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Persistent Coronary No Flow After Wire Insertion Is an Early and Readily Available Mortality Risk Factor Despite Successful Mechanical Intervention in Acute Myocardial Infarction

A Pooled Analysis From the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) Trials

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Objectives These studies sought to investigate the impact on mortality of coronary flow after passage of the wire through the culprit vessel in patients with ST-segment elevation myocardial infarction (STEMI) undergoing mechanical reperfusion.

Background Reduced spontaneous coronary flow before percutaneous coronary intervention influences mortality in patients with STEMI. Response to vessel wiring in patients with an occluded coronary artery before intervention might further discriminate outcomes irrespective of pre- and post-intervention coronary flow.

Methods Data from the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials were pooled: of 919 index procedures, 902 films (98%) were technically adequate for core laboratory TIMI (Thrombolysis In Myocardial Infarction) flow determination.

Results TIMI flow grade 0 was present before percutaneous coronary intervention in 59% of infarct vessels, TIMI flow grade 1 to 2 was found in 21%, whereas the remainder of infarct arteries presented with TIMI flow grade 3. In 49% of patients who showed persistent TIMI flow grade 0 after wire insertion (AWI), mortality was higher at 30 days (5.3%) and 1 year (9.4%) compared with patients in whom TIMI flow grade before percutaneous coronary intervention was either >0 (0.8%; $p < 0.003$ and 3.6%, $p < 0.008$) or improved from 0 AWI (1.5%, $p < 0.04$ and 3.6%, $p < 0.02$). After correcting for multiple imbalances, including baseline and final flow, persistent TIMI flow grade 0 AWI remained associated at 30 days to 2-fold (risk ratio [RR]: 2.1, 95% confidence interval [CI]: 1.08 to 5.00; $p = 0.038$) and at 1 year to almost 3-fold increases of mortality (RR: 2.7, 95% CI: 1.3 to 5.6; $p = 0.008$).

Conclusions STEMI patients displaying persistent no-flow AWI have a lower survival rate despite an apparently successful mechanical intervention. As an early marker for high residual mortality risk, persistent no-flow AWI may qualify STEMI patients for dedicated pharmacomechanical treatment strategies. (J Am Coll Cardiol Intv 2011;4:51–62) © 2011 by the American College of Cardiology Foundation

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Coronary flow before intervention, graded semiquantitatively according to the TIMI (Thrombolysis In Myocardial Infarction) angiographic scale, has been previously shown to influence short- (30 days) and medium-term (6 months) mortality in patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) (1,2). Importantly, the independent effect of initial flow in the culprit coronary artery on survival persisted even after correction for post-procedural flow (1), which suggests that

See page 63

early pre-PCI reperfusion has salutary benefits independent of promoting ultimate restoration of TIMI flow grade 3 (2). Early pre-PCI reperfusion may improve survival by enhancing myocardial recovery and/or by optimizing procedural success, of which final TIMI flow grade 3 is known to be a rather insensitive surrogate marker (3–7). A prognostic indicator for high residual mortality risk despite successful mechanical intervention in STEMI patients would be desirable to tailor intensity/complexity of treatment accordingly.

Abbreviations and Acronyms

ANOVA = analysis of variance

AWI = after wire insertion

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

We hypothesized that in patients presenting with occluded coronary artery before intervention, for whom prognosis is known to be unfavorable (1,8), response to vessel instrumentation through passage of the wire may further discriminate outcomes compared with both pre- and post-PCI coronary flow.

Methods

Patients. Data from 2 trials—STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) (9) (n = 175) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) (10) (n = 745)—were pooled in a computerized database. The major entry criteria of these trials were similar and deliberately nonrestrictive: 74% of all-comer patients who presented to the study sites with STEMI during recruitment period were included. The inclusion criteria were: 1) chest pain for >30 min with an electrocardiographic ST-segment elevation ≥1 mm in 2 or more contiguous electrocardiogram leads, or with a new left bundle-branch block; and 2) admission either within 12 h of symptom onset or between 12 and 24 h after onset with evidence of continuing ischemia. The exclusion criteria included administration of fibrinolytics in the previous 30 days, major surgery within 15 days, and active bleeding or previous stroke in the last 6 months. Moreover, for both trials, to minimize the potential for angiographic selection bias, protocols mandated inclusion of patients immediately after clinical eligibility criteria were met and before the visualization of coronary arteries through angiography (9,10). Follow-up visits were scheduled for the STRATEGY trial at 1, 6, and 12 months and at 1, 4, 8, and 12 months for the MULTISTRATEGY trial.

Study medications and intervention. At presentation, patients from both studies received aspirin (160 to 325 mg orally or 250 mg intravenously, followed by 80 to 125 mg orally indefinitely) and clopidogrel (300 mg orally and then 75 mg/day for at least 3 months). Heparin was given during transportation to the primary PCI facility or just in the catheterization laboratory at 40 to 70 U/kg, targeting an activated clotting time of at least 200 s. Before arterial sheath insertion, patients in both studies were randomly allocated with a 1:1 ratio to receive tirofiban, which was given as a bolus of 25 μg/kg, followed by an 18- to 24-h infusion at 0.15 μg/kg/min or abciximab, which was administered as a bolus of 0.25 mg/kg, followed by a 12-h infusion at 0.125 μg/kg/min. As part of a pre-specified subanalysis of both trials, the STRATEGY and MULTISTRATEGY protocols mandated acquisition of a coronary angiogram using the standard frame rate immediately after passage of the wire distal to the lesion to allow for central adjudication of TIMI flow grade after wire insertion (AWI) by an independent core laboratory. Stenting was the default strategy in patients with a reference vessel diameter ≥2.5 mm at visual estimation. Patients were randomized in both studies to sirolimus-eluting stent or any uncoated-stent type approved by the regulatory agency. The use of pre- or post-dilation and thrombus aspiration was left to the discretion of the treating physician.

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