EXPEDITED REVIEW

Myocardial Contrast Echocardiography Versus Thrombolysis in Myocardial Infarction Score in Patients Presenting to the Emergency Department With Chest Pain and a Nondiagnostic Electrocardiogram

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OBJECTIVES	We hypothesized that regional function (RF) and myocardial perfusion (MP) are superior to the Thrombolysis In Myocardial Infarction (TIMI) score for diagnosis and prognostication in patients presenting to the emergency department (ED) with chest pain (CP) and a nondiagnostic electrocardiogram.
BACKGROUND	Rapid diagnosis and prognostication is difficult in patients presenting to the ED with suspected cardiac CP.
METHODS	Contrast echocardiography was performed to assess RF and MP on 957 patients presenting to the ED with suspected cardiac CP and a nondiagnostic electrocardiogram. A modified TIMI (mTIMI) score was calculated from six immediately available variables. A full TIMI score also was derived after troponin levels were able to be accessed adequately. Follow-up was performed for early (within 24 h), intermediate (30 day), and late primary (death and myocardial infarction) or secondary (unstable angina and revascularization) events.
RESULTS	The mTIMI score was unable to discriminate between intermediate- compared to high-risk patients at any follow-up time point, whereas only 2 of 523 patients with normal RF had an early primary event. Regional function provided incremental prognostic value over mTIMI scores for predicting intermediate and late events. In patients with abnormal RF, MP further classified patients into intermediate- and high-risk groups. The full TIMI score could not improve upon these results at any follow-up time point.
CONCLUSIONS	Contrast echocardiography can rapidly and accurately provide short-, intermediate-, and long-term prognostic information in patients presenting to the ED with suspected cardiac CP even before serum cardiac markers are known. Integrating contrast echocardiography into the ED evaluation of CP may improve the risk stratification of such patients. (J Am Coll Cardiol 2005;46:920–7) © 2005 by the American College of Cardiology Foundation

Chest pain (CP) is a common complaint in patients seeking care from an emergency department (ED). The electrocar-

diogram (ECG) is effective in helping to diagnose 30% to 50% of patients with acute myocardial infarction (AMI) (1–3), and early determinations of serum cardiac enzymes

frequently are negative (4,5). The unreliability of these parameters results, on one hand, in the inadvertent discharge of approximately 5% of patients with ongoing AMI and, on the other hand, unnecessary hospital admissions (6).

Apart from the identification of ischemia, the accurate risk stratification of these patients also is important. Those patients who are at intermediate or high risk for an adverse outcome may require admission to a coronary care or telemetry unit, treatment with potent antiplatelet agents (7–9), or early referral for cardiac catheterization (10). The presence of elevated levels of troponin identifies those patients at increased risk and is a component of the Thrombolysis In Myocardial Infarction (TIMI) risk score (11). It may, however, not be elevated or immediately available at the time of patient presentation. Thus, complete risk stratification and initiation of therapy may be unnecessarily delayed. We hypothesized that an assessment of left ventricular (LV) regional function (RF) and myocardial perfusion (MP) would be superior to the TIMI score in patients presenting to an ED with suspected cardiac CP and no ST-segment elevation on the ECG.

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Abbreviations and Acronyms
AMI    = acute myocardial infarction
CE     = contrast echocardiography
CP     = chest pain
ECG    = electrocardiogram
ED     = emergency department
LV     = left ventricular
MP     = myocardial perfusion
mTIMI  = modified Thrombolysis In Myocardial
         Infarction
RF     = regional function
TIMI   = Thrombolysis In Myocardial Infarction
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METHODS

Patient population. This study was approved by the Human Investigation Committee at the University of Virginia. Patients >30 years of age who presented to the ED with a complaint of CP of >30 min in duration that was not easily attributable to an obvious noncardiac cause and who did not exhibit ST-segment elevation on the ECG were enrolled in the study. All patients had their contrast echocardiography (CE) study completed within 12 h of the onset of their symptoms. All patients provided written informed consent.

Determination of TIMI risk score. The TIMI risk score was calculated as previously defined (11). A score of 1 was assigned to each of the following seven variables when present: age >65 years, more than three coronary disease risk factors, known coronary luminal diameter narrowing of >50%, ST-segment deviation on ECG, two or more angina events in the previous 24 h, use of aspirin in the previous seven days, and elevated levels of troponin. The TIMI risk score was calculated as the sum of all scores.

We also wanted to evaluate the prognostic utility of a score derived from variables that are available immediately at the time of ED presentation. Because of inherent delays in receiving laboratory results and because troponin elevation may be delayed for many hours after the initial presentation, a modified TIMI risk score (mTIMI) that excluded this variable was derived (maximum score of 6).

Contrast echocardiography. An infusion of 3 ml of Optison (GE Healthcare, Princeton, New Jersey) diluted in 60 ml of saline was administered intravenously at a rate of 3 ml · min^{-1} using a syringe pump (model AS40A, Baxter, Deerfield, Illinois). Imaging was performed using a Sonos 5500 system (Phillips Ultrasound, Andover, Massachusetts). Regional function data were acquired using low mechanical index harmonic imaging and contrast for LV border delineation.

For MP, intermittent high mechanical index ultraharmonic imaging was performed using transmit/receive frequencies of 1.3/3.6 MHz, respectively, with ultrasound transmission gated to the ECG at end-systole. Images were acquired digitally at pulsing intervals of 1, 2, 3, 4, and 5 cycles. Compression was set at 75%, and all gain settings were optimized at the beginning of the study and then held constant. If a signal from myocardial regions was discernable despite optimization of ultraharmonic image settings, intermittent harmonic power Doppler was performed to achieve better tissue signal suppression. The transmit focus initially was set at the level of the mitral valve but was moved to the apex when an apical defect was observed to exclude the apical destruction artifact (Video A; see the online version of this article for all videos). Off-axis images were acquired as needed. Regional function and MP data were acquired digitally onto magneto-optical disks.

Regional function and MP studies were interpreted separately by experienced observers who were blinded to all data: both were scored visually using a 14-segment model as normal, abnormal, or not interpretable (12). The segments were then grouped into anteroapical, lateral, or inferoposterior territories. Studies were classified as normal if RF or MP in the majority of segments within each perfusion territory were normal. Studies were called abnormal if RF or MP was abnormal in one or more territories, even if all territories were not visualized. If a study could not be classified as previously mentioned, it was deemed not assessable.

Study protocol. All patients had a complete history and physical examination as well as a 12-lead ECG. Blood was drawn for troponin I at the time of ED presentation and repeated twice at 6-h intervals. Troponin I levels were measured using a direct chemiluminometric immunoassay (Bayer, Tarrytown, New York). Contrast echocardiography was performed as soon as possible after the patient's

Table 1. Early Events in Different mTIMI and TIMI Groups

Event, n (%)	mTIMI Risk Group			TIMI Risk Group		
	Low (n = 586)	Intermediate (n = 326)	High (n = 45)	Low (n = 560)	Intermediate (n = 305)	High (n = 92)
AMI	24 (4.1)	35 (11.0)	4 (8.9)	11 (2.0)	29 (9.5)	23 (26.0)
All-cause mortality	1 (0.2)	1 (0.3)	0 (0)	1 (0.2)	0 (0)	1 (1.1)
Total primary events	25 (4.3)	36 (11.3)	4 (8.9)	12 (2.2)	29 (9.5)	24 (27.1)
Unstable angina	11 (1.9)	28 (8.6)	9 (20.0)	8 (1.4)	25 (8.2)	15 (16.0)
PCI	1 (0.2)	7 (2.1)	1 (2.2)	1 (0.2)	6 (2.0)	2 (2.2)
CABG	1 (0.2)	2 (0.6)	0 (0)	1 (0.2)	1 (0.3)	1 (1.1)
Total secondary events	18 (3.1)	44 (13.3)	11 (24.4)	15 (2.7)	37 (14.8)	21 (22.6)

AMI = acute myocardial infarction; CABG = coronary artery bypass graft surgery; mTIMI = modified Thrombolysis In Myocardial Infarction; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.