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Effect of glycemic and lipid achievements on clinical outcomes type 2 diabetic, Chinese patients with stable coronary artery disease

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ABSTRACT

Aims: To describe the effect of glycemic and lipid achievements and their joint roles in future major adverse cardiovascular events (MACEs) prediction.
Methods: One thousand two hundred sixty consecutive, type 2 diabetic patients with stable coronary artery disease (CAD) were identified, they were followed up a median of 24.07 months.
Results: At baseline, 85.4% of patients with blood pressure less than 140/90 mmHg, while only a minority of patients met guideline-recommended hemoglobin A1C (HbA1C) (44.2%), low-density lipoprotein cholesterol (LDL-C) (24.7%), non high-density lipoprotein cholesterol (NHDL-C) (36.3%), or apolipoprotein B (apoB) levels (38.6%). After follow-up, patients achieving either glycemic or lipid goals experienced a lower rate of future events (HbA1C 35.4%, LDL-C 19.3%, NHDL-C 30.4%, apoB 26.7%). Dual-goal achievements of HbA1C and lipids showed the lowest event risk (adjusted relative risk, RR: HbA1C, 0.92 vs. LDL-C 0.75 vs. dual 0.27; HbA1C, 0.86 vs. NHDL-C 0.59 vs. dual 0.44; HbA1C, 0.74 vs. apoB 0.64 vs. dual 0.55). Patients with suboptimal goals (LDL-C 1.8–2.5 mmol/L, NHDL-C 2.5–3.4 mmol/L, or apoB 0.8–1.0 g/L) were at risk when compared to those with guideline-recommended goals.
Conclusions: Dual-achievement of glycemic and lipid goals based on a relative well-controlled condition of blood pressure conferred a better prognosis in type 2 diabetic patients with CAD.

1. Introduction

Coronary artery disease (CAD) is a frequently coexisting disorder for diabetes mellitus (DM) and presents as a major component of public health concerns and subsequent economic burdens worldwide. DM has been prominently positioned as a "super risk factor" or CAD risk equivalent in many position studies and guidelines (Kavousi et al., 2014). Early diagnosis of CAD coexisting with DM is a key factor for successful treatment outcome to reduce the risk of developing future major adverse cardiovascular events (MACEs) (Fox et al., 2007). Accordingly, international guidelines now recommend stringent lipid targets (ie, to levels of low-density lipoprotein cholesterol, LDL-C, <70 mg/dl; and non high-density lipoprotein cholesterol, NHDL-C, <100 mg/dl) in this high-risk population (Bays, Jones, Brown, & Jacobson, 2014; Stone et al., 2014).

Despite these statements, the management of CAD in asymptomatic DM once it is detected remains controversial. The effects of achievement of glycemic or lipid goal, and dual-achievement on the risk of MACE in the patients with concomitant DM and CAD are less evident, with recent data are predominantly observed in patients who are diagnosed with DM but free of CAD (Kontopantelis et al., 2015; Schulze et al., 2004; Shi et al., 2013).

Therefore, the primary objective of our study was to describe the current status of glycemic and lipid achievements that could offer insight into the potential cardiovascular risk, and their joint roles in MACE prediction in a Chinese, type 2 diabetic population with stable CAD.

2. Materials and methods

2.1. Study population

Our study complied with the Declaration of Helsinki and was approved by the hospital's ethical review board (Fu Wai Hospital & National Center for Cardiovascular Diseases, Beijing, China). Informed written consents were obtained from all patients enrolled in this study.

From April 2011 to January 2015, of 6153 consecutive patients scheduled for CAG because of angina-like chest pain and/or positive treadmill exercise test or clinically suspected CAD in our division, we

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identified 1260 type 2 diabetic patients with angiographic-proven CAD for the present analysis. Patients with acute coronary syndrome (ACS), heart failure (left ventricular ejection fraction, LVEF <45%), significant hematologic disorders, infectious or systematic inflammatory disease, thyroid dysfunction, severe liver and/or renal insufficiency and malignant disease were excluded from the current study.

2.2. Laboratory examinations

All patients underwent clinical examination and blood testing as our previous studies (Chen et al., 2015; Li et al., 2015). Blood samples were obtained from all patients from the cubital vein after a 12-hour overnight fast.

The concentrations of the plasma total cholesterol (TC), triglyceride (TG), HDL-C, LDL-C, apolipoproteinA-1 (apoA1), apoB were measured using an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan), and the TC, TG, HDL-C, and LDL-C levels were measured using an enzymatic assay. ApoA1, and apoB levels were measured using a turbidimetric immunoassay. NHDL-C was calculated as TC minus HDL-C. Hemoglobin A1C (HbA1C) was measured using Tosoh Automated Glycohemoglobin Analyzer (HLC-723G8, Tokyo, Japan). The concentrations of high-sensitive C-reactive protein (hs-CRP) were determined using immunoturbidimetry (Beckmann Assay 360, Bera, Calif., USA).

2.3. Follow-up

After the initial appointment, patients were prospectively followed up at 6, 12, 24, 48 months using telephone and/or interview by trained nurses or cardiologists, who were blinded to the results of the laboratory tests. The primary endpoints were first-time events of cardiac death, stroke, myocardial infarction (MI), post-discharge revascularization (PCI/CABG) or unstable angina (UA).

Cardiac death defined as a primary cause of acute MI, sudden cardiac death, congestive HF, arrhythmic heart disease, stroke, or other structural or primary cardiac cause of death. Stroke was defined on the basis of the presence of acute infarction as demonstrated by imaging or based on the persistence of symptoms. Diagnosis of MI was confirmed of the following: chest pain or equivalent symptom complex, positive cardiac biomarkers, and electrocardiogram changes typical of MI. Post-discharge revascularization was considered if coronary angioplasty or coronary surgery was performed during follow-up. UA without revascularization was defined as chest pain or chest pain equivalent with dynamic electrocardiogram changes such as ST depression or T wave inversion but without abnormal cardiac biomarkers and characterized by rest symptoms, new-onset angina (<2 months duration), or increasing duration or severity of previously stable anginal symptoms.

Statistical analysis

The values were expressed as the mean ± SD or median (Q1–Q3 quartiles) for the continuous variables and the number (percentage) for the categorical variables. The differences of clinical and biochemical parameters between groups were analyzed using independent sample t-test, Mann–Whitney U-test, χ^2-tests, and Fisher's exact test where appropriate. Univariate and multivariate Cox regression analyses were performed to estimate the association of glycemic and lipid achievement with CAD outcomes. A p-value <0.05 was considered statistically significant. The statistical analysis was performed with SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA).

Table 1
Baseline characteristics in type 2 diabetic patients with stable CAD.

	Total patients (n = 1260)	With MACE (n = 161)	Without MACE (n = 1056)	p-value
Cardiovascular risk factors				
Age (years)	59.04 ± 9.99	59.24 ± 11.40	58.97 ± 9.83	0.745
BMI (kg/m2)	26.19 ± 3.14	26.03 ± 3.08	26.23 ± 3.14	0.455
Gender, men% (n)	70.2 (885)	70.2 (113)	69.7 (736)	0.927
Hypertension, % (n)	74.0 (932)	79.5 (128)	73.2 (773)	0.101
Dyslipidemia, % (n)	30.8 (388)	34.2 (55)	30.0 (317)	0.314
Current smoking, % (n)	51.4 (648)	50.9 (82)	51.2 (541)	0.986
Previous PCI, %(n)	24.5 (309)	22.4 (36)	24.7 (261)	0.555
Previous CABG, %(n)	3.1 (39)	5.6 (9)	2.7 (28)	0.051
Family history of CAD, % (n)	14.8 (187)	17.4 (28)	14.6 (154)	0.451
Biomarkers				
SBP (mmHg)	129 ± 15	130 ± 12	129 ± 16	0.542
DBP (mmHg)	77 ± 10	78 ± 10	77 ± 10	0.102
TG (mmol/L)	1.60 (1.20–2.27)	1.58 (1.22–2.36)	1.60 (1.19–2.26)	0.744
TC (mmol/L)	4.09 ± 1.12	4.21 ± 1.16	4.07 ± 1.11	0.075
HDL-C (mmol/L)	1.02 ± 0.27	1.01 ± 0.30	1.02 ± 0.26	0.746
LDL-C (mmol/L)	2.46 ± 0.95	2.58 ± 0.99	2.44 ± 0.94	**0.041**
NHDL-C (mmol/L)	3.07 ± 1.06	3.20 ± 1.07	3.05 ± 1.06	**0.048**
Apo A1 (g/L)	1.32 ± 0.30	1.36 ± 0.34	1.31 ± 0.29	**0.037**
Apo B (g/L)	0.92 ± 0.30	1.01 ± 0.33	0.91 ± 0.30	**<0.001**
Glucose (mmol/L)	7.12 ± 2.29	7.46 ± 2.50	7.10 ± 2.25	**0.034**
HbA1C (%)	7.50 ± 1.39	7.76 ± 1.50	7.47 ± 1.37	**0.015**
Hs-CRP, mg/L	1.55 (0.77–3.27)	2.09 (0.99–6.37)	1.45 (0.73–3.04)	**<0.001**
Uric acid (umol/L)	344.57 ± 93.75	354.31 ± 97.10	343.04 ± 91.98	0.151
Prior drug treatment				
Statin, % (n)	69.7 (878)	69.6 (112)	70.3 (742)	0.916
Aspirin, n (%)	84.0 (1058)	82.6 (133)	84.3 (890)	0.634
Beta-blocker, % (n)	48.9 (616)	49.1 (79)	48.8 (515)	0.929
CCB, n (%)	19.5 (246)	16.1 (26)	19.6 (207)	0.297
ARB/ACEI, n (%)	27.0 (340)	28.6 (46)	26.4 (279)	0.421

Data shown are mean ± SD, median (Q1–Q3 quartiles) or n (%). The differences of clinical and biochemical parameters between groups were analyzed using independent sample t-test, Mann–Whitney U-test, χ^2-test where appropriate. The bold values indicated statistical significance. The MACE (major adverse cardiovascular events) consisted of cardiac death, stroke, myocardial infarction (MI), post-discharge revascularization or unstable angina (UA); BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CAD, coronary artery disease; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NHDL-C, non high-density lipoprotein cholesterol; Apo, apolipoprotein; HbA1C, hemoglobin A1C; Hs-CRP, high sensitively C reactive protein; CCB, calcium channel blocker; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker.