Observational Study

Medicine®

OPEN

Prognostic value of high-sensitivity troponin I after cardiac surgery according to preoperative renal function

Karam Nam, MD[a], Kyung Won Shin, MD[a], Tae Kyong Kim, MD, PhD[b], Kyung Hwan Kim, MD, PhD[c], Ki-Bong Kim, MD, PhD[c], Yunseok Jeon, MD, PhD[a], Youn Joung Cho, MD, PhD[a,*]

Abstract

Cardiac troponin levels can be elevated without myocardial injury in patients with renal impairment. However, the prognostic value of elevated troponin levels after cardiac surgery has not been well evaluated in patients with renal impairment. We evaluated the relationship between postoperative troponin levels and mortality following cardiac surgery according to preoperative renal function.

Among 3661 patients underwent cardiac surgery between March 2005 and December 2015, 1909 patients were analyzed after excluding those with insufficient laboratory data, preoperative myocardial infarction, underwent Cox-Maze or redo surgery, or with a follow-up period <30 days. The primary outcome was risk of 30-day mortality according to elevated postoperative high-sensitivity cardiac troponin I (hs-cTnI) levels in varying degrees of renal function. Secondary outcomes included long-term cardiac-cause and all-cause mortality during the median follow-up of 52 months.

After adjustment for risk factors, elevated peak postoperative hs-cTnI was associated with 30-day mortality [adjusted odds ratio 1.028, 95% confidence interval (CI) 1.013–1.043, $P < .001$], long-term cardiac-cause [adjusted hazard ratio (HR) 1.013, 95% CI 1.009–1.017, $P < .001$] and all-cause mortality (adjusted HR 1.013, 95% CI 1.009–1.016, $P < .001$), in patients with preoperative normal renal function [estimated glomerular filtration rate (eGFR) ≥60 ml/minute/1.73 m^2]. However, in patients with renal impairment (eGFR < 60 ml/minute/1.73 m^2), hs-cTnI levels were not associated with mortality following cardiac surgery.

Elevated hs-cTnI levels following cardiac surgery did not predict short- and long-term mortality in patients with preoperative renal impairment.

Abbreviations: AKI = acute kidney injury, CABG = coronary artery bypass graft, CI = confidence interval, COPD = chronic obstructive pulmonary disease, CPB = cardiopulmonary bypass, CRRT = continuous renal replacement therapy, cTnI = cardiac troponin I, cTnT = cardiac troponin T, EF = ejection fraction, eGFR = estimated glomerular filtration rate, EMR = electronic medical records, GFR = glomerular filtration rate, hs-cTnI = high-sensitivity cardiac troponin I, HR = hazard ratio, ICU = intensive care unit, IDMS = isotope dilution mass spectrometry, IRB = institutional review board, IQR = inter-quartile range, KDIGO = Kidney Disease: Improving Global Outcomes, LOS = length of stay, LV = left ventricular, MDRD = modification of diet in renal disease, MI = myocardial infarction, OR = odds ratio, SD = standard deviation.

Keywords: cardiac surgery, mortality, renal impairment, troponin I

Editor: Wilhelm Mistiaen.

Clinical registration number: clinicaltrials.gov; identifier, NCT03540511

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. All data generated or analyzed during this study are included in this published article [and its supplementary information files].

The author declares that they have no conflicts of interest.

Supplemental Digital Content is available for this article.

[a] Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul National University College of Medicine, [b] Department of Anesthesiology and Pain Medicine, SMG-SNU Boramae Medical Center, [c] Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea.

[*] Correspondence: Youn Joung Cho, Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea (e-mail: mingming7@gmail.com).

How to cite this article: Nam K, Shin KW, Kim TK, Kim KH, Kim KB, Jeon Y, Cho YJ. Prognostic value of high-sensitivity troponin I after cardiac surgery according to preoperative renal function. Medicine 2020;99:20(e20040).

Received: 2 January 2020 / Received in final form: 18 March 2020 / Accepted: 24 March 2020

http://dx.doi.org/10.1097/MD.0000000000020040

1. Introduction

An elevated troponin level is known to be related with adverse outcomes after cardiac surgery.[1] However, in patients with chronic renal disease troponin levels can be consistently elevated without myocardial injury.[2,3] Although cardiac troponin I (cTnI) is a sensitive and specific detector of myocardial injury even in renal insufficiency,[4] elevated troponin levels may not correlate with postoperative outcomes in patients with renal dysfunction following cardiac surgery. However, there are no sufficient data on the prognostic value of postoperative cTnI levels after cardiac surgery in patients with preoperative renal impairment. We hypothesized that the prognostic value of postoperative cTnI levels would differ according to different preoperative renal function in patients undergoing cardiac surgery.

To evaluate our hypothesis, we conducted a retrospective analysis of postoperative cTnI levels and short- as well as long-term mortality in patients undergoing cardiac surgery according to varying degrees of preoperative renal function.

2. Methods

2.1. Study design and setting

This retrospective observational study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (approval number 1804-117-939 on April 25, 2018) and was registered at ClinicalTrials.gov (identifier NCT03540511). The IRB did not require informed patient consent for a retrospective study. The study followed the STROBE statement.

Electronic medical records (EMR) of adult patients (age ≥20 years) who underwent cardiac surgery at Seoul National University Hospital between March 1, 2005, and December 31, 2015, were reviewed. During this period, all medical records were recorded in electronic manner. All laboratory results, including radiologic and echocardiographic images and readings, and all medical documents made by medical personnel were recorded by the electronic medical recording system, which is independently validated. Cardiac surgery included coronary artery bypass grafting (CABG), cardiac valve surgery, and their combined surgery. The exclusion criteria included a Cox-Maze procedure or cryoablation, redo surgery, preoperative myocardial infarction (MI) defined according to the existing guidelines,[5] and no preoperative creatinine levels or high-sensitivity cTnI (hs-cTnI) levels checked less than 2 consecutive values within the first 5 postoperative days. Patients who had follow-up period <30 days were also excluded.

2.2. Baseline characteristics and data collection

Baseline characteristics, including sex, age, height, weight, type of surgery, emergency procedures, comorbidities, smoking history, laboratory results, and medications were obtained from EMR. Perioperative data included the durations of operation and anesthesia, intraoperative transfusion, as well as records on cardiopulmonary bypass (CPB). Postoperative variables included new onset continuous renal replacement therapy (CRRT), postoperative reintubation, re-exploration, postoperative delirium, new onset atrial fibrillation, postoperative acute kidney injury (AKI), intensive care unit (ICU) and postoperative hospital length of stay (LOS). Postoperative AKI was defined as an increase in serum creatinine ≥0.3 mg/dl within 48 hours or an increase to ≥1.5 times baseline within 7 days following surgery as per the criteria of the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury.[6]

2.3. Assessment of renal function

The baseline glomerular filtration rate (GFR) was determined using preoperative serum creatinine concentration. Isotope dilution mass spectrometry (IDMS) was used to calibrate the measured serum creatinine level. The estimated GFR (eGFR) was calculated using the modification of diet in renal disease (MDRD) prediction equation[7]:

$$\text{IDMS MDRD eGFR} = 175 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ for women}).$$

Baseline renal function was categorized based on the 2012 KDIGO Clinical Practice Guideline[8] as follows: normal renal function was defined as an eGFR ≥90 ml/minute/1.73 m^2; while mild, moderate and severe renal dysfunction were defined as 60–89, 30–59, and <30 ml/minute/1.73 m^2, respectively. Patients with a baseline eGFR ≥60 ml/minute/1.73 m^2 were categorized as having normal renal function in this study due to the bias of the equation when the eGFR is ≥60 ml/minute/1.73 m^2.[9]

2.4. High-sensitivity cardiac troponin I measurements

Levels of hs-cTnI after cardiac surgery were identified from EMR. The hs-cTnI levels were evaluated at 6 hours, 12 hours, 24 hours, and then daily up to 7 days postoperatively and also by the discretion of clinicians in charge of postoperative patient care according to the postoperative status of the patients. Measurements of hs-cTnI were performed using an Abbott Architect Plus Analyzer (i2000SR; Flex Ltd., San Jose, CA), which has a limit of detection of 0.0011 μg/L and a limit of blank of 0.0007 to 0.0013 μg/L. The 99th percentile in the normal population was 0.028 μg/L, with a sex-specific upper reference range of 0.033 μg/L for men and 0.013 μg/L for women. The peak hs-cTnI value during the first 5 postoperative days was determined.

2.5. Study outcomes

The primary outcome of the study was 30-day mortality after cardiac surgery. The secondary outcomes included long-term cardiac-cause and all-cause mortality after the surgery. Cardiac-cause mortality was defined as death from MI, cardiac arrhythmia, worsening heart failure, cardiogenic shock or sudden death. Data on death were obtained from EMR and the National Population Registry of the Korean National Statistical Office. In South Korea, all citizens are obligated to register to the National Population Registry both at birth and death.

2.6. Statistical analyses

Data are expressed as means ± standard deviation (SD), the median (inter-quartile range [IQR]) or number (proportion). Continuous data were compared using the Kruskal–Wallis test or analysis of variance according to the distribution of data; categorical variables were compared using the χ^2 test. For time-to-event variables, survival functions were estimated using the

Kaplan–Meier method. Comparisons were made by the log rank test. The mortality risks of elevated peak hs-cTnI levels as continuous variables for varying degrees of renal function were evaluated using a binomial logistic regression for 30-day mortality and a Cox proportional hazard regression analysis for long-term mortalities. The relationship between the renal function groups and the peak postoperative hs-cTnI was analyzed with interaction terms between them in the regression models due to the small numbers and events in eGFR subgroups. To identify independent risks for the association between preoperative renal function, postoperative peak hs-cTnI and mortality, multivariable logistic and Cox regression models included all potential covariates based on previously defined risk factors known to affect postoperative outcomes after cardiac surgery.[10–12] Risk factors were adjusted and a significance level of 0.2 was used to enter a variable into the multivariable model or to remove it from the model. For multivariable model 1, odds ratios (ORs) for 30-day mortality were adjusted for age, emergency, type of surgery, duration of operation, preoperative left ventricular (LV) ejection fraction (EF) and hematocrit, chronic obstructive pulmonary disease (COPD) or asthma, atrial fibrillation, use of aspirin, beta-blockers, and statin, intraoperative transfusion. Hazard ratios (HRs) for cardiac-cause mortality were adjusted for sex, age, BMI, emergency, type of surgery, duration of operation, preoperative LV EF and hematocrit, COPD or asthma, atrial fibrillation, use of aspirin, diuretics, digoxin, and statin, intraoperative transfusion. HRs for all-cause mortality were adjusted for sex, age, BMI, emergency, type of surgery, duration of operation, preoperative LV EF and hematocrit, hypertension, diabetes mellitus, COPD or asthma, atrial fibrillation, use of aspirin, angiotensin receptor blockers, beta-blockers, diuretics, digoxin, and statin, intraoperative transfusion. In multivariable model 2, postoperative variables were included along with the variables in model 1: for ORs for 30-day mortality, postoperative CRRT, re-exploration, AKI, and ICU LOS; and for HRs for cardiac-cause and all-cause mortality, postoperative CRRT, re-exploration, delirium, AKI, and ICU and postoperative hospital LOS were included. Normal renal function (eGFR ≥60 ml/minute/1.73 m^2) was used as the reference group for different degrees of renal impairment. All results are reported as either ORs or HRs with 95% confidence intervals (CIs). The effect of the peak postoperative hs-cTnI in each renal function group was tested using Bonferroni-corrected significance level of 0.0167 (0.05/3) for each outcome.

To plot long-term survival curves, the best cut-off limits of postoperative peak hs-cTnI to predict mortality were obtained from patients with follow-up period ≥3 years (n = 937) by using receiver operating characteristic (ROC) curve analysis. The cut-off for hs-cTnI associated with maximum sensitivity and specificity was estimated with Youden J index. The area under the ROC curve, corresponding 95% CI and *P*-values were calculated. Statistical analyses were performed using SPSS (version 21.0; IBM Corp., Armonk, NY) and R software (version 3.4.3; R Development Core Team, Vienna, Austria) for Microsoft Windows. A *P* value <.05 was considered statistically significant.

3. Results

3.1. Study population

A total of 3661 patients EMR were reviewed. Patients with no data on preoperative creatinine (n = 136), who underwent Cox-Maze or cryoablation (n = 464), redo surgery (n = 331), preoperative MI (n = 172), postoperative hs-cTnI less than 2 consecutive results (n = 630) and those with a follow-up period <30 days (n = 19) were excluded. Finally, 1909 patients were included in the final analyses (Fig. 1). A total of 1309 (69%) patients had preoperative normal renal function, 459 (24%) moderate and 141 (7%) severe preoperative renal impairment.

3.2. Patients' baseline characteristics

The patients baseline characteristics are presented in Table 1. More patients with severe renal impairment had hypertension, diabetes mellitus and atrial fibrillation. Patients with renal impairment experienced longer durations of operation, anesthesia and CPB. More patients with preoperative renal impairment received emergency surgery and transfused with red blood cells intraoperatively than did those with normal renal function. The use of angiotensin receptor blockers, calcium channel blockers, and diuretics were more common in patients with renal impairment (see Table S1, Supplemental Content, http://links.lww.com/MD/E159, which shows medications of included patients).

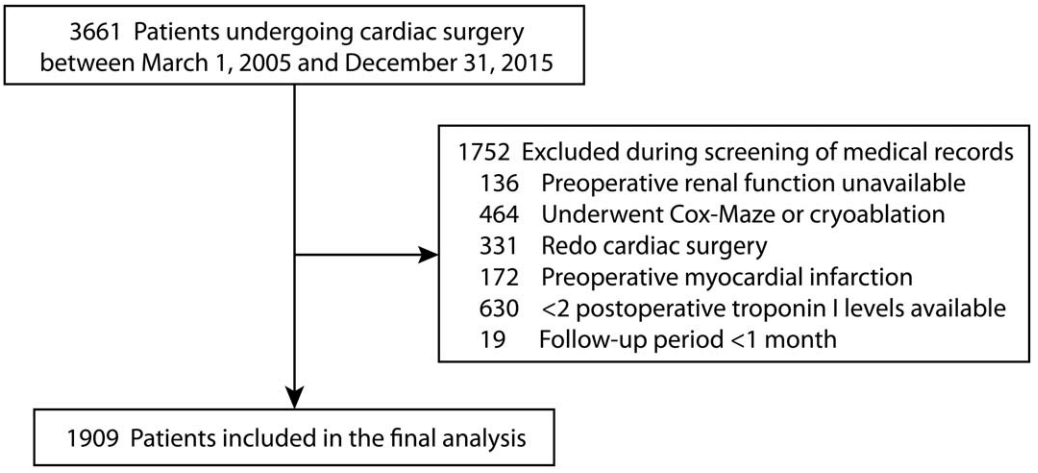

Figure 1. Study flow.

Table 1

Baseline characteristics of patients.

	eGFR (mL/min/1.73 m^2)			
	≥60 (n = 1309)	30 − 59 (n = 459)	<30 (n = 141)	*P* value
Demographics and medical history				
Age (y)	65 (57–71)	71 (64–76)	68 (61–72)	<.001
Male	953 (73%)	267 (58%)	100 (71%)	<.001
Body mass index (kg/m^2)	24.4 ± 3.2	24.7 ± 3.3	23.5 ± 2.7	.001
Current smoker	314 (24%)	65 (14%)	30 (21%)	<.001
Comorbidities				
Hypertension	729 (56%)	309 (67%)	111 (79%)	<.001
Diabetes mellitus	456 (35%)	221 (48%)	91 (65%)	<.001
Dyslipidaemia	385 (29%)	121 (26%)	30 (21%)	.080
Chronic obstructive pulmonary disease or asthma	36 (3%)	12 (3%)	6 (4%)	.563
Atrial fibrillation	112 (9%)	43 (9%)	27 (19%)	<.001
Preoperative haematocrit (%)	34 ± 5	34 ± 5	33 ± 4	.001
Preoperative LV EF (%)	56 ± 12	55 ± 12	51 ± 13	<.001
Operative data				
Duration of operation (min)	368 ± 80	381 ± 84	391 ± 89	<.001
Duration of anaesthesia (min)	441 ± 82	454 ± 85	470 ± 94	<.001
Use of cardiopulmonary bypass	340 (26%)	120 (26%)	37 (26%)	.996
Duration of cardiopulmonary bypass (min)	196 ± 65	204 ± 71	235 ± 76	.003
Emergency operation	216 (17%)	84 (18%)	42 (30%)	<.001
Intraoperative use of RBC (unit)	1 (0–3)	3 (1–4)	3 (2–5)	<.001
Type of surgery				<.001
CABG	998 (76%)	352 (77%)	108 (76%)	
Valve surgery	268 (21%)	70 (15%)	25 (18%)	
CABG + valve surgery	43 (3%)	37 (8%)	8 (6%)	
Peak postoperative hs-cTnI (μg/L)	1.00 (0.37–5.59)	1.70 (0.47–7.47)	1.62 (0.67–7.20)	<.001

Values are reported as median (inter-quartile range), number (%), or mean ± standard deviation. CABG = coronary artery bypass grafting, eGFR = estimated glomerular filtration rate, hs-cTnI = high-sensitivity cardiac troponin I, LV EF = left ventricular ejection fraction, RBC = red blood cell.

3.3. Postoperative troponin levels and in-hospital events

The renal impairment groups experienced higher postoperative peak hs-cTnI values compared to the normal renal function group (Table 1). New onset postoperative CRRT, reintubation, re-exploration, delirium, atrial fibrillation, and AKI were more common in preoperative renal impairment groups compared with the normal renal function group (see Table S2, Supplementary Content, http://links.lww.com/MD/E160, which shows postoperative events after cardiac surgery). The ICU and postoperative hospital LOS increased with increasing degrees of renal impairment (see Table S2, Supplementary Content, http://links.lww.com/MD/E160).

3.4. Study outcomes

Thirty three (1.7%) patients died within 30 days after cardiac surgery. During long-term follow-up of median (IQR) 52 (22–87) months (maximum 131 months), cardiac-cause mortality was 6.0% (115/1909) and all-cause mortality was 19.1% (364/1909). According to the degree of preoperative renal function, patients with renal impairment (eGFR <60 ml/minute/1.73 m^2) had higher mortality rates compared to those with normal renal function (Table 2).

Unadjusted and adjusted risks for mortality following cardiac surgery with increasing peak postoperative hs-cTnI in varying preoperative renal function groups are presented in Table 2. After adjustment, increased postoperative peak hs-cTnI was an independent predictor of 30-day, and long-term cardiac- and all-cause mortality following cardiac surgery in patients with preoperative normal renal function (all $P < .001$, Fig. 2 and Table 2). However, in patients with preoperative renal impairment (eGFR <60 ml/minute/1.73 m^2) elevated postoperative hs-cTnI was not related to short- or long-term mortality after cardiac surgery.

In additional analysis for impact of postoperative AKI on outcome, mortality after cardiac surgery was higher in patients with postoperative AKI than in those without (see Table S3, Supplementary Content, http://links.lww.com/MD/E161). After adjustment, increased postoperative hs-cTnI had predictive value for 30-day, and long-term mortality in patients developed postoperative AKI. However, it was not related to mortality in the absence of postoperative AKI, after adjustment for confounding variables.

In ROC curve analysis, the best cut-off limits to predict long-term cardiac-cause and all-cause mortality in normal renal function group were 1.055 μg/L and 1.365 μg/L, respectively (see Fig., Supplementary Content, http://links.lww.com/MD/E162, which illustrates ROC curve of long-term mortality). The cut-off value for predicting 30-day mortality was 7.345 μg/L. Survival curves according to increased postoperative hs-cTnI with cut-off limits in patients with preoperative normal renal function during the follow-up period are presented in Figure 3.

4. Discussion

Increased peak postoperative hs-cTnI following cardiac surgery was independently associated with increased 30-day mortality, and long-term cardiac-cause and all-cause mortality in patients with normal preoperative renal function. However, in patients with impaired preoperative renal function, postoperative hs-cTnI

Table 2

Odds ratios and hazard ratios for mortality after cardiac surgery according to preoperative renal function.

					Model 1		Model 2	
	eGFR (mL/min/1.73 m^2)	Incidence	Unadjusted OR (95% CI)	Unadjusted *P* value	Adjusted OR (95% CI)	Adjusted *P* value	Adjusted OR (95% CI)	Adjusted *P* value
30-day mortality				<.001*		<.001*		.017*
	≥60	12/1309 (0.9%)	1.034 (1.021–1.046)	<.001	1.031 (1.018-1.045)	<.001	1.028 (1.013–1.043)	<.001
	30–59	11/459 (2.4%)	1.009 (0.993–1.026)	.283	1.008 (0.989-1.027)	.419	0.999 (0.979–1.019)	.925
	<30	10/141 (7.1%)	1.003 (0.992–1.013)	.610	1.000 (0.986-1.013)	.970	0.999 (0.982–1.016)	.898
			Unadjusted HR (95% CI)	Unadjusted *P* value	Adjusted HR (95% CI)	Adjusted *P* value	Adjusted HR (95% CI)	Adjusted *P* value
Long-term cardiac-cause mortality				.009*		.029*		.089*
	≥60	51/1309 (3.9%)	1.013 (1.010–1.016)	<.001	1.013 (1.010–1.017)	<.001	1.013 (1.009–1.017)	<.001
	30–59	40/459 (8.7%)	1.012 (1.004–1.019)	.002	1.015 (1.007–1.023)	<.001	1.007 (0.999–1.016)	.077
	<30	24/141 (17.0%)	1.004 (0.999–1.009)	.143	1.004 (0.998–1.011)	.212	1.004 (0.995–1.012)	.384
Long-term all-cause mortality				<.001*		.001*		.002*
	≥60	157/1309 (12.0%)	1.012 (1.010–1.015)	<.001	1.013 (1.010–1.017)	<.001	1.013 (1.009–1.016)	<.001
	30–59	130/459 (28.3%)	1.004 (0.998–1.011)	.209	1.009 (1.001–1.016)	.026	1.005 (0.998–1.013)	.142
	<30	77/141 (54.6%)	1.002 (0.998–1.007)	.276	1.002 (0.997–1.007)	.521	1.001 (0.996–1.007)	.634

CI = confidence interval, eGFR = estimated glomerular filtration rate, HR = hazard ratio, OR = odds ratio.

* *P* value for interaction between preoperative renal function groups and the peak postoperative hs-cTnI levels.

had no prognostic value in regard to short- and long-term mortality.

Patients with renal impairment often exhibit elevated serum troponin levels, even in the absence of apparent myocardial injury.[3] Of patients visiting nephrology clinics with an eGFR ≤60 ml/minute/1.73 m^2, 38%, and 68% had abnormally elevated cTnI and cardiac troponin T (cTnT), respectively, without acute coronary disease.[2] However, it is not conclusively known whether the primary contributor to elevated troponin concentrations associated with renal dysfunction is reduced elimination or increased release.[13] Renal dysfunction therefore affects the diagnostic value of hs-cTnI for MI. Specificity and positive predictive values of hs-cTnI decreased with renal impairment, particularly at an eGFR <30 ml/minute/1.73 m^2, in patients presenting symptoms suggesting myocardial ischemia.[14] Additionally, it has been proposed that the cut-off values for hs-cTnT in diagnosing acute MI should be increased with increasing stages of chronic kidney disease.[3] In this context, the interpretation of elevated troponin levels in patients with renal impairment can be case-specific but not conclusive.

Troponin levels are well-known indicators predicting adverse outcomes in various clinical settings.[15,16] Increased troponin levels corresponded significantly with morbidity and mortality in non-surgical and non-cardiac surgical settings. Even in patients with chronic renal dysfunction with an eGFR <60 ml/minute/1.73 m^2 undergoing coronary angiography, hs-cTnI was a strong predictor of death, cardiac death and major adverse cardiac events during the median follow-up of 4.8 years.[17] Elevated troponin levels in the early postoperative period after non-cardiac surgery were associated with 30-day mortality.[18] Similarly, after intermediate- or high-risk non-cardiac surgery (orthopedic, gynecological, urological, vascular or other general surgery), elevated postoperative hs-cTnT was associated with a dose-dependent increase in 30-day and long-term mortality risk during the median follow-up of 2 years, in patients with preoperative eGFR ≥30 ml/minute/1.73 m^2.[19] However, there are insufficient data on prognostic value of postoperative troponin levels in patients with renal dysfunction undergoing cardiac surgery.

Following cardiac surgery, postoperative troponin release can be caused by intraoperative heart manipulations, which may increase serum cardiac troponin levels after the surgery.[20] Thus, increased troponin levels in the early postoperative period after cardiac surgery can be considered as a non-significant phenomenon that likely will not adversely impact patient outcomes. Nevertheless, postoperative cardiac troponin levels well predicted 30-day, 1-year, and 3-year mortality following cardiac surgery after adjusting for potentially confounding variables.[21,22] Elevated postoperative cTnI was also an independent predictor of death after CABG over a 2-year follow-up.[23] However, the relationship between preoperative renal function and postoperative troponin levels was not fully evaluated in previous studies.[23] Thus it is unclear whether the prognostic value of postoperative troponin maintains in patients with preoperative renal impairment undergoing cardiac surgery.

Evaluation of cardiac troponin release is an important part of post-cardiac surgery patient management that is widely used in clinical practice. Previous authors found that the best cut-off value was 4.25 μg/L of cTnI at 1 hour after CABG or valve surgery to predict hospital mortality from their registry database, without consideration of preoperative renal function.[24] Increased peak cTnI level until the next morning after aortic or mitral valve surgery was an independent risk factor for hospital mortality, but the results were not stratified with the degree of preoperative renal function.[25] In another study, elevated cTnI at 20 hours after CABG or valve surgery independently predicted in-hospital death, but the authors did not evaluate the influence of patients renal function.[26] In that study, the baseline creatinine clearance was 68 and 58 ml/minute in survivors and non-survivors, respectively ($P = .06$).

In the current study, elevated postoperative hs-cTnI was an independent predictor of 30-day, as well as long-term cardiac-cause and all-cause mortality following cardiac surgery only in

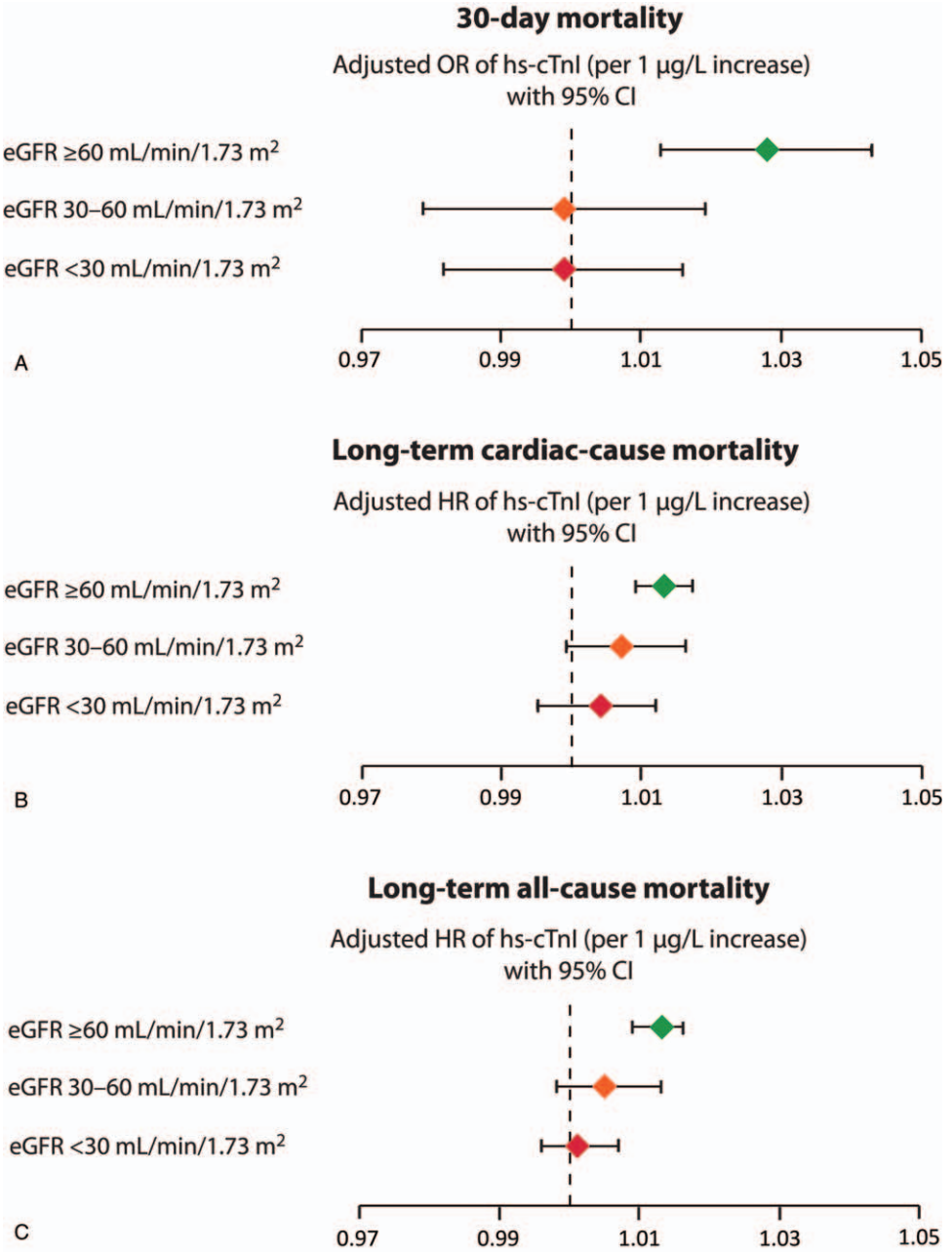

Figure 2. Forest plots of (A) 30-day, long-term (B) cardiac-cause and (C) all-cause mortality with increasing postoperative peak cardiac troponin I levels following cardiac surgery in different stages of preoperative renal function. eGFR = estimated glomerular filtration rate.

patients with normal renal function. The best cut-off value for predicting 30-day mortality was 7.345 μg/L in patients with preoperative normal renal function, which was partly corresponds to the optimal cTnI cut-off level of 7.97 μg/L within 12 hours after CABG surgery to identify MI related to surgery previously.[27] Therefore, the patients with higher than the cut-off limits in the early postoperative period would have increased risks for short- and long-term mortality following cardiac surgery if their preoperative renal function was normal.

However, in patients with renal impairment (preoperative eGFR <60 ml/minute/1.73 m^2), elevated postoperative hs-cTnI values were not associated with mortality following cardiac surgery in this study. It is partly explained that the renal dysfunction influences the diagnostic accuracy of cardiac troponin levels in detecting perioperative MI related to cardiac surgery.[28] Our results are in accordance with a previous study in high-risk patients for AKI (preoperative serum creatinine >2 mg/dl [177 μmol/L]) undergoing CABG or valve surgery, in which postoperative hs-cTnI was not correlated with 1- or 3-year mortality following surgery.[29] Therefore, according to these results, increased cardiac troponin levels may have little predictive value for postoperative short- or long-term mortality after cardiac surgery in patients with preoperative renal impairment. Elevated hs-cTnI levels following cardiac surgery in these patients should be interpreted in consideration of this relationship.

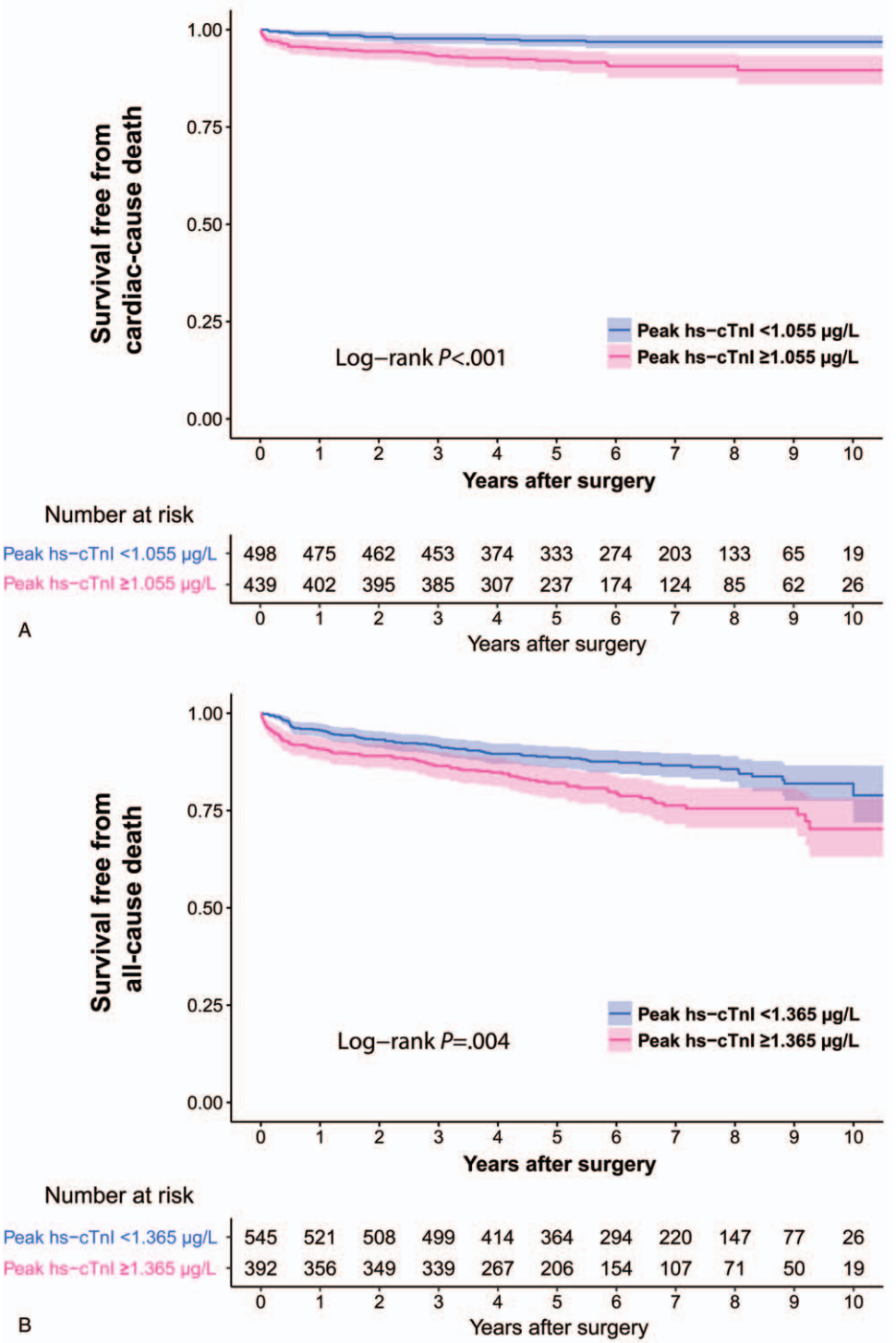

Figure 3. Kaplan-Meier survival curves depicting freedom from (A) cardiac-cause and (B) all-cause death according to the peak postoperative troponin I levels using the cut-off limits in patients with normal renal function. hs-cTnI = high-sensitivity cardiac troponin I.

In our sub-analysis, elevated postoperative hs-cTnI was an independent predictor for short- and long-term mortality in patients who developed postoperative AKI. Therefore, post-cardiac surgery patients superimposed with AKI may have greater risk for death with increasing postoperative hs-cTnI levels. However, hs-cTnI itself did not predict mortality after cardiac surgery after adjustment for other confounding variables in the absence of AKI.

5. Limitations

The limitations of this study include the insufficient data on preoperative troponin levels in this cohort. However, it is a practical aspect of real clinical practice because not all patients undergo troponin measurement preoperatively. We excluded patients with recent history of myocardial ischemia from analyses, therefore we believe that those with acutely elevated

troponin levels might have not been included in this study. Moreover, not only changes in troponin levels between the preoperative and postoperative periods but also the absolute value of postoperative troponin levels was an independent predictor of short-term mortality in a previous study.[30] EuroSCORE or STS risk scores were not included in this analysis due to the lack of information at the time of hospital admission from EMR. However, we included variables, many of which are mostly the components of those risk evaluation systems, in our multivariable analysis. Lastly, approximately 17% (630/3661) of patients were excluded because consecutive postoperative troponin levels were not available during the early postoperative period. Similarly, in a previous study evaluated the prognostic value of postoperative troponin levels in non-cardiac surgery,[19] about 27% (1287/4825) of cases were excluded because postoperative troponin levels were not obtainable. We believe that our study evaluated the relationship of currently available postoperative hs-cTnI levels and outcomes following cardiac surgery according to varying degrees of preoperative renal function in best clinical practice. Nevertheless, these results should be applied cautiously to other surgical patients and should be interpreted in consideration of practical limitations of the study. For further evaluation, prospective studies are required including preoperative troponin assessment and serial data on postoperative troponin measurements.

6. Conclusions

In conclusion, the peak hs-cTnI level in the early postoperative period following cardiac surgery had no prognostic value in patients with preoperative renal impairment (eGFR <60 ml/minute/1.73 m^2), while it was an independent predictor of mortality in patients with normal renal function. During management of patients undergoing CABG or cardiac valve surgery, elevated hs-cTnI levels in the early postoperative period should be interpreted in consideration of patients' preoperative renal function.

Acknowledgments

We thank to the Medical Research Collaborating Center for their advice concerning the statistical analyses.

Author contributions

Data curation: Karam Nam, Kyung Won Shin, Tae Kyong Kim, Kyung Hwan Kim, Ki-Bong Kim.
Formal analysis: Karam Nam, Youn Joung Cho.
Investigation: Karam Nam, Kyung Won Shin, Tae Kyong Kim, Kyung Hwan Kim, Youn Joung Cho.
Methodology: Karam Nam, Kyung Won Shin, Tae Kyong Kim, Ki-Bong Kim, Youn Joung Cho.
Validation: Karam Nam, Kyung Won Shin, Kyung Hwan Kim.
Visualization: Kyung Won Shin, Youn Joung Cho.
Supervision: Tae Kyong Kim, Kyung Hwan Kim, Yunseok Jeon.
Conceptualization: Ki-Bong Kim, Yunseok Jeon, Youn Joung Cho.
Resources: Ki-Bong Kim, Yunseok Jeon.
Project administration: Yunseok Jeon.
Writing – review & editing: Yunseok Jeon.
Writing – original draft: Youn Joung Cho.

References

[1] Mokhtar AT, Begum J, Buth KJ, et al. Cardiac troponin T is an important predictor of mortality after cardiac surgery. J Crit Care 2017;38:41–6.
[2] deFilippi C, Seliger SL, Kelley W, et al. Interpreting cardiac troponin results from high-sensitivity assays in chronic kidney disease without acute coronary syndrome. Clin Chem 2012;58:1342–51.
[3] Yang H, Liu J, Luo H, et al. Improving the diagnostic accuracy of acute myocardial infarction with the use of high-sensitive cardiac troponin T in different chronic kidney disease stages. Sci Rep 2017;7:41350.
[4] Freda BJ, Tang WH, Van Lente F, et al. Cardiac troponins in renal insufficiency: review and clinical implications. J Am Coll Cardiol 2002;40:2065–71.
[5] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). Circulation 2018;138:e618–51.
[6] KDIGO AKI Work GroupKDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012;2:1–38.
[7] Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145:247–54.
[8] Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int 2014;85:49–61.
[9] Stevens LA, Coresh J, Feldman HI, et al. Evaluation of the modification of diet in renal disease study equation in a large diverse population. J Am Soc Nephrol 2007;18:2749–57.
[10] Crawford TC, Magruder JT, Grimm JC, et al. Complications after cardiac operations: all are not created equal. Ann Thorac Surg 2017;103:32–40.
[11] Ellenberger C, Sologashvili T, Cikirikcioglu M, et al. Risk factors of postcardiotomy ventricular dysfunction in moderate-to-high risk patients undergoing open-heart surgery. Ann Card Anaesth 2017;20:287–96.
[12] Beller JP, Hawkins RB, Mehaffey JH, et al. Does preoperative troponin level impact outcomes after coronary artery bypass grafting? Ann Thorac Surg 2018;106:46–51.
[13] van der Linden N, Cornelis T, Kimenai DM, et al. Origin of cardiac troponin t elevations in chronic kidney disease. Circulation 2017;136:1073–5.
[14] Gunsolus I, Sandoval Y, Smith SW, et al. Renal dysfunction influences the diagnostic and prognostic performance of high-sensitivity cardiac troponin i. J Am Soc Nephrol 2018;29:636–43.
[15] Everett BM, Brooks MM, Vlachos HE, et al. Troponin and cardiac events in stable ischemic heart disease and diabetes. N Engl J Med 2015;373:610–20.
[16] Blankenberg S, Salomaa V, Makarova N, et al. Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. Eur Heart J 2016;37:2428–37.
[17] Sandesara PB, O'Neal WT, Tahhan AS, et al. Comparison of the association between high-sensitivity troponin i and adverse cardiovascular outcomes in patients with versus without chronic kidney disease. Am J Cardiol 2018;121:1461–6.
[18] Writing Committee for the VSI, Devereaux PJ, Biccard BM, et al. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. JAMA 2017;317:1642–51.
[19] Liem VGB, Hoeks SE, Grune F, et al. Prognostic value of postoperative high-sensitivity troponin T in patients with different stages of kidney disease undergoing noncardiac surgery. Br J Anaesth 2018;120:84–93.
[20] Nesher N, Alghamdi AA, Singh SK, et al. Troponin after cardiac surgery: a predictor or a phenomenon? Ann Thorac Surg 2008;85:1348–54.
[21] Mauermann E, Bolliger D, Fassl J, et al. Postoperative high-sensitivity troponin and its association with 30-day and 12-month, all-cause mortality in patients undergoing on-pump cardiac surgery. Anesth Analg 2017;125:1110–7. PMID: 28537984.
[22] Lurati Buse GA, Koller MT, Grapow M, et al. The prognostic value of troponin release after adult cardiac surgery - a meta-analysis. Eur J Cardiothorac Surg 2010;37:399–406.
[23] Fellahi JL, Gue X, Richomme X, et al. Short- and long-term prognostic value of postoperative cardiac troponin I concentration in patients undergoing coronary artery bypass grafting. Anesthesiology 2003;99:270–4.
[24] van Geene Y, van Swieten HA, Noyez L. Cardiac troponin I levels after cardiac surgery as predictor for in-hospital mortality. Interact Cardiovasc Thorac Surg 2010;10:413–6.

[25] Paparella D, Guida P, Caparrotti S, et al. Myocardial damage influences short- and mid-term survival after valve surgery: a prospective multicenter study. J Thorac Cardiovasc Surg 2014;148: 2373–9.
[26] Lasocki S, Provenchere S, Benessiano J, et al. Cardiac troponin I is an independent predictor of in-hospital death after adult cardiac surgery. Anesthesiology 2002;97:405–11.
[27] Jorgensen PH, Nybo M, Jensen MK, et al. Optimal cut-off value for cardiac troponin I in ruling out Type 5 myocardial infarction. Interact Cardiovasc Thorac Surg 2014;18:544–50.
[28] Cubero-Gallego H, Heredia-Rodriguez M, Tamayo E. Influence of impairment in renal function on the accuracy of high-sensitivity cardiac troponin T for the diagnosis of perioperative myocardial infarction after heart valve surgery. Interact Cardiovasc Thorac Surg 2018;27:234–7.
[29] Belley-Cote EP, Parikh CR, Shortt CR, et al. Association of cardiac biomarkers with acute kidney injury after cardiac surgery: A multicenter cohort study. J Thorac Cardiovasc Surg 2016;152:245–51.
[30] Brown JC, Samaha E, Rao S, et al. High-sensitivity cardiac troponin t improves the diagnosis of perioperative mi. Anesth Analg 2017;125: 1455–62.