Available online at www.sciencedirect.com

ScienceDirect

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

Original Article

Multimarker risk stratification approach and cardiovascular outcomes in patients with stable coronary artery disease undergoing elective percutaneous coronary intervention

Vimal Mehta [a], *Rishi Sukhija* [b], *Pratishtha Mehra* [a], *Anuj Goyal* [a], *Jamal Yusuf* [a], *Bhawna Mahajan* [c], *V.K. Gupta* [c], *Sanjay Tyagi* [a], *Chandrasekar Palaniswamy* [d,*], *Wilbert S. Aronow* [e]

[a] *Department of Cardiology, G.B. Pant Hospital, Delhi, India*
[b] *Department of Medicine, Division of Cardiology, IU Health La Porte Hospital, IN, United States*
[c] *Department of Biochemistry, G.B. Pant Hospital, Delhi, India*
[d] *Department of Medicine, Division of Cardiology, Mount Sinai Hospital, NY, United States*
[e] *Department of Medicine, Division of Cardiology, New York Medical College at Westchester Medical Center, Valhalla, NY, United States*

ARTICLE INFO

Article history:
Received 16 February 2015
Accepted 29 June 2015
Available online 18 January 2016

Keywords:
Biomarkers
Percutaneous coronary intervention
Periprocedural myocardial infarction
Major adverse cardiovascular event

ABSTRACT

Aims: We studied the utility of multimarker risk stratification approach to predict cardiovascular outcomes in patients with stable coronary artery disease, undergoing elective percutaneous coronary intervention (PCI).

Methods: We prospectively evaluated 302 consecutive patients with stable coronary artery disease and normal CPK-MB and cardiac troponin T levels, and who underwent elective PCI at our institution. The following cardiac biomarkers were measured before and between 12 and 24 h post-procedure: CK-MB, cardiac troponin T, hs-CRP, and NT-ProBNP. Patients were followed up for a minimum of 6 months.

Results: Post-PCI, CPK-MB levels were elevated but below myocardial infarction (MI) range in 70 patients (23%), and in the MI range in 6 patients (2%). Troponin T levels were detectable but below the 99th percentile (microleak) in 32 patients (10.6%) and elevated above the 99th percentile (periprocedural MI) in 104 patients (34.4%). At 9 months' follow-up, 1% died, 2% had stable angina, 10.3% had non-fatal MI, and 87.7% remained asymptomatic. There was no significant difference in clinical events among groups stratified by elevation of one biomarker or multiple biomarkers.

Conclusion: Single or multiple biomarker strategy in patients with normal baseline biomarkers failed to predict major cardiac events after PCI over medium-term follow-up.

* *Corresponding author.*
E-mail addresses: chandrasekar.palaniswamy@mountsinai.org, drpchandrasekar@gmail.com (C. Palaniswamy).

http://dx.doi.org/10.1016/j.ihj.2015.06.034
0019-4832/

1. Introduction

Myocardial damage after percutaneous coronary intervention (PCI) can result from procedural complications such as distal embolization, side-branch occlusion, coronary dissection, or disruption of collateral flow. The incidence of myocardial damage after PCI, based on significant elevation of cardiac biomarkers, is 1–30%.[1] Some of these episodes of periprocedural myocardial damage occur silently after uneventful PCI procedures. Although there is a consensus that troponin is probably the most relevant biomarker, the prognostic impact of troponin elevation after PCI is still debated.[2–4] The universal definition of myocardial infarction (MI) arbitrarily includes 'PCI-related MI' as patients with normal baseline troponin levels and a rise of troponin three times the 99th percentile of the upper reference limit (URL).[3] Cardiac troponins T (cTnT) and I (cTnI) are highly sensitive and specific markers of myocardial cell injury and necrosis. The prognostic value of troponins is now well established for patients presenting with acute coronary syndromes (ACS).[4–6] Elevation of troponin following routine PCI has also been found to be predictive of both short- and long-term major adverse cardiovascular events (MACE).[7,8] However, there are conflicting reports on the value of cTn in the setting of PCI in stable and unstable coronary disease.[9] Further, while the increasing sensitivity of cTn assays lowers the number of missed ACS diagnoses, it presents a diagnostic challenge because the gains in diagnostic sensitivity have inevitably come with a decrease in specificity.[10]

There is growing evidence that combining a biomarker of hemodynamic stress, such as B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP), and of inflammation, such as high-sensitivity C-reactive protein (hs-CRP), with a biomarker of necrosis (cardiac troponin) enhances risk assessment in patients with ACS.[11–14] Specifically, elevated levels of CRP and BNP at presentation identify patients who are at higher mortality risk, irrespective of whether or not there is detectable elevation of troponin.[15,16]

The present study evaluated the clinical impact of a multimarker risk stratification approach on cardiovascular outcomes in patients with stable coronary artery disease undergoing elective PCI. This study also evaluated the impact of micro-cTn leak on long-term outcomes following elective PCI.

2. Methods

We prospectively evaluated patients with stable coronary artery disease undergoing elective PCI at G.B. Pant Hospital, New Delhi, India from June 2010 to May 2011. To ensure that any post-procedural increase in cardiac markers was exclusively PCI-related, we only included patients with stable coronary disease or previously stabilized unstable coronary disease with normal cardiac markers before PCI. Inclusion criteria were (1) patients with troponin/creatine kinase MB (CK-MB) values that were assessed pre-PCI and 12–24 h post-PCI, and where pre-procedure values were within the normal range, and (2) patients with stable coronary artery disease. Exclusion criteria were (1) patients with cardiac biomarker elevation (Tn or CK-MB) immediately before PCI, (2) patients with ACS, and (3) patients with significant renal, hepatic, or any other systemic dysfunction.

Institutional ethical guidelines were followed. All patients were included after informed consent. All patients were evaluated after a detailed history, physical examination, and appropriate investigations. Demographic and clinical characteristics of patients were documented. Blood samples were collected at baseline and at 8–12 h and 18–24 h after the procedure, and were analyzed in a core biochemistry laboratory.

All patients were pre-treated with oral aspirin and clopidogrel 2–6 h prior to the procedure in accordance with the established protocol. All PCI procedures were performed using femoral access. Oral aspirin and clopidogrel were recommended post-PCI for at least 1 year. All patients undergoing PCI were given 70 IU/kg unfractionated heparin before PCI, while the use of glycoprotein IIb/IIIa inhibitor and coronary stent type (bare-metal or drug-eluting stent) was at the operator's discretion.

Patients with >70% stenosis of only 1 epicardial coronary artery vessel were classified as single-vessel disease and those with >70% stenosis of >1 epicardial coronary artery were classified as multivessel disease. Coronary artery lesions were classified qualitatively according to modified American College of Cardiology/American Heart Association (ACC/AHA) classification into type A, B, or C; types A and B1 lesions were categorized as simple, while types B2 and C were categorized as complex lesions. For each procedure, the duration and pressure of balloon inflation, number, and type of stents were recorded. Any complications occurring during or within the first 24 h of PCI were also recorded.

Angiographic success was defined as residual coronary artery stenosis <50% after balloon angioplasty or <20% after stent implantation, with normal TIMI 3 coronary flow. To rule out Q-wave MI during the procedure, a 12-lead electrocardiogram (ECG) was performed before and at 24 h post-procedure. Additional ECGs were obtained in patients with post-procedural chest pain.

Pre-PCI blood samples were taken to analyze baseline myocardial damage marker values. Four cardiac markers, namely CK-MB, cTnT, hs-CRP, and NT-proBNP, were measured before and between 12 and 24 h post-procedure. cTnT was determined using the electro-chemiluminescence analyzer. cTnT elevation was taken as >3 times laboratory's upper limit for normal (normal, <0.1 ng/ml, following the universal definition of AMI). The lower detectable ranges for serum NT-proBNP and cTnT were 5 pg/ml and 0.01 ng/ml, respectively. CK-MB elevation was taken as 3 times our laboratory's upper limit for normal (normal, <25 U/L). Lower detectable range for CK-MB was 3 U/L.

Plasma and serum samples were collected into aliquots and stored. cTnT and NT-proBNP levels were determined in serum samples taken at admission, 12, and 24 h, using the one-step enzyme immunoassay based on electro-chemoluminescence immunoassay by Roche Elecsys, modular Cobas 2010 e 411 (Mannheim, Germany) using commercially available kits. CK-MB measurements were done by the principle of immunoinhibition by commercially available kits by RANDOX Laboratories Ltd., Antrim, United Kingdom