electrocardiogram changes. Physicians are unlikely to immediately discharge that group. However, our findings suggest that AMI remains extremely unlikely and alternative diagnoses can be considered at an early stage.

Drs. Kavsak and Worster question the diagnostic performance of hs-cTnT using the limit of detection (LoD) (5 ng/l) rather than the limit of blank (LoB) (3 ng/l) as a cutoff. At the LoD cutoff, 272 (38.7%) patients would have had AMI immediately "ruled out" in our prospective cohort study. Three AMIs would have been missed. Thus, sensitivity fell to 97.7% (95% confidence interval [CI]: 93.4% to 99.5%) with a negative predictive value of 98.9% (95% CI: 96.8% to 99.8%). In our subsequent evaluation of hs-cTnT in clinical practice, 195 (21.3%) patients had an initial hs-cTnT below the LoD and only 2 developed elevated levels (>14 ng/l) on subsequent testing. Thus, sensitivity was 99.7% (95% CI: 98.8% to 100.0%) with negative predictive value 99.0% (95% CI: 96.3% to 99.9%). It remains to be decided whether these results can be confirmed in other datasets and whether the clinical community will find these results acceptable.

Recently, there has been discussion about reporting only down to the LoD rather than to the LoB. Our findings may influence that discussion. If the LoB provides important clinical data, this fact should be considered. Indeed, we reported a sensitivity of 100.0% at the LoB in our cohort study (Reichlin et al. [3] and, more recently, Christ et al. [4] also reported the same sensitivity) and a 99.8% value in a cohort from clinical practice. Our findings certainly suggest that further work is necessary to improve the analytical precision of troponin assays at that level.

In our cohort study, samples were not repeated when hemolysis was present, although we understand that hemolysis can lower hs-cTnT levels (4). Fifty-four (7.7%) of the samples in our cohort study showed some degree of hemolysis. Twelve of those samples had values <3 ng/l, which is below the LoB. We would advocate repeating the sample before excluding AMI at any cutoff whether it be the LoB or the LoD. No AMIs were missed using this approach, although the number of patients affected was small.

Our findings are preliminary. They require further prospective validation and subsequent evaluation in a randomized controlled trial. However, approaches like these are required to move the field forward by reducing the time taken to exclude AMI. We believe that we should, over time, be able to unencumber emergency departments by developing innovative approaches for ruling out AMI. Our investigation starts that important work.

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Microvolt T-Wave Alternans Testing Has a Role in Arrhythmia Risk Stratification

In one interesting aspect, the letter by Jackson et al. (1) pertains to risk stratification in general. They suggest that evidence-based cardiac risk assessment should be an automatic process devoid of individual clinical judgment. We disagree and maintain that any risk assessment requires careful interpretation by experienced physicians. Unfortunately, the Glasgow group misrepresented our guideline statement (2) not only in this respect.

The presence of abnormal T-wave alternans (TWA) has demonstrated clinical utility in stratifying risk for malignant arrhythmias and sudden cardiac death. This derives from prospective, peer-reviewed studies involving >12,000 patients. These data clearly show that patients with increased TWA levels have 2- to 23-fold independently higher risk of serious outcomes as compared with those with lower TWA levels. Elevated TWA provides risk information independent of left ventricular ejection fraction (LVEF), standard clinical variables (e.g., age and sex), and important cardiovascular risk markers (e.g., smoking, diabetes, hypertension, and medication usage). Our assertion, "it is reasonable to consider TWA evaluation whenever there is suspicion of vulnerability to lethal cardiac arrhythmias," concurs with prior statements by the American Heart Association (3,4), the American College of Cardiology (3,4), and the National Institutes of Health (5).

As with any risk stratification method, including LVEF, not all studies are consistent with the overall trend. Specifically, in the MASTER (Microvolt T-Wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients) trial and TWA substudy of SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial), TWA did not predict appropriate implantable cardioverter-defibrillator (ICD) therapy, sudden cardiac death, and/or ventricular tachycardia/fibrillation. As discussed in our document (2), there are plausible explanations for this departure from the bulk of the literature. Specifically, a recent systematic review and meta-analysis determined that

withdrawal of beta-adrenergic blockade before TWA assessment diminishes its predictive strength by nearly 4-fold (6). This observation also applies to the reduced predictivity in other prospective studies.

Furthermore, it carries the important implication that TWA is sensitive to chronic therapy (7), supporting our assertion that TWA assessment should be performed while patients are on their usual, chronic medications.

Regarding the potential application of TWA to guide therapy, we stated, "there is as yet no definitive evidence from interventional trials that it can guide therapy" (2). However, this conclusion does not connote an absence of evidence or the impossibility of using TWA to support other risk markers, especially in borderline cases. The ABCD (Alternans Before Cardioverter Defibrillator) trial demonstrated that TWA testing appears to be comparable to electrophysiological study in guiding ICD implantation and that the 2 methods may be complementary. Numerous studies outlined in our document demonstrate that TWA provides additive predictive value to LVEF and other risk stratifiers. These facts are reflected in our recommendation that TWA should not be used as a sole parameter either to rule in or to rule out the prescription of ICD therapy.

Thus, even without dedicated trials on therapy guidance, a sizeable number of prospective studies support TWA's utility in risk stratification for life-threatening arrhythmias and its potential value in clinical judgment.

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