The role of diabetes mellitus in the composition of coronary thrombi in patients presenting with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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Background Although diabetes mellitus (DM) is a predictor of poor outcomes in patients with ST-segment elevation myocardial infarction (STEMI), few studies have analyzed the impact of DM on the constituency of coronary thrombi.

Objectives Comparing morphologic and histopathologic aspects of coronary thrombi in STEMI patients with and without DM who underwent primary percutaneous coronary intervention.

Methods All consecutive patients with STEMI admitted to our institution between April 2010 and December 2012 (n = 1,548) were considered for inclusion. Thrombus material was obtained by aspiration thrombectomy; morphologic and histopathologic aspects were assessed by 3 independent pathologists blinded to clinical characteristics and outcomes. Patients with DM were compared with those without DM. A sensitivity analysis was performed using a propensity score.

Results During the study period, coronary thrombi material from 259 patients was obtained, of whom 19% (n = 49) had diabetes. Diabetic patients were older ($P = .10$), had a higher frequency of hypertension ($P < .01$) and dyslipidemia ($P = .03$), and had a trend to a longer time from the onset of chest pain to hospital arrival ($P = .08$). The number of retrieved fragments, the size of the thrombi and its composition (leukocytes, fibrin, and erythrocytes percent), and thrombus age and color were similar between patients with or without DM. There were also no statistically significant differences in thrombus constituency of the propensity score–matched patients (n = 92).

Conclusions In this study, morphologic and histopathologic constituency of coronary thrombi in the setting of a ST-elevation myocardial infarction was not significantly different between patients with or without DM. This finding was intriguing and deserves further investigation. (Am Heart J 2016;172:26-33.)

Acute coronary syndromes (ACS) are an important cause of morbidity and mortality in patients with diabetes mellitus (DM) who generally present atherosclerotic plaques more prone to rupture, with thinner fibrous caps and greater lipid cores.[1,2] ST-segment elevation acute myocardial infarction (STEMI) is the end-stage of the clinical spectrum of ACS and, in approximately 90% of cases, is caused by the rupture or erosion of an atherosclerotic plaque with superimposed coronary thrombosis.[3,4] Patients with DM who present with STEMI generally are at higher risk for adverse outcomes than nondiabetic patients,[5,6] due to more frequent comorbidities and functional changes in platelets and in the coagulation pathways.[4,5,7,8]

Primary percutaneous coronary intervention (pPCI) is the preferred reperfusion strategy for all patients with STEMI, and adjunctive aspiration thrombectomy (AT) has a class IIa recommendation in this setting.[9,10] The use of AT allows for a unique opportunity as examination of the retrieved coronary thrombi may be used to provide new

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Funding Sources: This work was funded by the Instituto de Cardiologia do Rio Grande do Sul, Fundação Universitária de Cardiologia, Porto Alegre, Brazil.
Uchechukwu Sampson, MD, served as guest editor for this article.
Submitted April 17, 2015; accepted October 6, 2015.
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0002-8703

http://dx.doi.org/10.1016/j.ahj.2015.10.003

insights into the pathophysiology of STEMI.[11–15] The objective of the present study is to compare morphologic and histopathologic aspects of coronary thrombi in STEMI patients with and without DM undergoing pPCI and adjunctive AT.

Methods

Patients

All consecutive patients with STEMI admitted to the Instituto de Cardiologia do Rio Grande do Sul, Fundação Universitária de Cardiologia, Porto Alegre, Brazil, between April 2010 and December 2012 (n = 1,548) were considered for inclusion. All patients enrolled in this study provided written informed consent. Because this was an observational study not involving additional procedures or changes in medical treatment, informed consent was obtained after pPCI to avoid delays in its performance. *ST-segment elevation acute myocardial infarction* was defined by resting chest pain lasting more than 30 minutes associated with ST-segment elevation of at least 1 mm in 2 leads in the frontal plane or at least 2 mm in the horizontal plane, or new left bundle-branch block. Exclusion criteria were chest pain lasting more than 12 hours, age <18 years, or refusal to participate. Patients had pPCI performed based on the clinical need for reperfusion therapy, according to the evaluation of the attending physician. The study was approved by the institutional review board of the Instituto de Cardiologia do Rio Grande do Sul, Fundação Universitária de Cardiologia.

Clinical and angiographic characteristics

Patients were evaluated on hospital admission, and clinical, angiographic, and laboratory information was collected in a dedicated database. During index hospitalization, patients were visited daily by one of the study investigators to assess in-hospital events. Diabetes mellitus was considered present when the patient had a previous diagnosis of this disease and was receiving medical treatment with insulin or oral hypoglycemic drugs, or if it was diagnosed during the index hospitalization for STEMI. *Delta t* was defined as the time between the onset of chest pain and hospital presentation. Door-to-balloon time comprehended the time between hospital presentation and first inflation of the balloon inside the infarct-related artery. Total ischemic time was the sum of these 2 periods.

Angiographic analyses were performed in at least 2 different views by experienced operators with a previously validated digital caliper system (Siemens Axiom Artis, Munich, Germany), and intracoronary nitroglycerin was routinely administered at a dose of 100 to 200 μg before measurements were performed. *Target vessel diameter* was defined as the mean diameter of the luminal segments proximal and distal to the lesion, and the severity of stenosis was measured in 2 orthogonal views. Lesion length was measured "shoulder to shoulder," and longer lesions were considered a single lesion when a short normal segment (<10 mm) lay between them. Coronary flow was assessed before and after the procedures according to the Thrombolysis in Myocardial Infarction (TIMI) criteria.[16] Myocardial perfusion was evaluated by the TIMI myocardial perfusion grade, as previously described by Gibson and coworkers.[17]

Interventional procedures

Our institution is a high-volume tertiary referral center for interventional cardiology (2,500 PCIs/y). Aspiration thrombectomy has been used in our institution for 4 years, and 3 different aspiration catheters were used: Export (Medtronic Vascular Inc, Santa Rosa, CA), Diver (INVATEC, Brescia, Italy), or Pronto (Vascular Solutions, Minneapolis, MN). In this study, the decision to perform AT was left to the discretion of the operator, as were technical aspects such as type and number of stents, use of any other devices, and glycoprotein IIb/IIIa use. In each case, AT was attempted before balloon dilation (as in the Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction [TAPAS] trial),[18] and several passages at the site of occlusion were performed. Aspirated blood and intracoronary material were collected in the filter. All patients were treated with 300 mg aspirin and 300 to 600 mg clopidogrel on hospital admission. Heparin (60-100 U/kg) was administered before coronary guide wire introduction, and all the procedures were performed according to standard PCI techniques.[19,20]

Thrombus analysis

All pathological analyses, including macroscopic and microscopic evaluation, were performed by 3 independent pathologists, blinded to the patient's characteristics and clinical outcomes. The intraobserver and interobserver agreement rates were assessed, and the κ coefficient was .90.

The sample was placed in 10% formalin immediately after retrieval and fixed for 24 hours. The number of fragments recovered and the dimensions of each were recorded. *Thrombus volume* was defined as the product of its length, height, and thickness. Thrombi were classified as "red" or "white" based on their color through macroscopic evaluation. Those thrombi with both red and white constituents were classified according to the predominant color. The material was then embedded in paraffin, entirely cut in 3-micra serial sections, and stained with hematoxylin-eosin at 8 or more levels. On histopathologic analysis, the thrombi were classified into recent thrombus (<1 day, composed of layered patterns of platelets, fibrin, erythrocytes, and intact granulocytes) or old thrombus (>1 day, characterized by areas of necrosis, apoptosis and karyorrhexis of leukocytes, and/or suggestive findings of organization) as previously