetic management (ie, stopping anticoagulant use before surgery, maintaining a normal coagulation state, and avoiding volume overload) and meticulous surgical management should be performed to reduce large volume blood transfusion during radical cystectomy.

We found that MINS was significantly associated with higher ICU admission rate, ICU stay duration, postoperative MACEs, and 1-year mortality in high-risk patients who underwent radical cystectomy. To our knowledge, the present study is the first to demonstrate the clinical effect of MINS on postoperative outcomes among high-risk cystectomy patients. Previous studies have reported the long-term and short-term prognostic significance of MINS in vascular, orthopedic, thoracic, and abdominal surgeries.[28,37,38] Ausset et al demonstrated that MINS was an independent predictor of postoperative MACEs in hip surgery, a finding consistent with that of the present study.[38] Levy et al conducted a meta-analysis of the long-term prognostic value of MINS,[37] reporting 1-year mortality rates after surgery of 6.2% and 30.4%, respectively, among patients without and with

MINS.[37] In the present study, the 1-year mortality after radical cystectomy was significantly higher in the MINS group than in the non-MINS group (28.6% vs 12.7%). These results suggest that MINS had a negative effect on postoperative outcomes among high-risk patients who underwent radical cystectomy. Therefore, serum troponin I measurement is necessary to evaluate MINS, especially in high-risk cystectomy patients.

This study has several limitations. First, the retrospective observational design meant that we could not evaluate all potential confounding factors that may affect our results. However, we collected and analyzed all possible factors to minimize bias and obtain reliable results. Second, this study could have been affected by a selection bias because we only included patients whose postoperative troponin I levels were measured at the discretion of the anesthesiologists and urologists. Therefore, our findings should be interpreted with caution before wider generalization.

5. Conclusion

The results of this study demonstrated that MINS occurred in 14.1% of patients and that E/E' ratio and large volume blood transfusion were independent risk factors for MINS in high-risk patients who underwent radical cystectomy. Furthermore, postoperative MACEs and 1-year mortality were significantly higher in the MINS group than in the non-MINS group. These results suggest that preoperative evaluation of risk factors for MINS may provide useful information to detect postoperative cardiovascular complications in high-risk patients undergoing radical cystectomy.

Author contributions

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