

EDITORIAL COMMENT

Behind the Times?

Optimal Timing of an Invasive Strategy in Non-ST-Segment Elevation Acute Coronary Syndromes*



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Ensuring consistent, evidence-based care across diverse patient populations and hospital networks is one of the principal challenges facing the U.S. health care system. For a small number of disease states, such as ST-segment elevation myocardial infarction (MI), clear evidence to support a specific strategy (i.e., emergent revascularization) and widespread adoption of care pathways to facilitate shorter door-to-balloon times have markedly reduced practice variation (1,2). Yet for most cardiovascular disease states, marked practice variations among hospitals and clinicians persist.

Non-ST-segment elevation myocardial infarction (NSTEMI) is representative of these latter conditions. NSTEMI is a heterogeneous diagnosis that encompasses multiple pathophysiological processes (e.g., type 1 vs. type 2 MI) (3) that are often difficult to differentiate at the time of initial patient evaluation. Although the weight of evidence supports a routine invasive strategy in higher risk patients with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) (4-6), some trials have not demonstrated a clear benefit for a routine invasive approach compared with a more selective invasive strategy (7). Similarly, the optimal timing of an invasive approach remains debated. TIMACS (Timing of Intervention in Acute Coronary Syndromes), the largest trial to date, enrolled 3,031 patients with NSTEMI-ACS to early (≤ 24 h) or delayed (≥ 36 h) coronary angiography. Overall, the results were neutral regarding the primary

endpoint of death, MI, or stroke. However, a clinical benefit for earlier angiography became more apparent when restricted to patients at higher risk (hazard ratio: 0.65; 95% confidence interval: 0.48 to 0.89). Earlier angiography also reduced the occurrence of the secondary composite outcome of death, MI, or refractory ischemia by 28%, a benefit that was driven largely by a 70% reduction in refractory ischemia.

Additional trials and substudies that have examined the optimal timing of angiography have not shown entirely consistent results, yet the bulk of the data support earlier angiography in higher risk patients. In contrast, the clinical benefit of early angiography is less apparent among patients at lower risk (5,7-10). These findings are reflected in the most recent American College of Cardiology/American Heart Association guidelines for the management of patients with acute coronary syndromes without ST-segment elevation (8), in which urgent (≤ 2 h) coronary angiography is recommended for patients with hemodynamic or electric instability, heart failure, or refractory angina, and early (≤ 24 h) angiography is recommended for patients without these features but at heightened risk, defined by an elevated GRACE (Global Registry of Acute Coronary Events) score (>140), temporal change in troponin, or new or presumably new ST-segment depression. For lower risk patients with NSTEMI-ACS, a delayed invasive strategy (25 to 72 h) is permitted for those who otherwise meet criteria for angiography (8).

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In this issue of *JACC: Cardiovascular Interventions*, Malta Hansen et al. (11) report their examination of the predictors and timing of coronary angiography in 138,688 patients hospitalized in the United States with NSTEMI who were enrolled in the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry database.

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The dataset included patient information from 661 percutaneous coronary intervention-capable sites between 2012 and 2014. Overall, 92% of patients (n = 127,402) underwent coronary angiography within 72 h, reflecting strong adherence to an invasive strategy. However, fewer than two-thirds of patients (n = 79,760 [57.5%]) underwent early angiography (defined by the investigators as ≤ 24 h), with wide variation across hospitals (21.7% to 100%). Unfortunately, we do not know what proportion of these patients would be advised to undergo angiography within 24 h under the existing American College of Cardiology/American Heart Association guideline recommendations, and it is therefore possible that many of these patients who underwent coronary angiography outside of 24 h were still appropriately managed.

Nonetheless, the investigators bring appropriate attention to several important issues. When they examined predictors of early (≤ 24 h) or delayed (> 24 to 72 h) angiography, it became apparent that some higher risk features that may predict benefit from earlier angiography were associated with a delayed approach. Early angiography was performed more commonly in men than women, whites than other, and those presenting on weekdays as opposed to weekends or holidays. In contrast, delayed angiography was more common in older patients and those with higher initial creatinine values, lower initial troponin values, and the presence of heart failure on presentation. In hospitals at which early angiography was more common, there appeared to be greater adherence to guideline-recommended therapies and higher “defect-free” quality scores. Although it is tempting to believe that differences in patient risk profiles explained differences in angiography timing across hospitals, it did not appear that patient characteristics were substantially different when

hospitals were categorized by tertiles of early angiography use.

Although the benefit of earlier angiography in a stable or low-risk patient with NSTEMI-ACS remains debated, the present analysis raises several important questions regarding factors that may overtly or subconsciously influence a medical professional's decisions regarding a patient's care. It is plausible that in some instances, clinicians were waiting for a patient's creatinine to stabilize before coronary angiography or that further testing was indicated to help distinguish type 1 from type 2 MI. However, clinicians are sometimes reluctant to bring older patients with unstable features or chronic kidney disease to the catheterization laboratory (12), despite evidence to indicate that they derive as much benefit as other populations from an invasive approach (13,14). Additional factors that appear to influence the timing of angiography, including race and insurance status, shine a spotlight on the role that socioeconomic factors play in existing health care disparities.

In summary, Malta Hansen et al. (11) have provided us with an important snapshot of contemporary NSTEMI management in the United States. They observed broad adherence to pursuing an invasive strategy in patients with NSTEMI, but further analysis should evaluate whether earlier angiography should be more frequently applied. Their work helps identify disparities in NSTEMI management on the basis of medical and socioeconomic variables that deserve additional investigation.

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