Comparison between the Effects of Pre- and Postoperative Myocardial Injuries on 30-Day Mortality After Non-Cardiac Surgery: A Retrospective Analysis Using an Inverse Probability Weighting Adjustment

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Abstract

**Background:** Although both pre- and postoperative myocardial injuries are strongly associated with an increased postoperative mortality, no study has directly compared the effects of pre- and postoperative myocardial injuries on 30-day mortality after non-cardiac surgery. Therefore, we evaluated and compared the effects of pre- and postoperative myocardial injury on 30-day mortality after non-cardiac surgery.

**Methods:** From January 2010 to December 2016, patients undergoing non-cardiac surgery were stratified into either the normal (n = 3,182), preoperative myocardial injury (n = 694), or postoperative myocardial injury (n = 756) groups. Myocardial injury was defined as a sole elevation of cardiac troponin value above the 99th percentile upper reference limit without ischemic symptom using the 4th universal definition of myocardial infarction. Patients in the preoperative myocardial injury group were further divided into the attenuated (n = 177) or persistent myocardial injury group (n = 517) according to the changes in postoperative cardiac troponin level. As the primary outcome, postoperative 30-day mortalities were compared among the groups using the weighted Cox proportional-hazards regression models with the inverse probability weighting.

**Results:** Compared with the normal group, postoperative 30-day mortality was increased significantly both in the pre- and postoperative myocardial injury groups (1.4% vs. 10.7%; hazard ratio [HR] 3.12; 95% confidence interval [CI] 1.62-6.01; \( p = 0.001 \) and 1.4% vs. 7.4%; HR 4.49; 95% CI 2.34-8.60; \( p < 0.001 \), respectively), however, there was no difference between the pre- and postoperative myocardial injury groups (HR, 1.44; 95% CI 0.79-2.64; \( p = 0.45 \)). In addition, the attenuated
myocardial injury group showed a significantly lower postoperative 30-day mortality than the persistent myocardial injury group (5.6% vs. 12.4%; HR 2.23; 95% CI 1.17–4.44; p = 0.02).

**Conclusion:** In patients undergoing non-cardiac surgery, preoperative myocardial injury also increased postoperative 30-day mortality to a similar degree of postoperative myocardial injury. In addition, attenuation of preoperative myocardial injury might decrease in 30-day mortality after non-cardiac surgery.

**INTRODUCTION**

More than 1% of patients aged 45 years or older die during early postoperative period after major non-cardiac surgery [1, 2]. This mortality rate is about 1000 times greater than anaesthesia-related intraoperative mortality that has currently decreased to less than 0.001% [3, 4]. Myocardial injury and infarction are considered as the leading causes of the postoperative mortality, accounting for a quarter of all postoperative deaths [5]. However, since most postoperative myocardial injury and/or infarction occurs within 2 days after non-cardiac surgery when cardiac symptoms can be masked by analgesic medication [6], postoperative myocardial injury sometimes can be identified only by the cardiac troponin (cTn) elevation.

Many previous studies have shown that pre- and postoperative cTn elevations, regardless of ischemic signs and/or symptoms, are strongly associated with postoperative mortality in patients undergoing non-cardiac surgery [1, 6–13]. In addition, myocardial injury was clearly differentiated from type 2 myocardial infarction based on the presence of signs and/or symptoms of clinical myocardial ischemia and specified into acute and chronic form according to the changes in hs-
cTn level in the recently published 4th universal definition of myocardial infarction [14].

However, to the best of our knowledge, there has been no study to compare the effects of pre- and postoperative myocardial injury on 30-day mortality after non-cardiac surgery directly. In addition, diagnostic criteria and clinical impact of perioperative myocardial injury based on the hs-cTn level changes appear not to be fully established. Considering that significant preoperative cTn elevation is found in more than 13% of patients [6] and that it is strongly associated with high postoperative mortality [10], the effect of preoperative myocardial injury on the postoperative deaths in non-cardiac surgery might need to be evaluated and compared, separately form that of postoperative myocardial injury. Therefore, the aim of our study was to evaluate and compare the effects of pre- and postoperative myocardial injuries, defined by the changes in hs-cTn level of the 4th universal definition of myocardial infarction, on 30-day mortality after non-cardiac surgery.

MATERIALS AND METHODS

This retrospective analysis included adult patients who had undergone non-cardiac surgery at Samsung Medical Center (Seoul, Korea). The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB No. 2017-10-109-003) and registered in Clinical Research Information Service (KCT0004348). This study was also conducted in accordance with the principles of the Declaration of Helsinki. Since the present study only used the routinely gathered patient data and had no risk of enrolled patients, the need for individual informed consent was waived by our Institutional Review Board.

Patients and Management
We included all adult non-cardiac surgical patients who had the hs-cTn results within 48 hours before and after surgery at Samsung Medical Center between January 2010 to December 2016. After excluding 7 patients in whom cardiopulmonary resuscitation was performed before postoperative hs-cTn measurement, 4,612 patients were enrolled into the analysis. According to the time point of serum hs-cTn elevation, the patients were stratified into either of the following three groups; the normal (n = 3,182), preoperative myocardial injury (n = 694), and postoperative myocardial injury (n = 756). Myocardial injury was defined as a sole elevation of cTn value above the 99th percentile of upper reference limit based on the 4th universal definition of myocardial infarction [14]. The patients in the preoperative myocardial injury group were further divided into the attenuated or persistent myocardial injury group according to the postoperative hs-cTn level (Fig. 1).

Perioperative evaluation and management including hs-cTn measurement were performed according to our institutional protocols mainly based on current guidelines. Hs-cTn I was measured selectively based on attending clinician’s decision. An automated analyzer with highly sensitive immunoassay (Advia Centaur XP, Siemens Healthcare Diagnostics, Erlangen, Germany) was used for measuring hs-cTn level. Lowest limit of detection was 6 ng/L, and normal upper limit was 40 ng/L according to the 99th percentile reference [15].

Data Collection and Extraction

Data were obtained from a paperless electronic medical record system of Samsung Medical Center. Initially, the patients with both pre- and postoperative hs-cTn measurement were identified with the aid of our Institutional Medical Information Department. Following the initial data collection, the “Clinical Data Warehouse Darwin-C” program which was designed for searching and retrieving the deidentified
medical records was used for the further data extraction. In this system, death of patients was consistently updated from the national database. An investigator (J.J. Min) who was blinded to the serum hs-cTn level organized baseline patients’ characteristics and postoperative clinical outcomes except death were collected through manual review of each patient’s medical records by the independent investigators (H. Cho and K.Y. Hong) who were blinded to the serum hs-cTn level and baseline characteristics.

Study Outcomes and Definitions

Definitions of clinical outcomes were based on a report on cardiovascular events in clinical trials by American College of Cardiology Foundation/American Heart Association task force [16]. The primary outcome was 30-day mortality. Secondary outcomes included in-hospital mortality, overall mortality, cardiovascular mortality, and type 1 myocardial infarction, coronary revascularization, stroke, newly developed atrial fibrillation, newly developed heart failure, and postoperative acute kidney injury during hospital stay. Type 1 myocardial infarction was defined as an angiographically proven myocardial infarction according to the 4th universal definition [14]. Heart failure was defined when the patient exhibits new or worsening symptoms of heart failure on presentation, has objective evidence of new or worsening heart failure, and receives initiation or intensification of treatment specifically for heart failure. Postoperative acute kidney injury was defined as either an increase in serum creatinine greater than or equal to 0.3 mg/dL within postoperative 48 hours or an increase to greater than or equal to 1.5 times baseline within seven days according to the Kidney Disease Improving Global Outcomes criteria [17].
Statistical Analysis

We used Analysis of variance tests or Kruskal-Wallis tests to compare differences in baseline characteristics, as applicable, and presented as mean ± standard deviation (SD) or median with interquartile range (IQR) for continuous variables. Kaplan-Meier estimates were used to construct survival curves and compared with the log-rank test. Cox regression was used to evaluate 30-day, in-hospital, overall and cardiovascular mortalities, and logistic regression was used to compare other outcomes during hospital stay. To further reduce selection bias and maximize the study power while maintaining a balance in confounding factors between the three groups, we conducted rigorous adjustment for differences in baseline characteristics of patients using the weighted Cox proportional-hazards regression models with the inverse probability weighting [18]. According to this technique, weights for patients with pre- and postoperative myocardial injury were the inverse of the propensity score and weights for the normal patients were the inverse of 1 - the propensity score. Inverse probability weighting adjusted cox regression was used to evaluate all-cause, 30-day and in-hospital mortality. We adopted a post hoc Bonferroni correction, which allowed for the primary outcome to be tested at an alpha level of 0.0167 (0.05 ÷ 3). The reduction in the risk of outcome was compared using either Cox or logistic regression model, as applicable. Adjusted hazard ratio (HR) or odds ratio (OR) with 95% confidence interval (CI) was reported for immediate clinical outcomes. Statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC) and R 3.5.3 (Vienna, Austria; http://www.R-project.org/). All tests were 2-tailed and p < 0.05 was considered statistically significant.

RESULTS
The flowchart of the patients is presented in Figure 1. Of the enrolled 4,612 patients, 694 (4.8%) patients with preoperative hs-cTn elevation were stratified into the preoperative myocardial group. After stratifying 756 (4.1%) patients with postoperative hs-cTn elevation into the postoperative myocardial group, the remaining 3,182 (91.1%) patients with normal hs-cTn level at pre- and postoperative measurements were stratified into the normal group. The patients in the preoperative myocardial group were further divided to the attenuated (n = 177, 25.5%) or persistent (n = 517, 74.5%) myocardial groups.

The baseline characteristics of the three groups are summarized in Table 1, and the types of surgery were described in Additional file 1: Table S1, Supplemental Digital Content 1. Regarding the normal group as a reference group, the preoperative myocardial injury group showed higher rate of diabetes, history of coronary revascularization, heart failure, arrhythmia, stroke, chronic kidney disease, chronic lung disease, and infectious state than the normal group. In addition, the preoperative group showed increased use of preoperative beta-blocker and decreased use of statin. The postoperative myocardial injury group showed higher rate of diabetes, history of coronary revascularization, heart failure, valve disease, chronic kidney disease, and aortic disease than the normal group. Preoperative beta-blocker therapy showed also higher incidence in the preoperative myocardial injury group. In the blood test, the pre- and postoperative myocardial injury group showed decreased hemoglobin and increased creatinine and liver enzyme levels than the normal group. Regarding the operative variables, the postoperative myocardial injury group showed higher incidence of high-risk operation than the other two groups. The rate of emergent operation, intraoperative inotropic and colloid use were higher in both myocardial injury groups compared to the normal
group. The postoperative myocardial injury group showed the longest operative duration. After an inverse probability weighting adjustment, balance between the three groups were improved and presented as the change of the standardized mean difference (Table 1).

Clinical outcomes were compared pairwise. The 30-day mortalities were 1.4 % in the normal group, 10.7% in the preoperative myocardial injury group, and 7.4% in the postoperative myocardial injury group, respectively. In univariate Cox regression analysis, both pre-and postoperative myocardial injury was significantly associated with increased 30-day mortality (HR, 8.31; 95% CI, 5.72–12.07; \(p<0.001\); HR, 2.36; 95% CI, 1.94-2.88; \(p<0.001\), respectively) (Table 2, Fig. 2). After inverse probability weighting adjustment, the result showed consistent 30-day mortality differences (HR, 3.12; 95% CI, 1.62–6.01; \(p = 0.001\); HR, 4.49; 95% CI, 4.49; 95% CI, 2.34-8.60; \(p<0.001\)), and it was not significantly different between the pre-and postoperative myocardial injury groups (HR, 1.44; 95% CI, 0.79–2.64; \(p = 0.45\)) (Table 2). Acute kidney injury was increased in both myocardial injury group (OR, 2.13; 95% CI, 1.43-3.19; \(p<0.001\); OR, 3.11; 95% CI, 2.30-4.21; \(p<0.001\), respectively) (Table 2). Other secondary outcomes were described in Table 2.

Additionally, the patients with attenuation of preoperative myocardial injury were compared to those with persistent myocardial injury (Additional file 1: Table S2). 30-day mortality was significantly lower for the attenuated myocardial injury group (5.6% vs. 12.4%; HR, 2.23; 95% CI, 1.17 - 4.44; \(p = 0.02\)) (Additional file 1: Table S3). The survival curves are shown in Figure 3.

**DISCUSSION**

Our study showed that both pre- and postoperative myocardial injuries were
associated with increased 30-day mortality after non-cardiac surgery and the mortality rates were similar between the patients with pre- and postoperative myocardial injuries based on the 4th universal definition of myocardial infarction. In addition, attenuation of preoperative myocardial injury appeared to be related with the improved postoperative outcomes.

In the fourth universal definition of myocardial infarction, type 2 myocardial infarction was classified into acute myocardial infarction and myocardial injury, which was previously integrated in the previous definition [14]. Myocardial injury is defined as a sole elevation of cTn value above the 99th percentile upper reference limit without ischemic symptom, and the definition of myocardial infarction requires a clinical evidence of acute myocardial ischemia in addition to myocardial injury [14]. Although Type 2 myocardial infarction and myocardial injury are frequently encountered in surgical patients [14, 19], discrimination between type 2 myocardial infarction and myocardial injury still remains challenging during the perioperative period, because clinical evidence of acute myocardial ischemia such as chest pain or dyspnea may be masked due to anaesthesia or analgesia.

Myocardial injury after non-cardiac surgery, which uses a cut-off point upper than 99th percentile as an upper-reference value of cTn [14], occurs in almost 20% of the patients who underwent non-cardiac surgery [20] and has been recently accepted as a strong predictor of early postoperative mortalities [6, 19]. Mortality within 30 days in patients with myocardial injury after non-cardiac surgery has been reported as around 10%, which represents a more than 5-fold increase from the background risk [21]. Considering that 30-day mortalities were 1.4% in the normal group, 10.7% in the preoperative myocardial injury group, and 7.4% in the postoperative myocardial injury group in the present study, our results are correspondent with
previous data. However, the incidences of pre- and postoperative myocardial injury were 4.8% and 4.1% in our study, respectively, which were lower than the previously reported incidences. We thought that separation of pre- and postoperative myocardial injuries and difference in surgical characteristics might have made this difference.

There have been relatively few studies for the effect of preoperative myocardial injury on the early postoperative mortalities, compared to that of postoperative myocardial injury [9–11]. Most of previous studies had been focused on postoperative cTn elevation and, in some studies, preoperative cTn elevation was excluded from the analysis since it was considered as chronic elevation [6, 20, 22]. However, serum cTn elevation persist for at least 5 days, despite its biological half-life of 120 minutes, reflecting a continuing release of this protein from disintegrating myofilaments [23]. Therefore, theoretically, patients with preoperative myocardial injury can be diagnosed as those with postoperative myocardial injury regardless of developing intra- or postoperative myocardial injury.

In addition, even in the studies for the effect of preoperative myocardial injury, no study has compared the effect of pre- and postoperative myocardial injury on 30-day mortality simultaneously. In the present analysis, 30-day mortality rates were similar between the patients with pre- and postoperative myocardial injuries. Our results suggest that preoperative myocardial injury would be also associated with an increased postoperative mortality to a similar degree of postoperative myocardial injury in patients who underwent non-cardiac surgery.

Interestingly, in the preoperative myocardial group, the patients with an attenuated myocardial injury after surgery showed significantly improved 30-day mortality compared to those with persistent myocardial injury. This finding suggests that
intraoperative and early postoperative management in patients with preoperative myocardial injury might change their postoperative outcomes. In addition, considering that preoperative, intraoperative, and postoperative risk factors are all related with developing myocardial injury after non-cardiac surgery [24], our results could be interpreted as showing the importance of appropriate intra- and postoperative management. However, further studies with larger registry should be needed to confirm our findings.

Our results should be appraised in the light of the following limitations. First, the present study is a single-center and retrospective analysis. Therefore, despite an adjustment with the inverse probability weighting, the results could be affected by the confounding factors since unmeasured variables were not able to be corrected even after an adjustment. Second, in our institution, the measurement of hs-cTn level is not a routine perioperative laboratory examination in non-cardiac surgery. Considering that the hs-cTn measurement is usually performed in the patients with a high cardiovascular risk, our results might have a chance to be exaggerated.

CONCLUSION

Our study showed that preoperative myocardial injury significantly increased 30-day mortality in the patients undergoing non-cardiac surgery to a similar degree of postoperative myocardial injury. In addition, it might be related with the improvement of 30-day mortality after non-cardiac surgery to attenuate the preoperative cTn elevation.

Declarations

Acknowledgements:
Authors’ contributions

SHL contributed to the design and conception of the work, and analysis and interpretation of the data and drafted the manuscript. JP contributed to the design and conception of the work and interpretation and revised the manuscript. JHL contributed to the design and conception of the work and interpretation of the data and revised the manuscript. JJM contributed to the design and conception of the work and revised the manuscript. KYH contributed to the design and conception of the work and data acquisition. HC contributed to the design and conception of the work, and data acquisition. KC contributed to the analysis and interpretation of the data and revised the manuscript. JA contributed to the analysis and interpretation of the data. All authors read and approved the final manuscript.

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Competing Interests:

The authors declare no competing interests.

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB No. 2017-10-109-003) and registered in Clinical Research Information Service (KCT0004348). Since the present study only used the routinely gathered patient data and had no risk of enrolled patients, the need for individual
informed consent was waived by our Institutional Review Board.

Abbreviations

cTn: cardiac troponin

Hs-cTn: high-sensitivity-cardiac troponin

SD: standard deviation

IQR: interquartile range

HR: hazard ratio

OR: odds ratio

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### Tables

| Table 1. Baseline Characteristics of the Study Population |
|--------------------------------------------------------|
| Normal \( (N = 3182) \) | Preoperative myocardial injury \( (N = 694) \) | Postoperative myocardial injury \( (N = 756) \) | \( p \)-value | SM D | IPW |
|---------------------------------|---------------------------------|---------------------------------|----------------|------|------|
| **Demographic variables**       |                                 |                                 |                |      |      |
| Male sex                        | 1957 (61.5)                     | 411 (59.2)                      | 484 (64)       | 0.17 | 6.0  |
| Age, years                      | 65.1 (±12.8)                    | 66.7 (±14.1)                    | 66.6 (±13.2)   | <    | 0.0  |
| BMI                             | 23.9 (±3.8)                     | 22.8 (±3.9)                     | 23.3 (±4.0)    |     |      |
| **Previous history**            |                                 |                                 |                |      |      |
| Hypertension                    | 1665 (52.4)                     | 368 (53.0)                      | 430 (56.9)     | 0.08 | 6.0  |
| Diabetes                        | 836 (26.3)                      | 246 (35.4)                      | 232 (30.7)     | <    | 0.0  |
| Current smoking                 | 410 (12.9)                      | 76 (11.0)                       | 86 (11.4)      | 0.25 | 4.0  |
| Old myocardial infarction       | 156 (4.9)                       | 78 (11.2)                       | 45 (6.0)       | <    | 0.7  |
| Coronary revascularization      | 417 (13.1)                      | 144 (20.7)                      | 153 (20.2)     | <    | 0.3  |
| Heart failure                   | 53 (1.7)                        | 59 (8.5)                        | 25 (3.3)       | <    | 0.0  |
| Arrhythmia                      | 285 (9.0)                       | 112 (16.1)                      | 89 (11.8)      | <    | 0.3  |
| Valve disease                   | 77 (2.4)                        | 27 (3.9)                        | 35 (4.6)       | 0.00 | 8.0  |
| Stroke                          | 410 (12.9)                      | 127 (18.3)                      | 129 (17.1)     | <    | 0.8  |
| Chronic kidney disease | 185 (5.8) | 164 (23.6) | 129 (17.1) | 1  <  0.00  1  0.3  4.7 |
|-----------------------|----------|-----------|-----------|-------------------------|
| Aortic disease        | 167 (5.2) | 38 (5.5)  | 84 (11.1) | 0.00  1  0.5  3.7 |
| PAD                   | 294 (9.2) | 75 (10.8) | 65 (8.6)  | 0.32  5  0.4  5.7 |
| PTE/DVT               | 64 (2.0)  | 21 (3.0)  | 6 (0.8)   | 0.01  11  0.9  0.1  34 |
| Cancer                | 696 (21.9)| 163 (23.5)| 158 (20.9)| 0.48  4.  0.2  6.8  |
| Chronic lung disease  | 380 (11.9)| 119 (17.1)| 98 (13)   | 0.00  1  0.2  6.2  |
| Infectious disease    | 1286 (40.4)| 521 (75.1)| 363 (48.0)| 0.00  1  0.4  4.9  |
| Preoperative medication|         |           |           |                      |
| Beta blocker          | 563 (17.7)| 147 (21.2)| 187 (24.7)| 11  0.4  4.7  |
| RAAS inhibitor        | 891 (28.0)| 180 (25.9)| 210 (27.8)| 0.54  3.  0.5  5.4  |
| Statin                | 853 (26.8)| 143 (20.6)| 218 (28.8)| 12  0.8  2.3  |
| Antiplatelet          | 975 (30.6)| 222 (32.0)| 272 (36.0)| 0.02  7.  0.8  1.5  |
| Preoperative blood test|         |           |           |                      |
| Hemoglobin            | 12.2 (±2.1)| 10.7 (±2.1)| 11.6 (±2.2)| 46  0.6  3.4  |
| Creatinine            | 1.03 (±1.19)| 2.05 (±2.46)| 1.53 (±1.79)| 36  0.6  2.8  |
| AST                   | 30 (±56)  | 87 (±291) | 44 (±187) | 18  0.1  4.5  |
| ALT                   | 3 (±50)   | 62 (±200) | 39 (±209) | 13  0.1  6.2  |
| Operative variables   |           |           |           |                      |
| ESC/ESA Risk          |           |           |           | 32  0.7  6.5  |
| High                  | 460 (14.5)| 74 (10.7) | 199 (26.3) |
| Intermediate          | 2396 (75.3)| 510 (73.5)| 503 (66.5) |
| Low                   | 326 (10.2)| 110 (15.9)| 54 (7.1)  |
| Operative duration, hours | 3.12 (±2.25)| 2.94 (±2.99)| 4.15 (±3.38)| 26  0.9  0.8  |
| General anesthesia     | 2892 (90.9)| 620 (89.3)| 685 (90.6)| 0.45  3.  0.1  8.2  |
| Emergent operation    | 650 (20.4)| 314 (45.2)| 226 (29.9)| 36  0.2  5.2  |
| Inotropic use         | 637 (20.0)| 281 (40.5)| 397 (52.5)| 47  0.6  3.3  |
| Table 2. Clinical Outcomes |
|---------------------------|
|                           | Univariate analysis | IPW analysis |
|                           | n (%)               | Unadjusted HR (95% CI) | p value | Adjusted HR (95% CI) | p value |
| **30-day mortality**      |                     |                        |         |                        |         |
| Normal                   | 44 (1.4)            | 1                      |         | 1                      |         |
| Preoperative myocardial  | 74 (10.7)           | 8.31 (5.72-12.07)      | <0.001  | 3.12 (1.62-6.01)       | 0.001   |
| injury                   | Postoperative       | 56 (7.4)               | 2.36 (1.94-2.88) | <0.001  | 4.49 (2.34-8.60)       | <0.001  |
| myocardial injury        | Pre- vs. postoperative myocardial | 0.67 (0.47-0.95) | 0.02 | 1.44 (0.79-2.64)       | 0.45 |
| injury                   |                        |                        |         |                        |         |
| **In-hospital death**    | 65 (2.0)            | 1                      |         | 1                      |         |
| Preoperative myocardial  | 97 (14)             | 3.33 (2.42-4.60)       | <0.001  | 2.87 (0.95-3.68)       | 0.011   |
| injury                   | Postoperative       | 71 (9.4)               | 1.62 (1.37-1.92) | <0.001  | 2.32 (1.16-4.65)       | 0.001   |
| myocardial injury        | Pre- vs. postoperative myocardial | 0.80 (0.59-1.09) | 0.16 | 1.24 (0.68-2.26)       | 0.34 |
| injury                   |                        |                        |         |                        |         |
| **Overall cardiovascular death** | 201 (6.3) | 1 | <0.001  | 1.30 (0.89-1.89)       | 0.18 |
| Normal                   | 71 (10.2)           | 2.07 (1.58-2.72)       | <0.001  | 1.30 (0.89-1.89)       | 0.18 |
| Preoperative myocardial  | 71 (9.4)            | 1.29 (1.13-1.48)       | <0.001  | 1.61 (1.16-2.23)       | 0.004   |
| injury                   | Postoperative       | 0.81 (0.58-1.13)       | 0.21 | 1.21 (0.70-2.10)       | >0.99   |
| myocardial injury        | Pre- vs. postoperative myocardial | 1.30 (1.20-2.10) | <0.001  | 1.51 (1.24-<0.001)     | <0.001 |
| injury                   |                        |                        |         |                        |         |
| **Overall all-cause death** | 596 (18.7) | 1 | <0.001  | 1.37 (1.08-1.74)       | 0.009   |
| Normal                   | 233 (33.6)          | 2.24 (1.92-2.60)       | <0.001  | 1.37 (1.08-1.74)       | 0.009   |
| Preoperative myocardial  | 218 (28.8)          | 1.30 (1.20-2.10)       | <0.001  | 1.51 (1.24-<0.001)     | <0.001 |
| Condition                        | Normal | Preoperative | Postoperative | Pre- vs. postoperative OR (95% CI) | p value | Adjusted OR (95% CI) | p value |
|---------------------------------|--------|--------------|---------------|-----------------------------------|---------|----------------------|---------|
| **myocardial injury**           |        |              |               |                                   |         |                      |         |
| Unadjusted OR (95% CI)          | 1      | 0.77 (0.64-0.93) | 0.006         | 1.85 (0.79-1.54) | >0.99   |                      |         |
| Adjusted OR (95% CI)            |        |              |               |                                   |         |                      |         |
| **Type 1 myocardial infarction**|        |              |               |                                   |         |                      |         |
| Normal                          | 10 (0.3) | 1              |               |                                   | 1       |                      |         |
| Preoperative myocardial injury  | 8 (1.2)  | 3.70 (1.41-9.41) | 0.006         | 2.07 (0.59-7.25) | 0.49    |                      |         |
| Postoperative myocardial injury | 16 (2.1) | 2.62 (1.77-3.96) | <0.001        | 7.12 (2.54-19.99) | <0.001  |                      |         |
| Pre- vs. postoperative myocardial injury | 1.85 (0.81-4.60) | 0.16 |                      | 3.44 (1.02-11.56) | 0.04    |                      |         |
| **Coronary revascularization**  |        |              |               |                                   |         |                      |         |
| Normal                          | 6 (0.2)  | 1              |               |                                   | 1       |                      |         |
| Preoperative myocardial injury  | 3 (0.4)  | 2.30 (0.48-8.73) | 0.24          | 2.08 (0.33-12.99) | 0.99    |                      |         |
| Postoperative myocardial injury | 8 (1.1)  | 2.38 (1.40-4.15) | 0.001         | 6.29 (1.58-24.98) | 0.004   |                      |         |
| Pre- vs. postoperative myocardial injury | 2.46 (0.71-11.28) | 0.18 |                      | 3.03 (0.49-18.83) | 0.44    |                      |         |
| **Atrial fibrillation**         |        |              |               |                                   |         |                      |         |
| Normal                          | 67 (2.1) | 1              |               |                                   | 1       |                      |         |
| Preoperative myocardial injury  | 52 (7.5) | 3.77 (2.59-5.45) | <0.001        | 3.34 (1.76-6.35) | <0.001  |                      |         |
| Postoperative myocardial injury | 47 (6.2) | 1.76 (1.45-2.12) | <0.001        | 2.61 (1.54-4.43) | <0.001  |                      |         |
| Pre- vs. postoperative myocardial injury | 0.82 (0.54-1.23) | 0.34 |                      | 0.78 (0.39-1.57) | 0.99    |                      |         |
| **Heart failure**               |        |              |               |                                   |         |                      |         |
| Normal                          | 3 (0.1)  | 1              |               |                                   | 1       |                      |         |
| Preoperative myocardial injury  | 8 (1.2)  | 12.36 (3.56-56.52) | <0.001       | 15.22 (2.49-93.16) | <0.001  |                      |         |
| Postoperative myocardial injury | 4 (0.5)  | 2.37 (1.11-5.35) | 0.02          | 4.15 (0.62-28.02) | 0.22    |                      |         |
| Pre- vs. postoperative myocardial injury | 0.46 (0.12-1.45) | 0.2  |                      | 0.27 (0.05-1.58) | 0.99    |                      |         |
| **AKI, any**                    |        |              |               |                                   |         |                      |         |
| Normal                          | 205 (6.4) | 1              |               |                                   | 1       |                      |         |
| Preoperative myocardial injury  | 172 (24.8) | 4.79 (3.83-5.98) | <0.001       | 2.13 (1.43-3.19) | <0.001  |                      |         |
| Postoperative myocardial injury | 219 (29.0) | 2.43 (2.19-2.71) | <0.001       | 3.11 (2.30-4.21) | <0.001  |                      |         |
| Pre- vs. postoperative myocardial injury | 1.24 (0.98-1.56) | 0.07 |                      | 1.46 (0.96-2.22) | 0.1     |                      |         |

AKI, acute kidney injury
Figures

Figure 1
The flowchart of the patients. Hs-cTnI, high sensitivity-cardiac troponin I.

Figure 2
Kaplan-Meier curves for the normal group (grey line), preoperative myocardial inj

Figure 3
Kaplan-Meier curves for the normal group (black line), attenuated myocardial inj

Supplementary Files
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