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RESEARCH LETTER

Direct Comparison of the 0/1h and 0/3h Algorithms for Early Rule-Out of Acute Myocardial Infarction

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et al

Patients with symptoms suggestive of acute myocardial infarction (AMI) account for ≈10% of all emergency department (ED) presentations.[1] The majority of patients are finally found to have diagnoses other than AMI.[2] Thus, the expeditious evaluation of such patients is important because delays in ruling out AMI may interfere with the detection of other underlying diseases. The 0/1 hour (0/1h) algorithm and the 0/3 hour (0/3h) algorithm are both recommended by the European Society of Cardiology with a Class I recommendation for the early rule-out of AMI.[1] The 0/1h algorithm and 0/3h algorithm are completely different protocols. Whereas the 0/1h algorithm uses high-sensitivity cardiac troponin (hs-cTn) concentrations at presentation and absolute changes within the first hour and hence takes optimal advantage of the increased diagnostic accuracy and precision of hs-cTn assays, the 0/3h algorithm uses a fixed threshold protocol based on the 99th percentile at presentation and 3 hours in conjunction with clinical criteria (GRACE [Global Registry of Acute Coronary Events] score <140 and the need to be pain free). It is currently unknown whether 1 algorithm is preferable to the other.

The aim of this study was to directly compare safety, quantified by the negative predictive value (NPV) and the negative likelihood ratio (LR) for the presence of AMI, and efficacy, quantified by the proportion of patients triaged toward rule-out in a large diagnostic multicenter study enrolling patients presenting with suspected AMI to the ED (URL: https://www.clinicaltrials.gov. Unique identifier: NCT00470587). The study was carried out according to the principles of the Declaration of Helsinki and approved by the local ethics committees. Written informed consent was obtained from all patients. Patients presenting with ST-segment–elevation MI were excluded. Triage toward rule-out by the 0/1h or the 0/3h algorithm was compared against the final adjudication performed by 2 independent cardiologists using all information, including cardiac imaging and serial hs-cTnT measurements. Analyses were performed with hs-cTnT and hs-cTnI. NPV and efficacy were compared by the McNemar test and Pearson χ^2 test, respectively. The 95% confidence intervals (CIs) were calculated with the Wilson score method without continuity correction.

Among 2547 patients eligible for analysis with hs-cTnT, AMI was the final adjudicated diagnosis in 387 patients (15%). The 0/1h algorithm provided safety similar to that of the 0/3h algorithm (NPV, 99.8% [95% CI, 99.4–99.9] and negative LR, 0.01 [95% CI, 0.00–0.03] versus NPV, 99.7% [95% CI, 99.2–99.9] and negative LR, 0.02 [95% CI, 0.00–0.05]) but allowed the rule-out of significantly more patients compared with the 0/3h algorithm (60% versus 44%; $P<0.001$). Among 2197 patients eligible for analysis with hs-cTnI, AMI was the final diagnosis in 327 patients (15%). The 0/1h algorithm provided higher safety compared with the 0/3h algorithm (NPV, 99.6% [95% CI, 99.1–99.9%] and negative LR, 0.02 [95% CI, 0.01–0.05] versus NPV, 97.8% [95% CI, 96.7–98.5] and negative LR,

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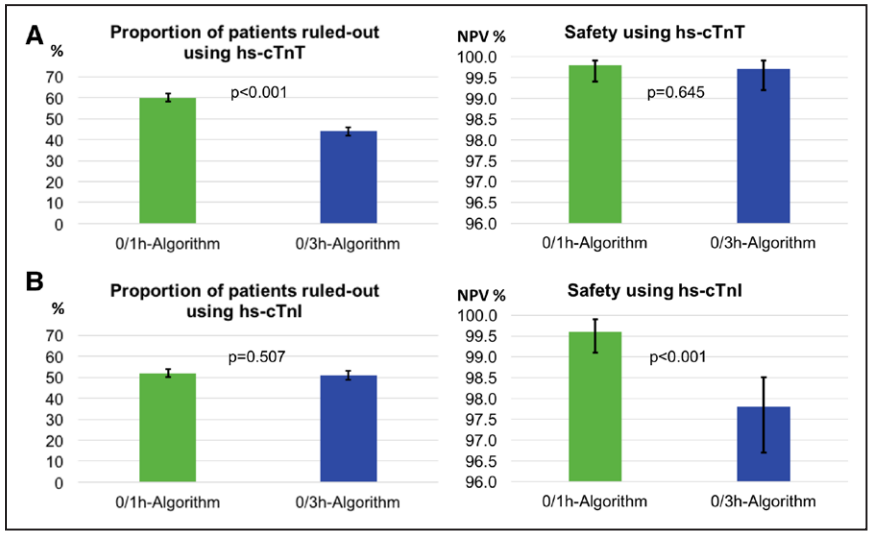

Figure. Direct comparison of the 0/1h and 0/3h algorithms for early rule-out of AMI using hs-cTnT (A) and hs-cTnI (B). The figure illustrates both coprimary end points: safety, as quantified by the negative predictive value (NPV; percent), and efficacy (proportion of patients assigned to ruled out; percent). Bars represent 95% confidence intervals. AMI indicates acute myocardial infarction; and hs-cTn, high-sensitivity cardiac troponin.

0.13 [95% CI, 0.09–0.19]) and allowed the rule-out of a similar portion of patients compared with the 0/3h-algorithm (52% versus 51%; *P*=0.507; Figure).

Overall, 711 patients (28%) presented within the first 2 hours from chest pain onset. Safety for the 0/1h and 0/3h algorithms with hs-cTnT was very high (NPV, 99.6% [95% CI, 98.4–99.9] versus 100% [95% CI, 98.9–100]) and comparable to late presenters (chest pain onset >2 hours) with 99.9% (95% CI, 99.5–100) versus 99.6% (95% CI, 98.9–99.9), respectively. The 0/1h algorithm allowed the rule-out of more patients compared with the 0/3h algorithm in early presenters (64% versus 49%; *P*<0.001) and in late presenters (59% versus 42%; *P*<0.001). Findings were confirmed with hs-cTnI and with 30-day survival used as an additional outcome measure for safety, with survival rates of 99.9% to 100% for patients triaged toward rule-out by both algorithms.

These findings corroborate and extend previous work on the development and validation of safe and effective rule-out strategies for AMI and have important clinical implications.[3–5] The excellent safety achieved with both algorithms documents the suitability of most of these patients for early discharge and outpatient management. Beyond the more favorable combination of safety and efficacy by the 0/1h algorithm versus the 0/3h algorithm, the following features may help physicians and institutions in the selection of their preferred triage algorithm. First, the 0/1h algorithm has the obvious and important additional advantage of allowing clinical decision making 2 hours earlier compared with the 0/3h algorithm. Because most patients triaged toward early rule-out are also candidates for direct discharge from the ED, it is very likely that it will reduce time to discharge and treatment cost in the ED. Second, the 0/1h algorithm does not require the use of a specific risk score, which further increases its feasibility. Previous studies have documented that omitting any of the 3 elements of the 0/3h algorithm (hs-cTn, GRACE score, pain-free criterion) in an effort to simplify the approach would worsen its safety and is therefore discouraged. Third, when putting our findings into clinical perspective, it is important to highlight that the 0/1h algorithm and the 0/3h algorithm should always be used in conjunction with all clinical information available. This is of paramount importance because, among patients presenting with acute chest discomfort to the ED, the rule-out of AMI is related to the possibility of rapid discharge and outpatient management but not identical to it.

In conclusion, the 0/1h algorithm is superior to the 0/3h algorithm using hs-cTnT as well as hs-cTnI because it more favorably combines safety with efficacy.

ARTICLE INFORMATION

Data sharing: The data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

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Disclosures

The authors designed the study, gathered and analyzed the data, vouched for the data and analysis, wrote the article, and decided to publish. Drs. Badertscher, Boeddinghaus, and Mueller had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors have read and approved the article. The sponsors had no role in designing or conducting the study and no role in gathering or analyzing the data or writing the article. The article and its contents have not been published previously and are not being considered for publications elsewhere in whole or in part in any language, including publicly accessible web sites or e-print servers. Dr. Boeddinghaus received speaker honoraria from Siemens and research grants from the University of Basel and the Department of Internal Medicine. Dr. Twerenbold has received research support from the Swiss National Science Foundation (P300PB-167803), the University of Basel, the University Hospital of Basel, and the Cardiovascular Research Foundation Basel, as well as speaker honoraria/consulting honoraria from Roche, Abbott, Brahms, Siemens, and Singulex. Dr. Rubini received speaker honoraria from Abbott and research support from the Swiss Heart Foundation. Dr. Reichlin has received research grants from the Goldschmidt-Jacobson-Foundation, the Swiss National Science Foundation (PASMP3-136995), the Swiss Heart Foundation, the Professor Max Cloëtta Foundation, the Uniscientia Foundation Vaduz, the University of Basel, and the Department of Internal Medicine, University Hospital Basel, as well as speaker honoraria from Brahms and Roche. Dr. Mueller has received research support from the Swiss National Science Foundation, the Swiss Heart Foundation, the KTI, the Stiftung für kardiovaskuläre Forschung Basel, Abbott, Alere, AstraZeneca, Beckman Coulter, Biomerieux, Brahms, Roche, Siemens, Singulex, Sphingotec, and the Department of Internal Medicine, University Hospital Basel, as well as speaker honoraria/consulting honoraria from Abbott, Alere, AstraZeneca, Biomerieux, Boehringer Ingelheim, BMS, Brahms, Cardiorentis, Novartis, Roche, Siemens, and Singulex. The other authors report no conflicts. The investigated hs-cTn assays were donated by the manufacturers, who had no role in the design of the study, the analysis of the data, the preparation of the article, or the decision to submit the article for publication.

APPENDIX

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