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Prevalence of unrecognized diabetes, prediabetes and metabolic syndrome in patients undergoing elective percutaneous coronary intervention

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Abstract

Background—Diabetes mellitus (DM) and metabolic syndrome are important targets for secondary prevention in cardiovascular disease. However, the prevalence in patients undergoing elective percutaneous coronary intervention is not well defined. We aimed to analyse the prevalence and characteristics of patients undergoing percutaneous coronary intervention with previously unrecognized prediabetes, diabetes and metabolic syndrome.

Methods—Data were collected from 740 patients undergoing elective percutaneous coronary intervention between November 2010 and March 2013 at a tertiary referral center. Prevalence of DM and prediabetes was evaluated using Haemoglobin A1c (A1c $\geq 6.5\%$ for DM, A1c 5.7–6.4% for prediabetes). A modified definition was used for metabolic syndrome [three or more of the following criteria: body mass index ≥ 30 kg/m²; triglycerides ≥ 150 mg/dL; high density lipoprotein <40 mg/dL in men and <50 mg/dL in women; systolic blood pressure ≥ 130 mmHg and/or diastolic ≥ 85 mmHg; and A1c $\geq 5.7\%$ or on therapy].

Results—Mean age was 67 years, median body mass index was 28.2 kg/m² and 39% had known DM. Of those without known DM, 8.3% and 58.5% met A1c criteria for DM and for prediabetes at time of percutaneous coronary intervention. Overall, 54.9% met criteria for metabolic syndrome (69.2% of patients with DM and 45.8% of patients without DM).

Conclusion—Among patients undergoing elective percutaneous coronary intervention, a substantial number were identified with a new DM, prediabetes, and/or metabolic syndrome.

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Conflicts of interest

Arthur Schwartzbard is on the speakers bureau for Takeda, Howard Weintraub is on the speakers bureau for Gilead, Novartis, Kowa, AstraZeneca and Abbott, and Edward Fisher is on the Merck Global Advisory Board for Atherosclerosis. All remaining authors have none declared.

Routine screening for an abnormal glucometabolic state at the time of revascularization may be useful for identifying patients who may benefit from additional targeting of modifiable risk factors.

Keywords

diabetes; prediabetes; metabolic syndrome; Haemoglobin A1c; glucose intolerance; cardiac catheterization

Introduction

Over the past several decades, rates of hyperlipidemia, hypertension and smoking have declined, as has cardiovascular mortality. However, the prevalence of obesity, diabetes mellitus (DM) and prediabetes have increased, possibly contributing to residual cardiovascular risk [1,2]. It is well recognized that DM increases the risk of cardiovascular disease, but prediabetes and metabolic syndrome also moderately increase the risk of cardiovascular disease and increase risk for overt DM [3]. The prevalence of glucometabolic abnormalities in populations with existing cardiovascular disease is uncertain, and despite current American Diabetes Association (ADA) guidelines, which recommend screening for DM every 3 years in adults with cardiovascular disease [4], screening in these patients by cardiology providers is not universally recommended [5–8]. The benefit in screening for prediabetes and metabolic syndrome in patients with cardiovascular disease lies in preventing the progression to diabetes through multifactorial interventions, such as in the Diabetes Prevention Program (DPP), improving the overall cardiovascular risk profile [9]. A cost-effectiveness analysis for treatment of prediabetes in the DPP trial was only \$9511 per quality-adjusted life-year (QALY), supporting the value of intervention at this stage [10].

In this study, we sought to evaluate the prevalence of undiagnosed DM, prediabetes and metabolic syndrome in patients undergoing elective percutaneous coronary intervention (PCI) by measurement of peri-procedural Haemoglobin A1c levels.

Materials and methods

Study population

A dedicated preventive cardiology consult service was established at New York University Langone Medical Center, a tertiary care facility, to identify and target modifiable cardiovascular risk factors in patients undergoing PCI. A preventive cardiology attending and fellow met with all patients undergoing elective PCI post-intervention. Between November 2010 and December 2012, the preventive cardiology team interviewed 822 patients undergoing elective PCI within 24 h post-procedure. All patients were referred for cardiac catheterization by outpatient internists or cardiologists. Among these patients, 10.0% ($n = 82$) were excluded from analysis because of missing A1c levels. New York University School of Medicine institutional review board approved this study, and all patients provided a signed written informed consent.

Variables of interest

A 145-question survey was administered by the preventive cardiology team and included data on demographics, medications, medical history and social habits. Data were obtained from patient interviews and the electronic medical record. History of coronary artery disease (CAD) was defined as either prior myocardial infarction, known CAD or prior coronary revascularization with coronary artery bypass graft surgery or PCI. History of DM was recorded from chart review, patient report or if on medical therapy for DM. Body mass index (BMI), blood pressure and A1c were recorded periprocedurally, and fasting lipid panel (total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein (HDL-C) and triglyceride level) measured within 2 weeks of procedure was obtained from chart review.

Outcomes of interest

Based on criteria from ADA guidelines, patients without known DM were reclassified into one of three groups using A1c levels: DM (A1c $\geq 6.5\%$), prediabetes (A1c 5.7–6.4%) or neither DM nor prediabetes (A1c $<5.7\%$) [4]. Metabolic syndrome was defined using the 2009 ‘harmonized’ criteria from the International Diabetes Federation task force on epidemiology and prevention, National Heart, Lung and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and the International Association for the Study of Obesity [11]. This definition was further modified using BMI criteria instead of waist circumference and A1c in lieu of fasting plasma glucose [12]. Therefore, metabolic syndrome was defined by the presence of three or more of the following criteria: (1) BMI ≥ 30 kg/m²; (2) triglyceride levels ≥ 150 mg/dL or on therapy (fibrates or fish oil); (3) reduced HDL-C (men <40 mg/dL, women <50 mg/dL); (4) systolic blood pressure >130 mmHg and/or diastolic blood pressure >85 mmHg or on anti-hypertensive medication; or (5) known history of DM or A1c $\geq 5.7\%$ or on glucose-lowering medication.

Statistical analysis

Data were compiled using Velos database software (Velos, Inc., Fremont, CA, USA) and statistical analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Normally distributed continuous variables are presented as mean $\pm$ standard deviation and compared using *t*-tests or analysis of variance for 2- and 3-way comparisons, respectively. Skewed continuous and ordinal variables are presented as median [interquartile range] and compared using the Mann–Whitney *U*-test and Kruskal Wallis test for two-way and three-way comparisons, respectively. Pearson’s chi-square analysis was used to compare proportions. Two-tailed *p*-values <0.05 were used to report statistical significance.

Results

Clinical characteristics of the overall study cohort are shown in Table 1. There was a significantly higher burden of comorbidities in those with known DM compared with those without. Clinical characteristics of patients without a known history of DM are shown in Table 2 and are reclassified as prediabetes, DM or neither based on A1c levels. There was a significantly greater proportion of non-Caucasians and patients with a history of peripheral

artery disease in those reclassified as having DM. Although there is a higher proportion of non-Whites in the group identified with DM, there were no other differences in cardiovascular risk factors or risk factor control by race. The remaining characteristics were similar across the three groups of glycemic status. Overall, two thirds of the patients without a known history of DM were reclassified as having prediabetes or DM by A1c criteria (Figure 1b), and over half of patients with known DM had an A1c level greater than 7% (Figure 1a, median A1c 5.6%). Of note, racial differences were found in risk factor control, with Hispanics patients having the highest proportion with A1c over 7% (71.9%) and Black patients with the highest proportion of blood pressure over 140/90 mmHg (48.0%) and total cholesterol above 200 mg/dL (31.6%).

Metabolic syndrome was present in over half the total population (54.9% overall, 69.2% of patients with DM and 45.8% of patients without DM). The proportion of patients with metabolic syndrome according to number of criteria fulfilled is shown in Figure 2.

Discussion

According to the National Cardiovascular Database and Registry, over half a million (544 869) non-urgent cardiac catheterizations with PCI performed between 2009 and 2011 [13]. Based on the findings in our study, over 45 000 of these patients would meet criteria for undiagnosed diabetes, and over 250 000 would meet criteria for prediabetes and/or metabolic syndrome.

Prior studies have shown that the presence of DM places patients with coronary disease at increased risk for recurrent cardiovascular events [14]. Prior studies have also shown that up to 50% of those with prediabetes may progress to DM within 5 years [15]. In addition, the presence of metabolic syndrome without a diagnosis of DM is associated with a fivefold risk of progression to DM compared with those without metabolic syndrome [16]. Growing evidence has supported the association of prediabetes and subsequent cardiovascular risk; a *meta*-analysis of 18 studies showed a small increase in risk for the development of cardiovascular disease (20%) in patients with pre-diabetes compared with those with normoglycemia [3]. While it has been shown that lifestyle changes, medical therapy and bariatric surgery can prevent progression to DM, it is not well understood if early detection and aggressive treatment of glucometabolic state improves cardiovascular outcomes [9,17–20]. Early intensive treatment of new DM in the United Kingdom Prospective Diabetes Study limited microvascular complications, myocardial infarction risk and death from any cause, while more recent studies in different diabetic populations have demonstrated either no benefit or increased adverse cardiovascular outcomes with intensive glycemic control [21–25].

The prevalence of undetected DM and prediabetes in our high-risk population is substantially higher than that observed in the general population [26]. Compared with unselected NHANES survey populations, we found a 4.5-fold higher prevalence of previously undetected DM (8.3% vs. 1.8%), and a more than 1.6-fold higher prevalence of prediabetes (58.0% vs. 35%) and metabolic syndrome (55% vs. 34%) [26,27]. While data exists on prevalence of hyperglycemia and DM in the setting of acute coronary syndrome

[28–30], few studies have assessed the prevalence in patients without known DM undergoing elective PCI. Two small European studies utilized oral glucose tolerance testing and found previously undetected DM in nearly 20% using oral glucose tolerance testing [31,32]. One study that used A1c levels in patients without known DM undergoing elective PCI found one-third of patients had levels greater than or equal to 6% [33]. At one-year follow-up, these patients had significantly higher rates of major adverse cardiac events, target vessel revascularization and cardiovascular mortality [33]. In our cohort, 40.5% of patients had an A1c of 6% or greater.

Detection of glucometabolic abnormalities with routine screening of A1c levels at the time of PCI may provide an opportunity for cardiovascular specialists to identify those who may benefit from targeted intervention to decrease the risk of progression to DM and its long-term sequelae. While A1c has been reported to be less sensitive for the diagnosis of DM than fasting blood glucose levels [30], the convenience of the non-fasting test allows for improved screening rates and therefore increased detection compared with standard methods. Currently, the ADA recommends screening for DM including the use of A1c in asymptomatic adults who have a BMI ≥ 25 kg/m² or one or more additional risk factors for DM, including cardiovascular disease; if normal, repeat testing is recommended every 3 years [15]. Despite this, a joint cardiovascular society recommendation that advocated for routine screening for DM in patients with cardiovascular disease was withdrawn, citing logistic difficulty with screening methods [34].

In our population, those with known diabetes had higher proportions of those with lipids and blood pressure at goal compared with those without known diabetes, suggesting that recognition of DM was associated with tighter risk factor control (Table 1). Although more research is needed, recognition of an abnormal glucometabolic state should lead to more aggressive lifestyle changes in combination with medical therapy targeted towards improvement of other cardiovascular risk factors.

The dedicated preventive cardiology consultation service at our center was established with the goal of increasing patient education, encouraging adherence to medication and lifestyle changes for the improvement of all cardiovascular risk factors. Further studies are underway to evaluate the efficacy of a periprocedural consultative service to improve risk factor optimization.

Limitations

Our study has several limitations. Ten percent of patients interviewed did not have A1c data available. Yet, when characteristics of those without A1c were compared with those with A1c present, we found no difference in demographics or cardiovascular risk factors (such as blood pressure control, history of coronary disease, lipid parameters or mean BMI), suggesting a balanced population sample. Not surprisingly, the only difference found was that those with a known history of diabetes had a higher proportion of A1c levels than those without a history of diabetes (94% vs. 88%). Second, the definition of metabolic syndrome was modified by using BMI >30 kg/m² and A1c $>5.7\%$; these have been used in prior studies separately, but the use of both has not been validated together. The use of BMI

instead of waist circumference may not fully account for the excess visceral fat that is central to the proposed risk associated with metabolic syndrome. The BMI was not adjusted for ethnicity as is suggested for waist circumference [35] which may have led to underdiagnosis of metabolic syndrome. In addition, the single blood pressure measurement recorded was taken within 24 h of PCI and may not be reflective of the patients' average blood pressure reading as this was performed periprocedurally as an inpatient, when they may have received intravenous fluids post-procedure or may feel anxious. Lastly, the population represented in this single center study may not be generalizable to everyone. Compared with that of the National Cardiovascular Data Registry, which collects ongoing data on patients undergoing cardiac catheterization across the United States, our patients were similar in age and gender, but our center had a higher proportion of non-White patients (42.3% vs. 16.7%) [36].

Despite these limitations, this remains one of the largest studies to evaluate the prevalence of undetected DM, prediabetes and metabolic syndrome in patients undergoing elective PCI.

Conclusions

In conclusion, we found a substantial proportion of patients with unrecognized DM, prediabetes and metabolic syndrome in a population undergoing elective PCI, supporting the need for a focus on routine screening by providers of cardiac patients. If identified early, treatment of diabetes has been shown to reduce micro and macrovascular complications. Treatment of prediabetes and metabolic syndrome can delay progression to diabetes, and more aggressive risk factor control overall in this population may reduce future cardiovascular risk. Further studies are needed to determine if targeted therapy can modify long-term cardiovascular risk. Given the substantial burden of prediabetes and metabolic syndrome in this population, identifying these patients prior to the development of diabetes provides an opportunity for significant risk reduction.

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Abbreviations

DM	diabetes mellitus
A1c	Haemoglobin A1c
BMI	Body Mass Index
PCI	percutaneous coronary intervention
CAD	coronary artery disease

LDL-C	Low Density Lipoprotein cholesterol
HDL-C	High Density Lipoprotein cholesterol

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Figure 1.

(A) Glycemic control in patients with a history of diabetes undergoing percutaneous coronary intervention ($n = 292$). (B) Proportions of non-diabetic patients reclassified as prediabetic and diabetic based on A1c levels ($n = 448$)

Figure 2.

Proportion of patients with metabolic syndrome according to number of criteria fulfilled ($N = 740$). Three or more criteria = metabolic syndrome. White = proportion with no history of diabetes ($n = 448$), Gray = proportion with history of diabetes ($n = 292$)

Table 1Comparison of characteristics of patients with and without a known history of diabetes mellitus ($n = 740$)

Characteristics	Overall ($N = 740$)	No history of DM ($n = 448$)	History of DM ($n = 292$)	p -value*
Median A1c, % (IQR)	6.1 (5.7, 6.9)	5.8 (5.6, 6.1)	7.6 (6.5, 8.4)	—
Age, years	66.9 (± 10.8)	66.7 (± 11.4)	67.2 (± 9.7)	NS
Body mass index, kg/m²	28.2 (25.6, 31.9)	27.7 (25.1, 31.3)	29.4 (26.1, 33.1)	NS
Sex, %				NS
Male	75.8	78.3	71.9	—
Female	24.2	21.7	28.1	—
Race, % ($n = 738$)				<0.001
Caucasian	57.7	63.5	49.0	—
Non-Caucasian	42.3	36.5	51.0	—
Current smoker, %	9.7	9.0	10.8	NS
Blood pressure <140/90, %	65.0	68.2	60.1	0.025
Medical history, %				
Coronary artery disease	57.2	53.0	63.7	0.004
Prior infarction	20.2	19.2	21.8	NS
Prior PCI	46.6	43.8	50.9	NS
Prior CABG	12.5	10.1	16.3	0.013
Hypertension	86.5	81.2	94.8	<0.001
Hyperlipidemia	84.4	79.6	91.7	<0.001
Stroke	5.8	4.0	8.7	0.009
Peripheral artery disease	12.3	9.2	17.0	0.002
Angina	29.6	30	29.1	NS
Medications, %				
Aspirin	85.8	85.2	86.6	NS
Beta blocker	65.1	63.6	67.5	NS
Clopidogrel	44.5	42.8	47.1	NS
Statin	77.8	76.1	80.5	NS
Lipid profile, mg/dL				
Total cholesterol <200	79.9	76.6	84.9	0.006
LDL-C <100	64.3	58.7	72.8	<0.001
HDL-C				
Men >40	69.0	70.9	65.7	NS
Women >50	55.9	60.8	50.0	NS
Non-HDL <130	66.2	62.3	72.3	0.005
Triglycerides <150	66.5	68.5	63.4	NS

DM, Diabetes Mellitus; PCI, Percutaneous coronary intervention; CABG, Coronary Artery Bypass Graft surgery; LDL-C, Low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol; IQR, interquartile range; NS, not significant

* Comparison between patients with *versus* without known history of diabetes mellitus

Table 2

Characteristics of patients without known history of diabetes mellitus reclassified as 'euglycemic', 'prediabetes' or 'diabetes' using Haemoglobin A1c criteria ($n = 448$)

	Euglycemic ($n = 149$)	Prediabetes ($n = 262$)	Diabetes ($n = 37$)	<i>p</i> -value
Median A1c, % (IQR)	5.4 (5.3, 5.5)	6.0 (5.8, 6.2)	6.7 (6.5, 7.1)	—
Age, years *	66.1 (± 11.2)	66.9 (± 11.6)	68.1 (± 11.5)	NS
Body Mass Index, kg/m²*	27.4 (24.4,30.8)	27.9 (25.6,31.6)	28.0 (26.0,31.1)	NS
Sex, %				NS
Male	77.9	78.2	81.1	—
Female	22.1	21.8	18.9	—
Race, % ($n = 446$)				0.002
White	71.1	62.3	40.5	—
Non-White	28.9	37.7	59.5	—
Current smoker, %	6.8	10.0	10.8	NS
Blood pressure <140/90	71.4	67.2	62.2	NS
Medical history, %				
Coronary artery disease	57.7	51.3	45.9	NS
Prior infarction	21.5	18.4	16.2	NS
Prior PCI	47.0	42.9	37.8	NS
Prior CABG	9.4	10.3	10.8	NS
Hypertension	79.2	81.6	86.5	NS
Hyperlipidemia	75.8	81.6	81.1	NS
Stroke	4.0	3.8	5.4	NS
Peripheral artery disease ($n = 445$)	7.4	8.5	21.6	0.023
Angina	29.5	29.1	37.8	NS
Medications, %				
Aspirin	85.2	86.2	78.4	NS
Statin	73.8	77.5	75.7	NS
Beta Blocker	57.0	66.4	70.3	NS
Clopidogrel	47.3	42.5	27.0	NS
Lipid profile, mg/dL				
Total Cholesterol <200	77.9	77.1	67.6	NS
LDL-C <100	61.5	58.2	51.4	NS
HDL-C				
Male >40	71.6	70.7	70.0	NS
Female >50	66.7	56.1	71.4	NS
Non HDL- <130	66.4	60.7	56.8	NS
Triglycerides <150	72.5	67.6	59.5	NS

DM, diabetes mellitus; PCI, Percutaneous coronary intervention; CABG, Coronary Artery Bypass Graft surgery; LDL-C, Low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol; IQR, interquartile range; NS, *3 way analysis by ANOVA