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Original article

Remnant cholesterol predicts periprocedural myocardial injury following percutaneous coronary intervention in poorly-controlled type 2 diabetes

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A R T I C L E   I N F O

A B S T R A C T

Background: Remnant cholesterol (RC) is receiving increasing attention regarding its relation to cardiovascular risk. Whether RC is associated with periprocedural myocardial injury (PMI) following percutaneous coronary intervention (PCI) in type 2 diabetes (T2D) is currently unknown.
Methods: We prospectively enrolled 1182 consecutive T2D patients who were scheduled for PCI but with baseline normal preprocedural cardiac troponin I (cTnI). Patients were divided according to their glycemic control status: group A [glycated hemoglobin (HbA1c) < 7%, $n = 563$] and group B (HbA1c $\geq$ 7%, $n = 619$). PMI was evaluated by cTnI analysis within 24 h. The associations of preprocedural RC and the RC to high-density lipoprotein cholesterol ratio (RC/HDL-C) with PMI were investigated.
Results: The associations of RC and RC/HDL-C with PMI were observed in group B (both $p < 0.05$) but not in group A (both $p > 0.05$). Patients in group B, a 1-SD increase of RC produced 30% and 32% increased risk for postprocedural cTnI > 3× upper limit of normal (ULN) and >5 × ULN, respectively. The odds ratios for RC/HDL-C were the highest compared with any cholesterol fractions including total cholesterol (TC)/HDL-C, low density lipoprotein cholesterol (LDL-C)/HDL-C, nonHDL-C/HDL-C, and triglyceride/HDL-C with 1.43 [95% confidence interval (CI): 1.10–1.88] for >3× ULN and 1.49 (95% CI: 1.13–1.97) for >5× ULN. However, no such associations were found in group A. Furthermore, patients with RC >27.46 mg/dL (third tertile) [RC $\leq$ 14.15 mg/dL (first tertile) as reference] were associated with a 1.57-fold and 2-fold increased risk for >3× ULN and >5× ULN in group B, respectively.
Conclusions: RC and RC/HDL-C might be valuable, independent predictors for PMI in poorly-controlled diabetic patients undergoing PCI.

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Introduction

Percutaneous coronary intervention (PCI) is one of the dominant methods for coronary revascularization in patients with coronary artery disease (CAD). Even though technical advances in PCI result in a safe procedure with minimal complications, PCI is frequently accompanied with periprocedural myocardial injury (PMI), especially with the use of high-sensitivity troponin [1]. Moreover, it has been well established that PMI is associated with increased subsequent mortality [2–4]. More importantly, previous studies suggested that patients with type 2 diabetes (T2D) had a 3-fold increased risk of CAD compared with normal subjects [5], and diabetic patients were also more prone to PMI as well as worse long-term outcome compared to those without diabetes [6].

Dyslipidemia is a common feature of diabetes and it is known to increase the risk of mortality and morbidity in diabetic patients [7]. Remnant cholesterol (RC) is defined as the cholesterol content of a subset of the triglyceride-rich lipoproteins called remnants, and associated with increased risk of cardiovascular disease [8–11]. The major triglyceride-rich lipoprotein in fasted subjects is very low density lipoproteins (VLDL) and to a lesser extent intermediate

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density lipoproteins (IDL), both apoB-100 containing, while in non-fasted subjects, VLDL in addition to chylomicron and VLDL remnants contribute to the pool [12]. Recently, studies have demonstrated that even after lowering low-density lipoprotein cholesterol (LDL-C) to recommended levels, there is a considerable residual risk of cardiovascular disease, and elevated RC levels may be one of the potential reasons [13]. In addition, elevated RC is also associated with reduced high-density lipoprotein cholesterol (HDL-C) [8], but it is also known that increased HDL-C levels have no benefit to reduce cardiovascular disease [14]. Therefore, elevated RC is likely to be a more potential causal factor than reduced HDL-C [8].

Of note, whether RC or RC/HDL-C was associated with PMI following PCI in patients with T2D is currently unknown, and the present study aimed to investigate these associations.

Methods

Study population

Between December 2010 and February 2014, 1252 consecutive diabetic patients with normal cardiac troponin I (cTnI) and creatine kinase-MB (CK-MB) levels without acute myocardial infarction (AMI) in the past 4 weeks who attempted to undergo elective PCI at our center were eligible for this study. The flowchart of inclusion and exclusion criteria for this study is demonstrated in Fig. 1. Finally, 1182 subjects (70.9% men, mean age 59.5 ± 9.3 years) were effectively included in the present study. The study complied with the Declaration of Helsinki, and was approved by the hospital ethic review board (FuWai Hospital & National Center for Cardiovascular Diseases, Beijing, China). Informed written consent was obtained from all patients included in this study.

Several guidelines suggest that the glycemic control goal is glycated hemoglobin (HbA1c) < 7% in diabetic patients [15,16]. Based on a cut-off of 7% for HbA1c, patients were divided into two groups: group A (HbA1c < 7%, $n = 563$, well-controlled) and group B (HbA1c $\geq 7\%$, $n = 619$, poorly-controlled).

Definitions

Adult patients with T2D were identified according to 2009 American Diabetes Association criteria for diabetes diagnosis: fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/l) or symptoms of hyperglycemia and a casual (random) plasma glucose ≥ 200 mg/dL (11.1 mmol/l) or 2-h plasma glucose ≥ 200 mg/dL (11.1 mmol/l) during an oral glucose tolerance test (OGTT). Atherogenic index of plasma (AIP) was defined as lg (triglyceride/HDL-C). Non-HDL-C was characterized as TC minus HDL-C. RC was equal to non-HDL-C minus LDL-C. Angiographic success of PCI was defined as residual stenosis less than 20% with stenting and residual stenosis less than 50% with balloon angioplasty only by visual estimation. Unstable angina was defined as rest angina, new-onset severe angina, and increasing angina within 2 months. PMI was defined as postprocedural cTnI $>3\times$ upper limit of normal (ULN), which was the diagnosis criterion of periprocedural myocardial infarction published in 2007 and postprocedural cTnI $>5\times$ ULN which was a requirement in the arbitrarily revised diagnosis criteria published in 2012 [17,18].

Percutaneous coronary intervention

The indication of PCI was based on the American College of Cardiology/American Heart Association (ACC/AHA) recommendations [19,20] and was performed by experienced interventional


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│ Inclusion criteria:         │   │ Consecutive patients │   │ 70 were not eligible:           │
│ ♦ Over 18 years of age      │   │ underwent PCI        │   │ ♦ 42 were excluded because a    │
│ ♦ Type 2 diabetes underwent │   │ n = 6588             │   │   total chronic occlusion could │
│   elective PCI              │   └──────────────────────┘   │   not be crossed with a wire    │
│ ♦ Normal cardiac markers    │              │               │ ♦ 3 patients were excluded      │
│   before PCI                │              ▼               │   because a subtotal chronic    │
│ ♦ Without AMI in the past 4 │   ┌──────────────────────┐   │   occlusion could not be        │
│   weeks                     │   │ Eligible patients    │   │   crossed with a wire           │
│ ♦ Without cardiac           │   │ n = 1252             │   │ ♦ 6 patients were excluded      │
│   dysfunction               │   └──────────────────────┘   │   because a severely calcified  │
│ ♦ Written informed consent  │              │               │   or tortuous lesion could not  │
└─────────────────────────────┘              ▼               │   be crossed with a balloon     │
                                 ┌──────────────────────┐    │ ♦ 5 patients were excluded      │
                                 │ Finally enrolled     │    │   because they were treated     │
                                 │ patients             │    │   with atheroablative, distal   │
                                 │ n = 1182             │    │   protection devices or         │
                                 └──────────────────────┘    │   aspiration thrombectomy       │
                                            │                │ ♦ 12 patients were excluded     │
                          ┌─────────────────┴─────────────┐  │   because the Remnant           │
                          ▼                               ▼  │   cholesterol values were       │
                 ┌─────────────────┐        ┌─────────────────┐ negative                        │
                 │ Group A         │        │ Group B         ││ ♦ 2 patients were excluded      │
                 │ Well-controlled │        │ Poorly-         ││   because lipid parameters      │
                 │ diabetic        │        │ controlled      ││   were lost                     │
                 │ patients        │        │ diabetic        │└─────────────────────────────────┘
                 │ (HbA1c <7%)     │        │ patients        │
                 │ n=563           │        │ (HbA1c ≥7%)     │
                 └─────────────────┘        │ n=619           │
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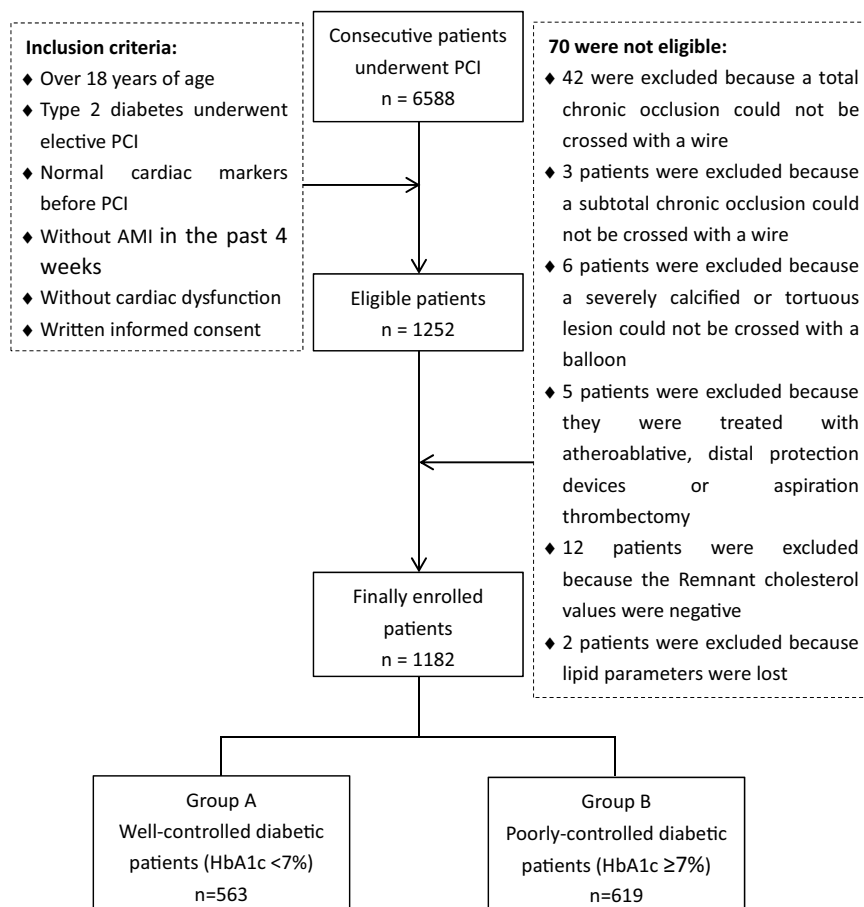
Fig. 1. Inclusion and exclusion criteria for this study. PCI, percutaneous coronary intervention; AMI, acute myocardial infarction; HbA1c, glycated hemoglobin.