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Impact of glycemic variability on the occurrence of periprocedural myocardial infarction and major adverse cardiovascular events (MACE) after coronary intervention in patients with stable angina pectoris at 6 months follow-up

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ABSTRACT

Background: We explored the impact of glycemic variability on the occurrence of periprocedural myocardial infarction and major adverse cardiovascular events (MACE) after coronary intervention in patients with stable angina pectoris (SAP) at 6 months follow-up.

Methods: From May 2015 to April 2016, a total of 746 patients with SAP were divided to high glycemic variability group (H group) (n = 261) and low glycemic variability group (L group) (n = 485). The primary end point was incidence of periprocedural myocardial infarction and MACE at 6 months follow-up.

Results: The occurrence of periprocedural myocardial infarction occurred in 18.8% of patients in H group and in 12.4% in L group (P = 0.03). The incidence of MACE at 6 months follow-up was 9.6% in H group and 4.5% in L group (P = 0.01). Multivariable analysis suggested that high glycemic variability conferred a 53% risk increment of 6 months follow-up MACE (odds ratio 2.13, 95% confidence interval 1.85–5.38; P = 0.01).

Conclusions: The trial shows that higher blood glucose variability was correlated with higher incidence of periprocedural myocardial infarction and MACE at 6 months follow-up.

1. Background

Recent research has been focused on how to improve prognosis after coronary intervention in patients with stable angina pectoris (SAP). A large number of clinical trials have reported the good effects of blood pressure lowering, lipid lowering and smoke quitting for secondary prevention and improved all-cause mortality. However, the limited ability of risk reduction associated with blood pressure lowering, lipid-lowering therapy and smoke quitting has attracted attention to the unmet need for residual clinical risk management. There is increasing evidence that glycemic variability has more detrimental effects on the coronary artery than chronic sustained hyperglycemia [1]. Epidemiological studies have suggested that glycemic variability may be a marker of increased progression of coronary disease [2]. However, it remains unknown whether glycemic variability may affect prognosis of patients after coronary intervention with SAP. The related clinical data is limiting. This study aimed to explore the impact of glycemic variability on the occurrence of periprocedural myocardial infarction and major adverse cardiovascular events (MACE) after coronary intervention in patients with stable angina pectoris (SAP) at 6 months follow-up.

2. Methods

2.1. Study population

This study was a prospective observational study of glycemic variability, periprocedural myocardial infarction and MACE after coronary intervention in patients with SAP at the department of cardiology, Xuanwu Hospital from May 2015 to April 2016. Consecutive patients with SAP who underwent percutaneous coronary intervention (PCI) at the first time were screened for eligibility. The study protocol was approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University and was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients gave written informed consent.

There were 3 inclusion criteria that had to be present simultaneously: (1) SAP patients undergoing a first PCI were included to the study. SAP was defined according to guidelines of and the American College of Cardiology (ACC)/American Heart Association (AHA) [3,4],

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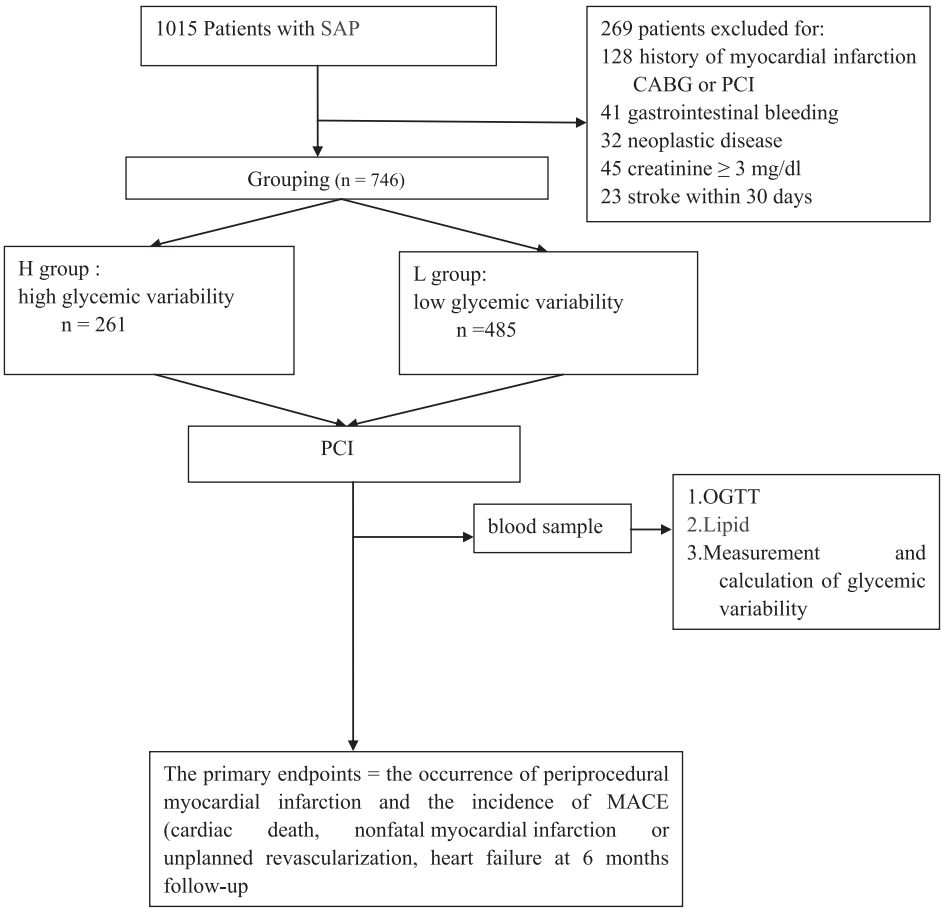

Fig. 1. Study design.
The flow chart shows the design of the trial. SAP = stable angina pectoris, CABG = cardiac artery bypass grafting, PCI = percutaneous coronary intervention, OGTT = Oral Glucose Tolerance Test, MACE = major adverse cardiovascular events.

angina classification was used according to Canadian Cardiovascular Society (CCS) class; (2) patients ranging from 18 to 80 y; (3) ≥ 75% stenosis at the native coronary artery.

We excluded patients with any of the following characteristics: (1) acute coronary syndrome; (2) history of myocardial infarction, PCI and coronary artery bypass surgery; (3) acute exacerbation of chronic obstructive pulmonary disease (COPD) with pulmonary infection; (4) history of peptic ulcer and/or gastrointestinal bleeding; (5) renal failure with a creatinine ≥ 3 mg/dl and/or estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2; (6) stroke within the previous 30 days; (7) history of hyperthyroidism; (8) Severe non cardiac organic disease or neoplastic disease, estimated survival time < 6 months and (9) refusal to sign informed consent to participate in the study.

2.2. Study design and clinical follow-up

A total of 1015 patients fulfilling the inclusion criteria were initially evaluated but 269 (26.5%) were excluded per the exclusion criteria described above (Fig. 1). The remaining 746 patients were divided into high glycemic variability group (H group) and low glycemic variability group (L group). All patients were treated with optimized drug-therapy including angiotensin-converting enzyme inhibitors, β-blockers, aspirin, clopidogrel, lipid lowering drugs and glucose lowering drugs. All patients were treated with PCI. An 18-lead electrocardiogram (ECG) was recorded every morning or in the case of ischemic symptoms and the occurrence of periprocedural myocardial infarction. The primary end point was incidence of periprocedural myocardial infarction and MACE at 6 months follow-up. Periprocedural myocardial infarction was defined according to the Society for Cardiovascular Angiography and Interventions (SCAI) definition [5]: elevation of Creatine Kinase-Myocardial Band (CK-MB) values ≥ 10 × upper reference limit (URL) and/or Troponin T(TNT) values ≥ 70 × URL. MACE was defined as the composite of cardiac death, nonfatal myocardial infarction or unplanned revascularization, heart failure.

2.3. Data collection, procedure, periprocedural medications and blood sampling

Clinical data were obtained through a review of the medical records. All baseline and procedural cineangiograms were reviewed and analyzed. In all cases, the interventional strategy and instrumentation used were at the discretion of the interventional cardiologists. Coronary angioplasty was performed in the conventional manner, and coronary stents or other procedures/devices were used only when required. The administration of periprocedural antiplatelet and antithrombotic medications was based on the operator's discretion and current guidelines. Lifelong aspirin (100 mg/day) was prescribed to all patients. At least 12 months of clopidogrel (75 mg/day) was recommended to all patients.

Blood samples were routinely obtained from all of the patients before and after the procedure. To identify periprocedural myocardial infarction, cardiac biomarkers and electrocardiograms were systematically assessed before and after PCI. Creatine kinase-MB (CK-MB) and cardiac troponin T measurements were scheduled before PCI and 6–18 h after PCI, with subsequent serial measurements for relevant complaints or biomarker increases, until peak increase was established.

2.4. Measurement and calculation of glycemic variability

Fingertip blood samples were obtained on admission, before and 2 h after meals and before bedtime (6 am, 9 am, 11 am, 1 pm, 5 pm, 7 pm and 9 pm) daily for measurement of blood glucose for three days after