Journal of Cardiology 63 (2014) 29–34

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Association of prediabetes with diffuse coronary narrowing and small-vessel disease

Cagatay Ertan (MD)[a], Ozcan Ozeke (MD)[b,*], Murat Gul (MD)[b], Dursun Aras (MD)[b], Serkan Topaloglu (MD)[b], Halil Lutfi Kisacik (MD)[b], Ahmet Duran Demir (MD)[a], Sinan Aydogdu (MD)[b], Bulent Ozin (MD)[c]

[a] *Acibadem University, Department of Cardiology, Eskisehir, Turkey*
[b] *Turkiye Yuksek Ihtisas Education and Research Hospital, Department of Cardiology, Ankara, Turkey*
[c] *Baskent Universitesi, Department of Cardiology, Ankara, Turkey*

ARTICLE INFO

Article history:
Received 15 May 2013
Received in revised form 19 June 2013
Accepted 24 June 2013
Available online 5 September 2013

Keywords:
Prediabetes
Diffuse coronary narrowing
Coronary artery size

ABSTRACT

Background: A significant number of patients may not benefit from conventional techniques of myocardial revascularization due to diffuse coronary artery disease (CAD) or small coronary arterial sizes because of smaller arteries causing anastomotic technical difficulties and poor run-off. Diabetic patients have a more severe and diffuse coronary atherosclerosis with smaller coronary arteries limiting the possibility to perform a successful and complete revascularization, but this has not been examined in prediabetics.
Objective: To evaluate whether there is an association between prediabetes and the coronary arterial size.
Methods: We prospectively studied 168 consecutive patients with CAD and 172 patients with normal coronary artery anatomy (NCA). Patients were divided into three groups according to hemoglobin (Hb) A1c levels as "normal," "prediabetic," and "diabetic" groups, and the coronary artery sizes and Gensini scores were analyzed.
Results: There were 78 female patients and 90 male patients in the CAD group, and 87 female patients and 85 male patients in the NCA group. There was a statistically significant difference in distal and proximal total coronary arterial size among the CAD and NCA groups for both genders. There was a positive correlation between the HbA1c subgroups and Gensini score (Spearman's ρ: 0.489, $p < 0.001$ in female group; Spearman's ρ: 0.252 $p = 0.016$ in male group).
Conclusion: We found that prediabetic patients have a smaller coronary size and diffuse coronary narrowing for both genders, particularly in distal coronary arterial tree of left anterior descending coronary artery. The early detection of prediabetes in daily cardiology practice may provide more appropriate coronary lesion for percutaneous or surgical revascularization.

Introduction

Cardiovascular diseases are the leading cause of morbidity and mortality in insulin-resistant individuals with glycemic disorders. The risk for death among people with diabetes is about twice that of people of similar age but without diabetes [1,2]. However, epidemiologic evidence suggests this morbidity–mortality relationship begins early in the progression from normal glucose tolerance to overt diabetes. Since both increased insulin resistance and impaired β-cell function are present long before overt hyperglycemia becomes evident, indeed, most diabetic patients already show signs of cardiovascular disease upon diagnosis [1,2]. Overt diabetes is usually preceded by a condition known as "prediabetes," which refers to an intermediate stage in which individuals have blood glucose or glycated hemoglobin (hemoglobin A1c, HbA1c) levels higher than normal but not high enough to be classified as diabetes [2]. Subjects with prediabetes have an increased risk for future overt diabetes with a conversion rate of ~5–10% per year [3,4]. This risk increase has found to be a continuum and begins at a level below the cut point for impaired fasting glucose (IFG, 100 mg/dl) [5]. The prevalence of diabetes and prediabetes is substantial among adults with coronary artery disease (CAD) and likely underestimated because of suboptimal screening [6,7]. In 2010, the American Diabetes Association (ADA) proposed a "diabetes" diagnosis based on an HbA1c ≥ 6.5%, and 'prediabetes' [including IFG or impaired glucose tolerance (IGT)] as an HbA1c 5.7–6.4% [2].

Diabetic patients have a more severe, extensive-diffuse and rapidly progressive form of coronary atherosclerosis with an unfavorable angiographic anatomy limiting the possibility to perform

* Corresponding author at: Türkiye Yüksek İhtisas Hastanesi, Kardiyoloji Klinigi, Ankara, Turkey. Tel.: +90 505 3836773; fax: +90 312 2206100.
E-mail address: ozcanozeke@gmail.com (O. Ozeke).

0914-5087/$ – see front matter © 2013 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jjcc.2013.06.015

a successful and complete revascularization [3,8–10]. Compared to those without diabetes, diabetics have had worse outcomes with percutaneous transluminal coronary angioplasty, bare-metal stents, and drug-eluting stents. The reasons for this trend are because patients with diabetes have smaller-caliber vessels, a diffuse disease that often progresses rapidly, a greater burden of atherosclerotic disease, and exaggerated neointimal hyperplasia. Patients with small vessels present a higher risk for an adverse outcome after percutaneous coronary intervention (PCI) [10,11], because of a higher incidence of restenosis and an increased risk of major adverse cardiac events [12,13] and a higher risk after coronary artery bypass grafting (CABG) due to more technically challenging operative procedures and lower long-term patency rates [14–17] due to difficulties in anastomoses between saphenous vein grafts or internal mammary conduits to small caliber native coronary arteries particularly in diabetics [18] or women [19–21]. In the Coronary Artery Surgery Study, small body size and coronary artery caliber were the strongest predictors of perioperative mortality [22].

In general, CAD in diabetic patients is detected at an advanced stage, whereas the disease in its premature (prediabetes) or asymptomatic stages (undiagnosed diabetics) remains unfortunately undetected [23,24]. Such observations impose an aggressive approach to diagnostic strategies in diabetic patients to detect CAD at an early asymptomatic stage, which is probably characterized by a more favorable coronary vessel anatomy. Despite the remarkable advances in revascularization strategies made during the past decade, a significant proportion of patients are excluded from either PCI or CABG because of unsuitable or ungraftable coronary anatomy including diffuse severe CAD, extremely calcified vessels, chronic total occlusions, or small vessel caliber. In diabetics, the coronary arteries and their branches have been shown to have smaller diameters than normal subjects [25,26], but also appear to be narrower in prediabetic patient in daily cardiology practice. We aimed to evaluate whether there was an association between prediabetes and diffuse coronary narrowing and/or coronary artery sizes.

Methods

We planned to compare the coronary artery sizes separately in patients with normal coronary artery (NCA) findings in all 3 major epicardial and the left main coronary arteries, and patients with CAD. We prospectively studied 172 consecutive patients with NCA anatomy, and 168 consecutive CAD patients referred for elective coronary angiography. Those with known valvular heart disease, congenital heart disease, chronic kidney disease, anemia, or hemoglobinopathies were excluded from the study [27–29]. Patients were classified according to HbA1c levels in accordance with 2010 ADA Guidelines [2] into three groups: HbA1c lower than 5.7% (normal control group), HbA1c: 5.7–6.4% (prediabetic group), and HbA1c higher than 6.4% (diabetic group), and the coronary artery sizes and Gensini scores were analyzed. All measurements were performed by the same cardiology specialist blinded to the subjects' clinical and laboratory status.

Fasting blood specimens were collected to measure fasting plasma glucose (FPG), lipid profile, creatinine, and HbA1c levels. Other risk factors for cardiovascular disease and demographic parameters (age, gender, and body mass index) at the moment of enrollment in the study were evaluated by history-taking and physical examination results.

Selective coronary angiography was performed with the standard Judkins approach. Significant CAD was defined as the presence of >50% luminal diameter narrowing of one or more major epicardial arteries or its major branches. Segments of each epicardial coronary artery were measured in locations defined by Dodge et al. [30] and Mosseri et al. [25] as follows:

(a) The left main artery (LM) was measured at its midpoint,
(b) the left anterior descending artery (LAD) was divided into three segments, the proximal LAD (pLAD) was measured at its midpoint between its origin and the first branch (first septal-1S or diagonal-1D) of the pLAD, the mid-LAD (mLAD) was measured between 1S and 1D, and the distal LAD (dLAD) was measured after the diagonal branch of the LAD, apical LAD was measured in its distal 1.0 cm before the distal bifurcation, commonly referred to as the "pitchfork," "moustache," or "whale's tail",
(c) the circumflex (Cx) was also divided into two segments, the proximal Cx (pCx) was measured at its midpoint between its origin and the first obtuse marginal (1 M), the distal Cx (dCx) was measured at the origin of the second obtuse marginal branch (2 M); and finally the 1 M was measured at its origin,
(d) the right coronary artery (RCA) was divided into two segments: the proximal RCA (pRCA) was measured 15 mm from the ostium and the distal RCA (dRCA) was measured at the ostium of the posterior descending artery (PDA). In the CAD group, measurements of artery size were done on the most proximal disease-free part of each segment. In this respect, totally occluded segments were not evaluated in statistical analysis. Intracoronary nitrate was not administered to patients before the coronary angiography. Quantitative coronary angiographic analysis of all three coronary arteries was performed using the edge-detection method. The diameter of the catheter after contrast filling was used as a reference for calculating true arterial diameters. Measurements were taken in two orthogonal views for each of the major epicardial coronary arteries. The average of the two measurements was used for each coronary artery.

The sum of the pLAD, pCx, and pRCA was calculated and defined as total proximal coronary diameter (pTCD). The sum of diameters of the distal segments including dLAD, dCx, and dRCA was calculated and defined as total distal coronary diameter (dTCD).

The SPSS statistical software package (version 16.0; SPSS Inc., Chicago, IL, USA) was used to perform all statistical calculations. Continuous variables were expressed as mean ± SD. Since the coronary diameters in men are greater than women [31], all comparisons were made separately for both genders. The analysis of variance (ANOVA) with post hoc Tukey's HSD or Chi-square test was used for the statistical analysis of the results. Relationships between the continuous variables were evaluated by Pearson's correlation analysis when data were normally distributed or by Spearman's correlation analysis when they were not normally distributed. For all tests, a value of $p < 0.05$ was considered significant.

Results

There were 78 female patients and 90 male patients in the CAD group (Table 1) and 87 female patients and 85 male patients in the NCA group (Table 2). There were no statistically significant differences at baseline in any demographic or baseline variables between the groups (Tables 1 and 2). There were statistically significant differences in proximal and distal total coronary arterial sizes between the CAD (Table 1) and NCA (Table 2) groups for both genders particularly in LAD. There was a positive correlation between the patient subgroups (diabetic, prediabetic, and normal groups) and Gensini score (Spearman's ρ: 0.489, $p < 0.001$ in the female group; Spearman's ρ: 0.252, $p = 0.016$ in the male group).