JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 7, NO. 3, 2014

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2013.08.016

Impact of Nonculprit Vessel Myocardial Perfusion on Outcomes of Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndromes

Analysis From the ACUITY Trial (Acute Catheterization and Urgent Intervention Triage Strategy)

Alexandra J. Lansky, MD,* Vivian G. Ng, MD,* Stephanie Meller, MD,* Ke Xu, PhD,† Martin Fahy, MSc,† Frederick Feit, MD,‡ E. Magnus Ohman, MD,§ Harvey D. White, MD,‖ Roxana Mehran, MD,¶ Michel E. Bertrand, MD,# Walter Desmet, MD,** Martial Hamon, MD,†† Gregg W. Stone, MD†

New Haven, Connecticut; New York, New York; Durham, North Carolina; Auckland, New Zealand; Lille and Normandy, France; and Leuven, Belgium

Objectives This study evaluated the impact of nonculprit vessel myocardial perfusion on outcomes of non–ST-segment elevation acute coronary syndromes (NSTE-ACS) patients.

Background ST-segment elevation myocardial infarction patients have decreased perfusion in areas remote from the infarct-related vessel. The impact of myocardial hypoperfusion of regions supplied by nonculprit vessels in NSTE-ACS patients treated with percutaneous coronary intervention (PCI) is unknown.

Methods The angiographic substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial included 6,921 NSTE-ACS patients. Complete 3-vessel assessments of baseline coronary TIMI (Thrombolysis In Myocardial Infarction) flow grade and myocardial blush grade (MBG) were performed. We examined the outcomes of PCI-treated patients according to the worst nonculprit vessel MBG identified per patient.

Results Among the 3,826 patients treated with PCI, the worst nonculprit MBG was determined in 3,426 (89.5%) patients, including 375 (10.9%) MBG 0/1 patients, 475 (13.9%) MBG 2 patients, and 2,576 (75.2%) MBG 3 patients. Nonculprit MBG 0/1 was associated with worse baseline clinical characteristics. Patients with nonculprit MBG 0/1 versus MBG 3 had increased rates of 30-day (3.0% vs. 0.7%, $p < 0.0001$) and 1-year (4.4% vs. 1.0%, $p < 0.0001$) death. Similar results were found among patients with pre-procedural TIMI flow grade 3 in the culprit vessel, where nonculprit vessel MBG 0/1 (hazard ratio: 2.81 [95% confidence interval: 1.63 to 4.84], $p = 0.0002$) was the strongest predictor of 1-year mortality.

Conclusions Reduced myocardial perfusion in an area supplied by a nonculprit vessel is associated with increased short- and long-term mortality rates in NSTE-ACS patients undergoing PCI. Furthermore, worst nonculprit MBG is able to risk-stratify patients with normal baseline flow of the culprit vessel. (J Am Coll Cardiol Intv 2014;7:266–75) © 2014 by the American College of Cardiology Foundation

From the *Division of Cardiovascular Medicine, Yale University School of Medicine, New Haven, Connecticut; †Division of Cardiology, Columbia University Medical Center and the Cardiovascular Research Foundation, New York, New York; ‡Division of Cardiology, New York University School of Medicine, New York, New York; §Department of Medicine, Duke University School of Medicine, Durham, North Carolina; ‖Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; ¶Division of Cardiology, Mount Sinai Medical Center, New York, New York; #Department of Cardiology, Hôpital Cardiologique, Lille, France; **Department of Cardiology, University Hospital Gasthuisberg, Leuven, Belgium; and the ††Department of

Although initial assessments of the coronary vasculature are focused on evaluating and optimizing epicardial flow, subsequent work has revealed that normal epicardial flow does not necessarily equate to normal tissue perfusion (1,2). Furthermore, changes in epicardial and myocardial perfusion may not be limited to the vessel with the culprit lesion. In ST-segment elevation myocardial infarctions (STEMIs), alterations in myocardial perfusion can occur both in areas supplied by and areas remote from the occluded culprit vessels (3–5) and may persist even after revascularization of the culprit lesion (6). These changes in nonculprit vessel myocardial perfusion have been noted in patients with non ST-segment elevation acute coronary syndromes (NSTE-ACS) (7).

In the prospective, multicenter ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial, moderate- to high-risk patients with NSTE-ACS underwent early invasive management and were subsequently triaged to treatment with medical management, percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) (8,9). We analyzed the impact of abnormal myocardial perfusion in an area subtended by a nonculprit vessel on 30-day and 1-year outcomes of PCI patients. Furthermore, we studied whether abnormal myocardial perfusion in a nonculprit vessel could further stratify outcomes of PCI patients with normal culprit vessel epicardial flow.

Methods

The ACUITY study design, major inclusion and exclusion criteria, endpoints, definitions, and results have been previously described in detail (8,9). In summary, 13,819 patients with moderate- or high-risk NSTE-ACS were prospectively randomized in an open-label fashion to either heparin (unfractionated heparin or enoxaparin) plus a glycoprotein IIb/IIIa inhibitor, bivalirudin plus a glycoprotein IIb/IIIa inhibitor, or bivalirudin alone. Dosing regimens were described previously (9). All patients underwent angiography within 72 h of randomization and were subsequently triaged to PCI, CABG, or medical management at the discretion of the physician. Primary clinical endpoints were adjudicated by an independent clinical events committee blinded to treatment assignment. The major 30-day primary endpoints were composite ischemic events (death from any cause, myocardial infarction [MI], or unplanned revascularization for ischemia), non–CABG-related major bleeding (protocol-defined), and net clinical outcomes (composite ischemia or major bleeding). The major 1-year primary endpoint was composite ischemic events.

Angiographic analysis. The pre-specified angiographic substudy of the ACUITY trial was composed of the first 6,921 consecutive patients enrolled at U.S. centers. Clinical sites were instructed and trained to acquire protocol-guided 3-vessel diagnostic angiograms prior to intervention. Site training and prospective protocol for angiography included administration of intracoronary nitroglycerin, hand or injector contrast injection, and imaging of each coronary and its myocardial territory for at least 4 cardiac cycles in a minimum of 2 orthogonal views using a 5-F or larger catheter. Comprehensive quantitative coronary angiography of baseline and final angiograms was performed by an independent angiographic core laboratory. All angiograms were evaluated by reviewers blinded to treatment assignment using validated quantitative methods (Medis, Leiden, the Netherlands). Complete baseline 3-vessel and post-procedural culprit lesion angiographic data were available in 3,627 of 3,826 (89.5%) patients undergoing PCI. Baseline TIMI (Thrombolysis In Myocardial Infarction) flow grade and myocardial blush score assessed on a scale of 0 to 3 was performed at baseline in all 3 (culprit and nonculprit) epicardial vessels (1,10). All angiograms were analyzed by trained analysts and over-read for accuracy by a second physician (A.J.L. or E.C.), who was blinded to clinical outcomes. The methodology for myocardial blush analysis used (derived from the original Zwolle description) (1,10) has been previously described and has been shown to have high intra- and interobserver reproducibility for prior technicians, and for the current analysis (C kappa = 0.87 and 0.82 for inter- and intraobserver variability, respectively). Angiograms were considered technically adequate for blush analysis only if the

Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
MBG = myocardial blush grade
MI = myocardial infarction
NSTE-ACS = non–ST-segment elevation acute coronary syndrome(s)
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

Cardiology, University Hospital, Normandy, France. The ACUITY trial was sponsored and funded by The Medicines Company and Nycomed. Dr. Feit has received consulting fees from The Medicines Company; and is a shareholder in Boston Scientific, Johnson & Johnson, Medtronic, and The Medicines Company. Dr. Ohman has received grant support from Daiichi Sankyo, Eli Lilly, and Gilead Sciences; has received consulting fees from Abiomed, AstraZeneca, Biotie, Ikaria, Ivivi, Janssen, Liposcience, Pozen, Sanofi-Aventis, The Medicines Company, and WebMD; and has served on the Speakers' Bureaus of Gilead Sciences and Liposcience. Dr. White has unrestricted research grant support from AstraZeneca, Merck Sharp & Dohme, Roche, Regado Biosciences, Sanofi-Aventis, Eli Lilly, The Medicines Company, the National Institutes of Health, GlaxoSmithKline, and Daiichi Sankyo. Dr. Mehran has received institutional research grant support from The Medicines Company, Bristol-Myers Squibb/sanofi, and Lilly/Daichii Sankyo; and has received consulting fees from Abbott Vascular, AstraZeneca, Boston Scientific, Covidien, Janssen (Johnson & Johnson), Regado Biosciences, Maya Medical, and Merck & Co. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received April 11, 2013; revised manuscript received August 8, 2013, accepted August 30, 2013.