European Journal of Internal Medicine 37 (2017) 69–74

Contents lists available at ScienceDirect

European Journal of Internal Medicine

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

Original Article

Prospective study of the impact of diabetes mellitus newly diagnosed by glycated hemoglobin on outcomes in patients undergoing percutaneous coronary intervention

Muhammad Abu Tailakh [a,b], Michael Friger [b], Doron Zahger [c], Aviel Sidi [c], Efrat Mazor-Dray [c], Victor Novack [a,d,*]

[a] Clinical Research Center, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel
[b] Department of Public Health, Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel
[c] Department of Cardiology, Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel
[d] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA

ARTICLE INFO

Article history:
Received 23 August 2016
Accepted 9 September 2016
Available online 21 September 2016

Keywords:
Diabetes mellitus
HbA1c
Percutaneous coronary intervention

ABSTRACT

Background: We sought to determine the prevalence of diabetes mellitus (DM) newly diagnosed by elevated glycated hemoglobin (HbA1c) in patients undergoing percutaneous coronary intervention (PCI) and its association with 1-year clinical outcomes.
Methods: We prospectively enrolled consecutive patients undergoing PCI (2011–2013). HbA1c levels were assessed during the index hospitalization and newly diagnosed DM was defined as HbA1c ≥ 6.5% in the absence of the previous diagnosis. The primary outcome was MACCE (Major Adverse Cerebro- and Cardiovascular Events) defined as death, stroke, PCI or acute myocardial infarction at 1 year.
Results: Diabetes was previously diagnosed in 391 (34%) patients (DM group), 221 (19%) had newly diagnosed DM based on the HbA1c level and 539 (47%) did not have diabetes (Non-DM). In DM group HbA1c was 7.80 ± 1.36% as compared with 7.62 ± 1.30% in patients with newly diagnosed DM ($p < 0.001$). These patients were younger (62.0 ± 11.3 years) compared to DM (67.9 ± 10.4 years) and non-DM (63.7 ± 13.0) patients, $p < 0.001$. 1-year MACCE rates were 14.8%, 19.5% and 27.96% in the non-DM, newly diagnosed DM and DM groups, respectively ($p < 0.001$). Multivariate analysis showed that compared to non-DM, the adjusted one-year hazard ratios for MACCE were 1.75 and 1.40 in patients with known DM and newly diagnosed DM, respectively ($p < 0.05$ for both).
Conclusion: Newly diagnosed DM based on peri-procedural HbA1c is common and associated with increased short and long term risk for adverse outcomes. Our results may warrant routine screening for DM in all patients undergoing PCI.

1. Introduction

Recent studies estimated the prevalence of diabetes mellitus (DM) in patients undergoing percutaneous coronary interventions (PCI) at 31–40% [1,2]. Following PCI, both short and long term ischemic outcomes are worse in patients with DM compared to those without DM [3]. Furthermore, patients with DM undergoing PCI have an increased risk of restenosis and stent thrombosis [4,5,6]. Even in the drug-eluting stent (DES) era, repeat revascularization rates are higher in DM patients [7,8,9].

In 2008 the International Expert Committee recommended the use of glycosylated hemoglobin (HbA1c) levels above 6.5% for the diagnosis of diabetes. It was shown that 18% of patients undergoing PCI have newly diagnosed diabetes [10]. Glycemic control assessed by HbA1c levels at the time of the PCI can independently predict six months restenosis [11]. Furthermore, Corpus et al. [12] observed that patients with DM but with HbA1c levels ≤7% who underwent elective PCI had one-year target vessel revascularization (TVR) rates comparable to patients without diabetes. However, the full prognostic value of HbA1c for short and long term post-PCI outcomes in unselected patients is yet to be fully elucidated.

In the present study we prospectively evaluated association between DM newly diagnosed by elevated HbA1c and one year composite outcome of major adverse cerebro- and cardiovascular events (MACCE) comprising all cause death, revascularization, stroke and myocardial infarction in an unselected population of patients undergoing PCI.

* Corresponding author at: Soroka University Medical Center, P.O.B. 151, Beer-Sheva 84101, Israel.
E-mail address: victorno@clalit.org.il (V. Novack).

http://dx.doi.org/10.1016/j.ejim.2016.09.007
0953-6205/

2. Methods

2.1. Population

This prospective study enrolled all consecutive patients undergoing percutaneous coronary intervention between July 2011 and July 2013 at Soroka University Medical Center (SUMC). This tertiary 1000 bed-hospital is the only medical center for Southern Israel (population of 700,000) and therefore is the sole provider of acute care for patients with acute coronary syndromes in this region.

We collected demographic data, clinical characteristics, medications and laboratory tests including fasting glucose on the second day of hospitalization. The hospital Ethics Committee approved the study informed consent and the study participants are continued to be followed for five years from the index procedure.

2.2. Measurement of HbA1c

Blood samples for HbA1c levels were collected within 24 h of admission. All tests were performed by a single laboratory at SUMC, utilizing BIO-RAD VARIANT II TURBO HbA1c Kit-2.0 based on ion-exchange high-performance liquid chromatography (HPLC) for HbA1c testing [13].

2.3. Diabetes mellitus status

Patients were stratified into three groups based on their diabetes mellitus status. Known diabetes (DM) was defined based on the family physician's record, appropriate history or regular use of medications. Newly diagnosed diabetes mellitus (UDM) was defined based on HbA1c ≥6.5%, in the absence of known diabetes. The rest of the study population was assigned to the group without diabetes mellitus (Non-DM).

2.4. Study outcomes

The primary outcome was MACCE—a composite outcome comprising overall mortality, recurrent non-fatal myocardial infarction and cerebro-vascular events at one year. Secondary outcomes included individual components of MACCE, in-hospital death, length of stay, thirty days MACCE and recurrent acute coronary syndrome after discharge, as defined by European Society of Cardiology and American College of Cardiology guidelines [14,15].

We have collected other relevant clinical variables: hypertension, history of previous MI, hyperlipidemia, chronic renal disease, smoking, congestive heart failure and obesity. From ECHO report we have extracted the systolic function stratified based on Recommendations for Chamber Quantification [16] and severe left ventricular dysfunction was defined as ejection fraction less than 30%.

2.5. Statistical analysis

Patient characteristics are presented as mean ± SD for continuous variables and as percentage for categorical variables. Categorical variables were compared using the chi-square test. Continuous variables were examined using one way ANOVA with Fisher's Least Significant Difference (LSD) post-hoc tests. Continuous variables that are not normally distributed are reported as median (IQR) and compared by Kruskal Wallis test.

The rates of outcomes at 1-year were estimated using the Kaplan–Meier method, and differences were assessed by the log-rank test. We performed Cox proportional hazards regression analyses to investigate the effect of DM status on clinical outcomes at one year. We have included the following variables statistically and clinically associated with the components of the primary outcome (MACCE) into the multivariate models: demographics (age, gender), clinical (hypertension, dyslipidemia, smoking, obesity, systolic function, type of acute coronary syndrome), laboratory (eGFR) and angiographic characteristics (number of diseased vessels). All clinical and angiographic variables that were significantly different between study groups by univariate analysis ($p < 0.10$) were included in the first step of the model. Backward stepwise regression was utilized, eliminating variables with non-significant association ($p > 0.10$) with the outcome. DM group status was forced into the models.

Proportionality of hazards test was assessed by the evaluation of the interaction between log (survival time) and variable of interest. Hazard ratios (HRs) and 95% confidence intervals were estimated for each variable in the final parsimonious models.

All statistical analyses were performed using IBM SPSS version 22 (Chicago, USA).

3. Results

3.1. Population

Out of 1151 patients enrolled, DM had previously been diagnosed in 391 (34%) patients, 221 (19.2%) had newly diagnosed DM (UDM) and 539 (46.8%) did not have diabetes.

Baseline clinical characteristics for patients stratified by diabetes status are presented in Table 1. Patients with newly diagnosed DM were significantly younger and had less comorbidity compared to DM group. Presentation with STEMI (ST-segment Elevation Myocardial Infarction) was more common in patients with newly diagnosed DM and in non-DM compared to patients with DM ($p < 0.001$). Thirty seven percent of the study population was treated with antiplatelet agents ($p = 0.80$ for difference between the groups) prior to the admission. In DM patients group 100 (26%) received metformin, 22 (5.6%) sulfonamides and 54 (13.8%) were treated with insulin prior to the admission.

Table 1
Baseline demographic, clinical and laboratory characteristics in patients without diabetes, with known DM and newly diagnosed DM.

Characteristics	No DM N = 539	Previously known DM N = 391	Newly diagnosed DM N = 221	P-value
Age (yr's) mean ± SD	63.7 ± 13.0	67.9 ± 10.4	62.0 ± 11.3	<0.001
Male gender (%)	424 (78.7)	245 (62.7)	165 (74.7)	<0.001
Heart failure (%)	26 (4.8)	44 (11.3)	21 (9.5)	0.001
Old myocardial infarction (%)	75 (13.9)	115 (29.4)	31 (14)	<0.001
Hypertension (%)	276 (51)	279 (71.4)	131 (59.3)	<0.001
Acute coronary syndrome (%)	428 (79.4)	281 (71.9)	181 (81.9)	0.005
ST elevation myocardial infarction (%)	230 (42.7)	80 (20.5)	92 (41.6)	<0.001
Drug eluting stent (%)	173 (32.1)	158 (40.4)	82 (37.1)	0.03
One vessel (%)	179 (33.3)	84 (21.6)	75 (34.2)	<0.001
Two vessels (%)	202 (37.6)	123 (31.6)	82 (37.4)	0.14
Three vessels (%)	156 (29.1)	182 (46.8)	62 (28.3)	<0.001
Severe L.V systolic dysfunction	47 (10.3)	56 (18.0)	27 (13.4)	0.008
Smoking (%)	231 (43)	74 (19)	103 (47)	<0.01
Hyperlipidemia (%)	394 (73)	338 (86)	179 (81)	<0.01
Obesity (%)	98 (18)	107 (27)	71 (32)	<0.01
Glucose mg/dL Mean ± SD	126 ± 38	213 ± 115	202 ± 111	<0.001
Creatinine mg/dL Mean ± SD	0.96 ± 0.48	1.55 ± 1.82	0.97 ± 0.96	<0.001
eGFR mL/min/1.73 m^2 Mean ± SD	95 ± 25	76 ± 33	97 ± 24	<0.001
WBC (1000/mm^{-3}) Mean ± SD	10.5 ± 4	9.7 ± 4	11 ± 4	<0.001
PLT (1000/mm^{-3}) Mean ± SD	236 ± 71	244 ± 77	253 ± 77	0.02

Values are mean ± SD or N (%).
WBC—white blood cells.
eGFR—estimated Glomerular Filtration Rate calculate by using the Mayo Quadratic formula [36].