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Acute kidney injury is an independent risk factor for myocardial injury after noncardiac surgery in critical patients

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ABSTRACT

Background: Myocardial injury after noncardiac surgery (MINS) contributes to mortality and morbidity. However, risk factors accelerating its development remain unclear. The aim of this study was to identify the incidence and risk factors of MINS.

Methods: A retrospective and observational cohort study of critical patients (n = 1087) after noncardiac surgery was carried out at a large and tertiary university hospital from January 2012 to January 2013. The clinical data including medical history as well as intraoperative and postoperative variables were recorded. The primary outcome was the occurrence of MINS. Secondary outcomes included 30-day all-cause mortality and the incidence of 30-day major adverse cardiac events (MACE) after surgery. The risk factors of MINS in critical patients were analyzed using logistic regression.

Results: MINS had occurred in 188 (17.3%) of the 1087 critical patients. Fifty-seven patients (5.2%) had postoperative acute kidney injury (AKI), wherein stage 1 accounted for 82.5% (47/57), stage 2 accounted for 12.3% (7/57), and stage 3 accounted for 5.3% (3/57). The independent risk factors of MINS in critical patients were emergency surgery (odds ratio [OR], 2.64; 95% confidence interval [CI], 1.60-4.35; $P < .001$), a longer time of operation (OR, 1.10; 95% CI, 1.03-1.17; $P = .004$), postoperative AKI (OR, 2.09; 95% CI, 1.15-3.79; $P = .015$), vasopressor drugs used within 24 hours after operation (OR, 2.27; 95% CI, 1.40-3.67; $P = .001$), and a higher Acute Physiology and Chronic Health Evaluation II score (OR, 1.05; 95% CI, 1.02-1.08; $P = .002$). All-cause mortality and MACE after surgery were not related to postoperative AKI ($P = .544$ for mortality; $P = .663$ for MACE).

Conclusions: The incidence of MINS in critical patients is high. Postoperative AKI is an independent risk factor of MINS in critical patients. It is recommended that postoperative kidney functions be routinely assessed in all critical patients after noncardiac surgery.

1. Introduction

Major adverse cardiac events (MACE) after noncardiac surgery are a leading cause of morbidity and mortality [1]. The reported incidence of postoperative myocardial infarction (POMI) among patients undergoing noncardiac surgery is between 3% and 6% [2-4]. Prevention of POMI by the inhibition of platelet function or by perioperative suppression of the compensatory sympathetic effects of surgery has not benefited from several major clinical trials [2,3,5]. Early recognition and timely treatment of POMI after surgery are very important [1]. Therefore, routine monitoring of cardiac troponin has been recommended to identify patients at risk of early postoperative cardiovascular events after surgery [6]. Myocardial injury after noncardiac surgery (MINS) [7] is defined as follows: myocardial injury caused by ischemia (that may or may not result in necrosis), has prognostic relevance, and occurs during or within 30 days after noncardiac surgery. MINS can be measured by postoperative troponin elevation in the presence or absence of clinical symptoms. MINS occurs in 8% to 22% of adults undergoing major noncardiac surgery [7,8]; MINS is an independent predictor for 30-day and 1-year mortality [7,8]. To date, there have been few studies investigating the risk factors of MINS in critical patients. We aimed to identify the incidence and risk factors of MINS in critical patients.

2. Materials and methods

2.1. Study design

The study was a retrospective and observational cohort study of critical patients undergoing noncardiac surgery at a large and tertiary university hospital from January 2012 to January 2013. This study was approved by the Peking University People's Hospital Medical Ethics Committee (acceptance number 2016PHB001). Because no treatment interventions were mandated and no protected health information was collected or analyzed, signed patient consent was waived. All data were anonymized before analysis.

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2.2. Patients

This study recruited all adult critical patients admitted to the intensive care unit (ICU) undergoing noncardiac surgery. Patients were eligible if they were aged 18 years or more, were undergoing elevated-risk noncardiac surgery under general or spinal anesthesia, and had an expected length of postoperative hospital stay of at least 48 hours. For patients who underwent surgery more than once, the first surgery was included in the analysis. Exclusion criteria were (1) pregnancy, (2) perioperative myocardial injury caused by a documented nonischemic etiology (eg, pulmonary embolism, sepsis, cardioversion), and (3) heart failure (New York Heart Association class III and IV).

2.3. Data collection

Data were collected retrospectively and consecutively. All data input was done by trained physicians and research nurses who were not aware of the study and had not participated in the management and care of the patients. All data were obtained from electronic medical records. Preoperative, surgical, and postoperative data were documented. Data quality was assessed by reviewing a random sample of 10% of all medical records. All reported events were confirmed by reviewing hospital charts or by contacting the physicians. Follow-up was conducted in all patients using medical records or telephone interviews.

2.4. Potential confounders and risk factors

We collected patient characteristic data and potential perioperative variables for MINS. These included the following clinical variables:

2.4.1. Preoperative variables included sex, age, history of hypertension, coronary artery disease (CAD), diabetes mellitus, stroke, and chronic kidney disease. The definitions for the history of CAD were as follows: (1) those who had stable angina pectoris or other symptoms associated with CAD; (2) those who were previously symptomatic with known obstructive or nonobstructive CAD but become asymptomatic after treatment; and (3) those who had a history of acute coronary syndrome (including ST-segment elevation acute MI, non–ST-segment elevation acute MI, and unstable angina) but had been free of an acute coronary event for 12 months. The history of stroke included the history of ischemic stroke and hemorrhagic stroke. Hypertension was defined by a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg and/or those patients receiving antihypertensive medications. Diabetes mellitus was diagnosed in patients who had previously undergone dietary treatment for diabetes, had received additional oral antidiabetic or insulin medication, or had a current fasting blood glucose level of ≥7.0 mmol/L or a random blood glucose level of ≥11.1 mmol/L. Chronic kidney disease was defined as a serum creatinine (SCr) ≥2 mg/dL and an estimated glomerular filtration rate <60 mL/min per 1.73 m^2 based on Kidney Disease Outcome Quality Initiative guidelines [9].

2.4.2. Surgical variables included the type of surgery (no matter whether abdominal surgery was performed or not), emergency surgery, operational time, intraoperative hemorrhage, intraoperative hypotension, and vasopressor used during operation. The type of surgery included abdominal surgery and nonabdominal surgery (thoracic surgery, orthopedic surgery, brain surgery, major vascular surgery, and peripheral vascular surgery). Intraoperative hypotension was defined if any one of the following was met: systolic blood pressure <90 mm Hg or a 35% decrease in the mean arterial blood pressure for >5 minutes or the use of vasopressive agents to treat blood pressure. The types of vasopressor included epinephrine, norepinephrine, vasopressin, dopamine, and phenylephrine.

2.4.3. Postoperative variables included immediate postoperative Pao_2/fraction of inspired oxygen (Fio_2) ratio, immediate postoperative hemoglobin, immediate postoperative blood lactic acid, postoperative acute kidney injury (AKI), vasopressor drugs used within 24 hours after operation, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score. The types of vasopressor were the same as those used during operation.

2.4.4. Acute kidney injury was defined by an SCr increase ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or an SCr increase ≥1.5 times that of the baseline value and was known or presumed to have occurred within the prior 7 days; or urine volume < 0.5 mL/(kg h) for 6 hours [10]. According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines for AKI [10], we categorized the patients into 3 groups: stage 1, with one of the following conditions: the Scr level increased to 1.5 to 1.9 times that of the baseline value, Scr increased >0.3 mg/dL (26.5 μmol/L), urinary output <0.5 ml/(kg h) during a 6-hour period; stage 2, with one of the following conditions: the Scr level increased to 2.0 to 2.9 times that of the baseline value, urinary output <0.5 mL/(kg h) during two 6-hour periods; stage 3, with one of the following conditions: the Scr level increased to >3 times that of the baseline value, Scr increased to >4.0 mg/dL (353 μmol/L), initiation of renal replacement therapy, urinary output <0.3 mL/(kg h) after more than 24 hours, or anuria lasted for more than 12 hours.

2.5. Outcomes

The main outcome was the occurrence of MINS. *MINS* was defined as myocardial injury caused by ischemia (that may or may not result in necrosis), with prognostic relevance and occurring during or within 30 days after noncardiac surgery [7]. The diagnostic criterion for MINS was a peak cardiac troponin I (cTNI) level of 0.034 ng/mL or higher that was judged as the result of myocardial ischemia. Each incidence of elevated cTNI was evaluated to ensure an ischemic etiology. Myocardial injury mainly occurs within 3 days after surgery, so we checked the cTNI level immediately after noncardiac surgery and at 24 and 48 hours after noncardiac surgery. Secondary outcomes included 30-day all-cause mortality and the incidence of 30-day MACE after surgery. MACE [11] included nonfatal cardiac arrest, acute MI, congestive heart failure, new cardiac arrhythmia, and angina. To identify events that met any MACE definition, patients with postoperative complications were evaluated by consulting the medical records in real time as they were developed. Clinical follow-up was scheduled at 30 days.

2.6. Statistical analysis

The NCSS-PASS 11 Statistical data analysis software was used to calculate the sample size of a logistic regression model. This study was undertaken to investigate the relationship between MINS and AKI. The AKI rate was thought to be 5% among MINS patients. We expected a sample size large enough to detect an odds ratio (OR) of 2.0 with 80% power at the .05 significance level using a 2-sided test. After calculation, the sample size required was 1030. One hundred eighty-eight MINS and 19 variables were used in the study. Therefore, a sample size of 1087 patients was considered large enough to be able to construct a logistic regression model with at least 10 MINS per variable [12].

Data were expressed as mean ± standard deviations (SD) for continuous variables, median (25th percentile, 75th percentile) for nonnormal distributions of continuous variables, and percentages for categorical variables. For comparisons between each risk factor and MINS, a Student *t* test was used for continuous variables, a nonparametric Mann-Whitney *U* test was used for nonnormal distributions of continuous variables, and a Pearson χ^2 test was used for categorical variables. Rates of missing data were <1% for all variables, missing continuous covariates were imputed to the median nonmissing value, and missing categorical covariates were imputed to the value of the most frequent group.

Collinearity diagnostics were evaluated for all risk factors. If any condition indexes were 30 or greater, a bivariate correlation matrix was constructed to evaluate pairwise correlations. Groups of variables with a pairwise correlation of .70 or greater were deemed to demonstrate

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