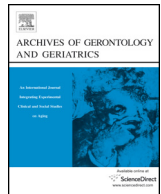




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Major adverse cardiac events in elderly patients with coronary artery disease undergoing noncardiac surgery: A multicenter prospective study in China

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ABSTRACT

Background: Major adverse cardiac events (MACEs) are important causes of perioperative morbidity and mortality for elderly patients undergoing non-cardiac surgery. Treatment and control rates for coronary artery disease (CAD) in Chinese patients are poorer than rates in western countries. However, no previous prospective study has focused on perioperative MACE in this population. Our aim was to ascertain the incidence and risk factors associated with MACEs in Chinese patients.

Methods: Consecutive CAD patients, aged ≥ 60 years, who underwent non-cardiac surgery at five medical centers in China, were prospectively enrolled. Clinical variables, including electrocardiogram and troponin I levels, were evaluated to estimate MACEs. The main outcome was occurrence of at least one perioperative MACE from admittance to 30 days after surgery, defined as any of the following complications: cardiac death, nonfatal cardiac arrest, acute myocardial infarction (MI), congestive heart failure (CHF), and angina. MACE independent risk factors were based on the Andersen–Gill multiplicative intensity model.

Results: Of the 1422 patients recruited, 129 (9.1%) developed at least one MACE, and cardiac death occurred in 11 patients (0.8%). The independent risk factors contributing to postoperative MACE included age ≥ 75 years, female gender, history of MI, history of hypertension, high-risk surgery, intraoperative hypotension, and intraoperative hypoxemia.

Conclusions: The incidence of MACE in Chinese elderly patients with CAD who underwent non-cardiac surgery was 9.1%. Seven independent risk factors for a perioperative MACE were identified. Preventing intraoperative hypoxemia and hypotension may reduce the occurrence of MACE in these high risk patients.

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1. Introduction

China has the largest and most rapidly growing elderly population in the world. The percentage of elderly in China is projected to triple, from 8% in 2006 to 24% in 2050 (England, 2005). With a growing elderly population, the number of patients with underlying coronary

artery disease (CAD) is concomitantly on the rise. This fact, coupled with an increased availability of advanced surgical techniques, indicates that more elderly patients with CAD will undergo elective non-cardiac surgery. Elderly CAD patients have increased rates of peri-operative morbidity and mortality, in part due to major adverse cardiac events (MACEs) that are caused by both the response to surgery as well as underlying CAD (Freeman & Gibbons, 2009; Landenberg et al., 2009).

To date, most studies reported in the literature focus on patients from western countries. Anesthesiologists in China rely on results from these studies to evaluate the peri-operative risk of their patients with CAD (Goldman et al., 1977; Lee et al., 1999; Fleisher et al., 2007, 2014). This may not be a suitable strategy, as Chinese

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elderly CAD patients have unique characteristics. A 2010 survey showed that the incidence of CAD was 15.9% in Beijing residents aged over 70 years (Zhang et al., 2010). However, the treatment rate and control rate of Chinese CAD patients are lower than that of Europe and in the United States (US). A study including 7962 CAD patients with a mean age of 72 years from 165 hospitals in 26 provinces of China showed that only 27.5% of the Chinese elderly CAD patients received percutaneous artery intervention (PCI), and only 2.6% received coronary artery bypass grafting (CABG). The control rate of Chinese elderly CAD patients was only 50.8% (Li et al., 2012). On the contrary, a 2010 US study showed that 32.8% and 20.0% of CAD patients with a mean age of 65 years received PCI and CABG, respectively (Yusuf et al., 2011). In addition, in Chinese elderly CAD patients, 70.3% were treated with antiplatelet drugs, 54.9% with statins, and 47.5% with a β -blocker; compared to European patients, of which 91% were treated with antiplatelet drugs, 78% with statins, and 80% with β -blockers (Kotseva et al., 2009).

We previously conducted a retrospective study that enrolled 482 elderly patients with CAD undergoing non-cardiac surgery in Peking Union Medical College Hospital from 2004 to 2008. For these patients, the incidence of a MACE was 12.7% and the mortality rate was 2.1% (Liu et al., 2013), which was much higher than reported for studies in Japan, Europe, and North America (Seki et al., 2005; Sabate et al., 2011; Devereaux et al., 2011). This finding drew attention from the Chinese Health Administration. Of note, Peking Union Medical College Hospital is the top general hospital in China and often receives severely sick patients transferred from other area hospitals. Therefore, the results of this one hospital may not be representative for all hospitals in China. In addition, it was a retrospective study and has inherent limitations in the results. To determine the incidence and predictors of MACE in Chinese elderly patients with CAD who undergo intermediate- to high-risk non-cardiac surgery, we conducted a multi-center clinical prospective study in five hospitals located in different areas of China.

2. Methods

2.1. Patients

This multicenter prospective study included consecutive patients undergoing non-cardiac surgery between March 1, 2008 and February 28, 2010, at five university hospitals located in different regions of China. After approval from the local medical ethics committee, patients with a history of CAD were eligible if they were at least 60 years old and were undergoing intermediate- to high-risk non-cardiac surgery based on the American College of Cardiology/American Heart Association guidelines (Fleisher et al., 2014). Exclusion criteria included: patients who underwent emergency surgery or low risk surgery; patients who met the

American Society of Anesthesiologists (ASA) classification of V or VI; and patients with congenital heart disease or cardiomyopathy.

2.2. Data collection

Research data were collected in parallel with clinical data. Before surgery, a study physician performed a routine clinical evaluation and chart review. In addition, all patients were subjected to a 12-lead electrocardiogram, heart and chest X-rays, transthoracic echocardiography, and complete laboratory tests. For each patient, we determined the Canadian Cardiovascular Society classification of angina, the New York Heart Association classification of heart failure, the cardiac-risk index, and the ASA classification of overall health status. A history of arrhythmia within the past 6 months was collected and included the occurrences of bradycardia, sick sinus syndrome, supraventricular tachycardia, atrial fibrillation, frequent ventricular premature, or conduction abnormalities. Criteria for ST-T segment abnormalities were defined using the Minnesota code. In addition, we analyzed pre-operative data including the history of claudication, stroke, transient ischemic attack, smoking, limitation of activity (<4 Metabolic Equivalent of Tasks, METs). Medication history was analyzed for perioperative medications. Blood loss, total fluids infused, and the duration of anesthesia and surgery were recorded.

2.3. Clinical care and monitoring

Clinical decisions were not affected by the study protocol. Routine monitoring during surgery included intra-arterial pressure, five-lead electrocardiogram, pulse oximetry, and end tidal CO_2 by mass spectroscopy. Intraoperative hypotension was defined as a systolic pressure $<30\%$ of baseline value, a systolic pressure <90 mmHg, or diastolic pressure <60 mmHg lasting over 10 min. Intraoperative hypoxemia was defined as $\text{PaO}_2 < 60$ mmHg or $\text{SaO}_2 < 90\%$ lasting over 5 min. Use of vasoactive agents during surgery was recorded.

Patients were monitored continuously for 72 h post-operatively. A 12-lead electrocardiogram was obtained and reviewed immediately after surgery, on post-operative day one, and when indicated. Troponin I was measured before surgery and on post-operative days 1–3. Finally, patients were followed up 30 days after the surgery.

2.4. Outcomes

The occurrence of an intra- or postoperative MACE was the main outcome. Definitions of MACE are shown in Box 1. A MACE was recorded if any of these complications were present from admission to the operating theatre to 30 days after the surgery. To find events that fulfilled any MACE definition, patients with

Box 1. Definitions of MACEs.

Cardiac death: any death, unless an unequivocal non-cardiac cause could be established (Cutlip et al., 2007).
Non-fatal cardiac arrest: an absence of cardiac rhythm or presence of chaotic rhythm requiring any component of basic or advanced cardiac life support.
Acute myocardial infarction: increase and gradual decrease in troponin level (Cutlip et al., 2007) or a faster increase and decrease of creatine kinase isoenzyme as markers of myocardial necrosis in the company of at least one of the following: ischemic symptoms, abnormal Q waves on the ECG, ST-segment elevation or depression; or coronary artery intervention (e.g., coronary angioplasty) or a typical decrease in an elevated troponin level detected at its peak after surgery in a patient without a documented alternative explanation for the troponin elevation (Devereaux et al., 2005).
Congestive heart failure: new in-hospital signs or symptoms of dyspnea or fatigue, orthopnea, paroxysmal nocturnal dyspnoea, increased jugular venous pressure, pulmonary rales on physical examination, cardiomegaly, or pulmonary vascular engorgement.
Angina: dull diffuse substernal chest discomfort precipitated by exertion or emotion and relieved by rest or nitroglycerin.

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