Increased coronary intervention rate among diabetic patients with poor glycaemic control: A cross-sectional study

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Abstract

The relationship between glycaemic control and coronary artery disease (CAD) in type 2 diabetes mellitus (T2DM) is controversial. In the current cross-sectional study, we addressed the relationship between Hemoglobin A1c (HbA1c) values and the need for revascularization among diabetic patients undergoing coronary angiography. A total of 301 consecutive patients with known T2DM (age 61.8±10.1 years, 46.2 % women) requiring coronary angiography due to CAD symptoms were included. T2DM patients were categorized into two groups based on their HbA1c values: 93 (30.9%) diabetics with good glycaemic control (HbA1c≤7 %), and 208 (69.1%) diabetics with poor glycaemic control (HbA1c>7 %). A total of 123 patients (40.9%) required revascularization. The revascularization rate was 28.0% among T2DM patients with good glycaemic control and 46.6% among T2DM patients with poor glycaemic control, respectively (p=0.002). In a logistic regression analysis, the need for revascularization was predicted by poor glycaemic control (Odds Ratio [OR] 2.26, 95% Confidence Interval [CI] 1.32-3.82; p=0.003) adjusted for age, gender, Body-Mass-Index and diabetes duration. Moreover, there was a linear relationship between HbA1c values and number of affected coronary arteries (r= 0.169; p=0.003). Our data suggest that there is a close association between poor glycaemic control and increased revascularization rate in T2DM, which should be considered in primary and secondary prevention models.

KEY WORDS: Diabetes mellitus, glycaemic control, coronary artery disease, revascularization

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) continues to be one of the most common and expensive public health problems worldwide [1]. It is also a major risk factor for cardiovascular disease [2]. Glycaeted hemoglobin is an integrated summary of circadian blood glucose during the preceeding 6-8 weeks, equivalent to the lifespan of erythrocytes [3], and glycaeted hemoglobin A1c (HbA1c) is a useful measure of glycaemic control, which plays an important role in the management of the T2DM patients. Optimal glycaemic control (defined as HbA1c ≤7%) results in lower incidence of microvascular complications [1]. There is, for instance, a well-defined relationship between increased HbA1c levels and the incidence or worsening of diabetic retinopathy [4]. However, although an association between T2DM and coronary artery disease (CAD) exists (current registries estimate that approximately one-third of patients undergoing Percutaneous Coronary Intervention (PCI) have T2DM [5]), there is still a lack of evidence regarding the glycaemic control and macrovascular complications, including CAD. An increasing number of CAD patients undergo PCI or Coronary Artery Bypass Grafting (CABG) with a considerable risk of relapse of the CAD in the years following the intervention [6, 7]. In this context, the impact of glycaemic control in these patients is controversial [2, 8]. In the current cross-sectional study, we aimed to address the association between glycaemic control and coronary intervention rate in a consecutive cohort of T2DM patients undergoing coronary angiography due to CAD symptoms.

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MATERIALS AND METHODS

Study population

This is a retrospective study conducted at 29 Mayıs Hospital, Ankara between March 2009 and January 2012. A total of 301 consecutive patients (age 61.8±10.1 years, 46.2% women) with known T2DM undergoing coronary angiography due to CAD symptoms for decision/intervention were enrolled. T2DM was defined as previous history of the physician diagnosed T2DM based on the hospital records, or the use of an oral antidiabetic agent and/or insulin at the time of the coronary angiography. The patients were scheduled for coronary angiography on the basis of current guidelines for ischaemic heart disease [9] and categorized into two groups based on their HbA1c values obtained within the 21 days proceeding and 16 days following the coronary angiography (95% within the same week): "Good glycaemic control was defined as HbA1c≤7 %, and "poor glycaemic control" as HbA1c>7 % [10]. The baseline anthropometrics, smoking habits and medical history as well as medications were also obtained from the medical records.Body Mass Index (BMI) was calculated according to the formula body weight divided by height squared, and obesity was defined as a BMI ≥30 kg/m² [11]. The study was approved by the hospital ethical committee and conducted in conformity with the Declaration of Helsinki.

Procedure

Selective coronary angiography was performed through the femoral artery using Seldinger technique. Under use of non-ionic contrast media (Iomeron 400/250ml) standard multiangulated cinegraphies were obtained. Angiograms were assessed visually by an experienced angiographer for the diagnosis of CAD and the decision for an intervention was made by the cardiology and cardiovascular surgery team of the hospital independently of the current retrospective study design.

Blood samples

HbA1c values in percentage according to the Diabetes Control and Complications Trial (DCCT) / National Glycohemoglobin Standardization Program (NGSP) were obtained on a Beckmann Coulter Olympus AU 400 auto analyzer using the commercially available Tina-quant hemoglobin A1c Gen.3 reagent with the whole blood application. We also determined lipid profile and fasting plasma glucose by standard laboratory methods.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 for Windows® system (SPSS® Inc., Chicago, Illinois, USA). Independent sampled T-test was used for comparison of continuous variables, and chi-square test was applied for comparison of the categorical variables. A univariate logistic regression analysis was used to address the relationship between the need for revascularization and poor glycaemic control as well as anthropomorphic and clinical variables. Corrected odds ratios (OR) was calculated from the regression coefficients. All ORs are presented with their 95% confidence intervals (CI). Moreover, univariate and multivariate linear regression analysis were also executed to evaluate the correlation between HbA1c levels and the number of affected coronary vessels. Unstandardized coefficient (B) is presented with 95% CI. Results are given as mean ± SD, and categorical variables as numbers (percentages). All statistical tests were two-sided, and *p*-values less than 0.05 were considered significant.

RESULTS

In the whole group, the majority (N=208; 69.1%) of the T2DM patients had poor glycaemic control with mean HbA1c levels >7.0%. There was no significant difference between the patients with good glycaemic control versus poor glycaemic control regarding age, gender, BMI, obe-

TABLE 1. Characteristics of the study population based on the glycaemic control

Variable	Good Control (n=93)	Poor Control (n=208)	p Value
Age (yrs)	61.8 ± 10.0	61.8 ± 10.2	0.984
Female gender (%)	49.5	44.7	0.445
BMI (kg/m²)	29.3 ± 4.4	28.9 ± 4.7	0.461
Obesity (%)	61.5	68.3	0.237
Current smokers (%)	24.7	20.7	0.432
Former revascularization (%)	28.0	30.3	0.682
Diabetes duration (yrs)	8.2 ± 7.8	10.1 ± 7.9	0.057
Hypertension (%)	83.9	82.2	0.725
Atrial fibrillation (%)	3.2	6.7	0.287
Stroke (%)	6.5	4.8	0.563
Diabetes treatment			
Diet only (%)	8.6	2.4	
Oral antidiabetics (%)	79.6	58.9	
Insulin (%)	5.4	16.4	
Oral antidiabetics + Insulin (%)	4.3	19.8	< 0.001
Other medications			
ASA (%)	68.8	76.4	0.163
Clopidogrel (%)	20.4	34.6	0.017
Warfarin (%)	2.2	4.3	0.352
Beta blockers (%)	54.8	55.8	0.881
Diuretics (%)	43.0	28.8	0.016
Calcium channel blockers (%)	21.5	21.2	0.945
ACE inhibitors (%)	30.1	37.5	0.215
Angiotensin II antagonists (%)	40.9	28.8	0.040
Lipid lowering agents (%)	67.7	67.3	0.941

*Continuous variables are expressed as mean ± SD, statistics by unpaired Student's *t* test. Comparison of groups by chi-squared test. *Definition of abbreviations* BMI = Body-Mass-Index; ASA = Acetylsalycilic acid; ACE = Angiotensin Converting Enzyme

TABLE 2. Laboratory and angiography results of the study population based on the glycaemic control

Variable	Good Control (n=93)	Poor Control (n=208)	p Value
Blood samples			
Plasma triglyceride, mg/dl	197.9 ± 174.1	203.6±143.7	0.795
Plasma LDL cholesterol, mg/dl	117.8 ± 35.6	128.6 ± 36.7	0.019
Plasma HDL cholesterol, mg/dl	44.1 ± 10.7	42.4 ± 9.4	0.204
Plasma glucose, mg/dl	128.0 ± 35.3	207.9 ± 86.0	< 0.001
HemoglobinA1c (%)	6.1 ± 0.5	9.1 ± 1.8	< 0.001
Coronary angiography results			
No vessel involvement (%)	48.4	28.8	
One-vessel disease (%)	17.2	27.9	
Two-vessel disease (%)	14.0	19.7	
Three-vessel disease (%)	20.4	23.6	0.009
Decision for coronary intervention (%)	28.0	46.6	0.002
PCI (%)	18.3	34.6	
CABG (%)	9.7	12.0	

*Continuous variables are expressed as mean ± SD, statistics by unpaired Student's *t* test. Comparison of groups by chi-squared test. *Definition of abbreviations* LDL = Low Density Lipoprotein; HDL = High Density Lipoprotein; PCI = Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Grafting.

TABLE 3. The relationship between anthropomorphic as well as clinical variables and the need for coronary intervention in T2DM patients with CAD symptoms

Univariate analysis	OR	95% CI	p Value
Age	1.05	1.03-1.07	<0.001
Male gender	1.55	0.97-2.46	0.067
BMI	1.01	0.96-1.06	0.835
Obesity	0.85	0.52-1.38	0.507
Current smoking	1.00	0.58-1.75	0.993
Hypertension	1.02	0.56-1.88	0.938
Diabetes duration in years	1.05	1.02-1.08	0.002
Uncontrolled T2D	2.25	1.33-3.82	0.003
HbA1C	1.19	1.07-1.34	0.002
Plasma HDL cholesterol	0.98	0.95-1.01	0.147
Plasma LDL cholesterol	1.01	1.00-1.01	0.101
Plasma Triglycerides	1.00	1.00-1.00	0.890
Multivariate model I			
Uncontrolled T2DM	2.26	1.05-1.33	0.003
Age	1.04	1.01-1.06	0.002
Male gender	2.01	1.21-3.37	0.007
Diabetes duration in years	1.03	0.99-1.06	0.119
Multivariate model II			
HbA1C	1.19	1.05-1.34	0.005
Age	1.03	1.01-1.05	0.006
Male gender	2.01	1.21-3.37	0.007
Diabetes duration in years	1.02	0.99-1.06	0.113

Definition of abbreviations T2DM = Type 2 Diabetes Mellitus; OR = Odds ratio; CI= Confidence interval; BMI = Body-Mass-Index; HbA1C = Hemoglobin A1c; HDL = High Density Lipoprotein; LDL= Low Density Lipoprotein.

sity, current smoking, and other comorbidities. However, plasma LDL cholesterol levels were significantly higher in the poor glycaemic control group though the proportion of patients on the lipid lowering agents did not differ significantly (Tables 1 and 2). The T2DM patients with good glycaemic control seemed to have higher usage of diuretics and angiotension II antagonists while proportionally more patients among the poor glycaemic control group were on clopidogrel therapy (Table 1). The mean duration of T2DM was longer in the poor glycaemic control group (10.1 *vs* 8.2 yrs), and those patients were more likely to be treated with insulin, or oral antidiabetics and insulin in combination. In total, 123 T2DM patients (40.9%) undergoing coronary angiography required revascularization. As shown in Table 2, the revascularization rate was 28 % among diabetics with good glycaemic control, while almost half of the poor glycaemic control group had two or three-vessel disease with requirement for revascularization. The poor glycaemic control group was predominant both within the PCI and CABG procedures. In a logistic regression analysis, the need for revascularization was associated with age, diabetes duration, poor glycaemic control and HbA1c levels but not with gender, BMI, obesity, current smoking, hypertension and blood lipid levels (Table 3). In a multivariate model, the need for revascularization was predicted by poor glycaemic control (Odds Ratio [OR] 2.26, 95% Confidence Interval [CI] 1.32-3.82; p=0.003) adjusted for age, gender, BMI and diabetes duration. As shown in Figure 1, HbA1c levels were higher among the groups with more than one vessel involved, and there was a linear relationship between HbA1c values and the number of affected coronary arteries (r= 0.169; p=0.003).

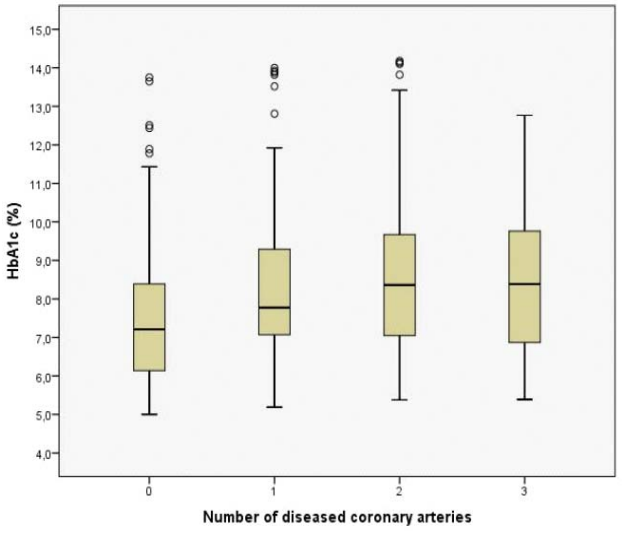

FIGURE 1. HbA1c levels in T2DM patients based on the affected arteries during coronary angiography

DISCUSSION

The main finding of our study was that poor glycaemic control was significantly associated with the need for revascularization in this consecutive cohort of T2DM patients undergoing coronary angiography due to CAD symptoms. Our results are in accordance with several other previously published studies reporting increased risk of cardiovascular outcome in patients with uncontrolled T2DM. Zoungas et al. [12] demonstrated that the threshold HbA1c was 7% for macrovascular events, moreover every 1% higher mean HbA1c level above this threshold was associated with a 38% higher risk . In a study by Xu et al. [13], addressing all-cause and coronary heart disease mortality in T2DM patients, a higher HbA1c threshold (8.5%) came out to be predictive. A recent study showing the relationship between HbA1c-levels and clinic outcomes in diabetic patients following elective stenting also had similar results; diabetic patients with poor glycaemic control were 2.1 times more at risk of developing major advance cardiovascular events than good controlled diabetic patients using the HbA1c threshold of 7% [10]. However, although an association between T2DM and CAD exists, the impact of glycaemic control in these patients remains controversial [2, 8]. The predictive value of high preprocedural glycaemia levels has been reported in diabetic patients undergoing PCI, especially in the context of acute myocardial infarction [14, 15, 16]. In contrary, there is also data from larger prospective studies, suggesting the absence of the benefit in macrovascular complications of a strict glycaemia control [8]. Regarding the HbA1c thresholds, Currie et al. [17] found an approximately U-shaped pattern between HbA1c categories and all-cause mortality, suggesting that low (6.4%) and high (10.6%) mean HbA1c levels were associated with increased all-cause mortality when compared with those having modest glucose control (7.5%). The reason for the increased mortality in low mean HbA1c values remains unknown. An association with higher rates of severe hypoglycaemia was reported in the ACCORD study [18]. It should also be kept in mind that the controversies within glycaemic control in literature refer mainly to the CAD cohorts. Kauffman et al. [19] suggested that in a closely monitored setting, with aggressive control of cardiac risk factors and implementation of secondary prevention therapies, HbA1c values at the time of an incident cardiac event may not be predictive of a recurrent cardiac event in patients with CAD. It has also been suggested that care of patients with CAD should focus primarily on management of cardiovascular risk factors, rather than improvement of suboptimal HbA1c values at the time of the cardiac event [19].

The prognostic value of glycaemic control in T2DM patients in respect of incident CAD also needs to be better defined. Less is known regarding the association between glycaemic control and the need for coronary revascularization among T2DM patients with CAD symptoms. To the best of our knowledge, our cross-sectional study is the first to address this relationship in a consecutive T2DM cohort undergoing coronary angiography for suspicion of CAD. Based on the previous reports and the current guidelines of the American Diabetes Association, we also chose HbA1c <7% as the threshold for good glycaemic control. The univariate predictors of the need for revascularization were age, diabetes duration, poor glycaemic control and HbA1c levels but not gender, BMI, obesity, current smoking, hypertension and blood lipid levels in this cohort. However, there was a tendency for increased risk for revascularization in males, which also came out to be significant in the multivariate model. The given HbA1c threshold seemed to be suggestive for our hypothesis, and there was a positive dose-response relationship between HbA1c levels and the number of affected coronary arteries. Our study is not without limitations. Our patients were required to have only one HbA1c value for inclusion in the study, which reflects ambient mean glycaemia over 2-3 months period in relation to the angiographic procedure. A longer period over 1 year with several HbA1c controls could have been much better to reflect the real relationship. Due to the retrospective character of our study, we did not have complete data regarding earlier HbA1c values as many of those patients were referred for coronary angiography from centers other than our own hospital. As many patients with T2DM have symptoms suggestive of CAD, and suspicious exercise stress testing or myocardial perfusion scintigraphy findings, the negative coronary angiography results do not exclude coronary microangiopathy [20]. However, our findings have clinical implications in predicting the need for coronary revascularization among T2DM patients based on the glycaemic control.

CONCLUSION

In conclusion, our data suggest that there is a close association between poor glycaemic control, based on the HbA1c threshold of 7%, and the need for revascularization in T2DM, which should be considered in primary and secondary cardiovascular prevention models.

DECLARATION OF INTEREST

The authors declare that there is no conflict of interest.

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