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Original Contributions

RETROSPECTIVE EVALUATION OF TWO FAST-TRACK STRATEGIES TO RULE OUT ACUTE CORONARY SYNDROME IN A REAL-LIFE CHEST PAIN POPULATION

Martin Schønemann-Lund, MD,* Mikkel Malby Schoos, MD, PHD,† Kasper Iversen, MD, DMSC,‡ Steen I. Hansen, MSC ENGINEERING,§ Jørgen Thode, MD, DMSC,§ Peter Clemmensen, MD, DMSC, FESC, FSCAI,|| and Rolf Steffensen, MD, MPA¶

*Department of Internal Medicine, Hudiksvalls Sjukhus, Hudiksvall, Sweden, †Department of Cardiology, Køge Sygehus, Køge, Denmark, ‡Department of Cardiology, University Hospital of Copenhagen, Herlev Hospital, Herlev, Denmark, §Department of Clinical Biochemistry, University Hospital of Copenhagen, Hillerød Hospital, Hillerød, Denmark, ||Department of Cardiology, Nykøbing Falster Sygehus, Nykøbing Falster, Denmark ¶Department of Cardiology, University Hospital of Copenhagen, Hillerød Hospital, Hillerød, Denmark

Reprint Address: Martin Schønemann-Lund, MD, Department of Internal Medicine, Hudiksvalls Sjukhus, Ås 203, Delsbo 82060, Sweden

□ **Abstract—Background: The European Society of Cardiology (ESC) guideline on non-ST-elevation acute coronary syndrome (N-STE ACS) proposed a new ACS rule-out protocol. Objectives: To evaluate this new tool, which uses diagnostic levels of high-sensitivity troponin T (hs-TnT; > 14 ng/L) in a slightly modified version and compare this to a recently proposed approach using undetectable levels of hs-TnT to rule out patients. Methods: There were 534 consecutive patients with suspected ACS included. Protocol 1: symptom duration, hs-TnT at 0 and 6–9 h, Global Registry of Acute Coronary Events (GRACE) score, and symptom status at 6–9 h. Protocol 2: a single blood sample of hs-TnT. The primary endpoint was a discharge diagnosis of ACS by blinded adjudication. Secondary endpoints were ACS re-admission < 30 days and 1-year mortality. Results: Protocol 1 classified 434/534 (81%) patients, with 27.9% being ruled out. All myocardial infarctions were correctly ruled in, but 15 cases of unstable angina were missed, resulting in a sensitivity and negative predictive value of 87.3% (79.6–92.5%) and 87.6% (80.4–92.9%), respectively. Protocol 2 ruled out 17.5% of the population, yielding a sensitivity and negative predictive value of 94.1% (88.2–97.6%) and 90.8% (81.9–96.2%), respectively. Both protocols correctly ruled in 2/3 patients with ACS re-admission < 30 days and 55/56 1-year fatalities. Conclusion: The present study confirms the diagnostic value of a modified version of the ESC rule-out protocol (Protocol 1) in N-STE ACS patients, but also suggests that a simpler protocol using undetectable levels of hs-TnT (Protocol 2) could provide a similar or even superior sensitivity.** © 2015 Elsevier Inc.

□ **Keywords—acute coronary syndrome; sensitivity; specificity; triage; troponin; undetectable levels; limit of detection**

INTRODUCTION

Patients presenting to the emergency department (ED) with symptoms suggestive of acute coronary syndrome (ACS) represent the second most common patient type in the ED (1). The prevalence of ACS in chest pain patients presenting to the ED is 30% (2,3). Furthermore, ACS is one of the most common and potentially life-threatening diseases where symptoms can be deceiving at presentation. Consequently, large numbers of chest pain patients are admitted for observation and investigation, thereby placing a heavy burden on health care costs (4). Despite this, the diagnosis of ACS is missed in approximately 2% of cases (5,6).

The pivotal decision of patient admittance still relies on the clinical skill set of the physician accessing the

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patient (7,8). These skills are prone to a number of important biases (9–11). Accordingly, there continues to be a need for improved and objective diagnostic tools that safely rule in and rule out a suspected diagnosis of ACS.

In recent years, a growing body of evidence has suggested the possibility of identifying a low-risk group of patients that can be discharged safely for outpatient evaluation and treatment (12–15). Accordingly, the new guidelines from the European Society of Cardiology (ESC) on the treatment of non-ST-elevation ACS (NSTE ACS) suggests a fast-track protocol to rule-out ACS consisting of high-sensitivity cardiac troponin, Global Registry of Acute Coronary Events (GRACE) risk score, and symptom status (16). However, this strategy differs from previously proposed fast-track protocols and needs evaluation in a clinical setting. Furthermore, a strategy of ruling-out patients with initial undetectable levels of high-sensitivity troponin T (hs-TnT) has gained attention, demonstrating high negative predictive values (NPV) for a subsequent diagnosis of ACS (15,17). The aim of this study was to determine the safety and efficacy of a slightly modified version of the ESC rule-out protocol (Protocol 1) and compare it with the approach using undetectable levels of hs-TnT (Protocol 2).

MATERIALS AND METHODS

The present study is a sub-study of the Hillerød Heart Study, a prospective, observational, single-center study designed to evaluate the diagnostic and prognostic value of several new biomarkers in ACS. The local ethics committee (J.nr. H-2-2009-097) and the national data agency (J.nr. 2010-41-5621) approved the study. Methods and results are reported according to the recommendations from the Standards for Reporting of Diagnostic Accuracy (STARD) initiative (18). The decision to undertake the present sub-study was taken after termination of the inclusion period for the original study.

Population

Between January 1, 2011 and April 30, 2011, all patients above the age of 18 years assessed for acute nontraumatic chest pain that had blood drawn for troponin analysis as a part of their diagnostic work-up, triggered an additional simultaneous specimen collection. Patients identified by this automated process comprised the recruitment population. Due to logistic reasons, patients were not included in the time interval between 2:00 p.m. Friday and 2:00 p.m. Sunday.

Consenting participants were mainly recruited from the Coronary Care Unit (CCU) situated in the Department of Cardiology (n = 383) and from the ED (n = 107). Patients with a high likelihood of ACS are transferred directly to the CCU after an initial evaluation in the ED. Patients with a lower likelihood of ACS are evaluated and discharged directly from the ED or transferred to another ward according to the preliminary diagnosis set by the referring physician.

The rest of the participants were recruited from other medical or surgical departments of the hospital if they developed symptoms suggestive of ACS during admission, and consequently became subjects for testing of cardiac troponins, which triggered the automated specimen collection mentioned previously (n = 44).

Exclusion criteria consisted of not being able to provide informed consent; admitted to the Intensive Care Unit at time of testing; ST-elevation myocardial infarction; cardiac arrest at time of admission or prehospital or implantable cardioverter defibrillator shock prior to admission, as well as admission to a hospital other than Hillerød Hospital at time of first blood sample (Figures 1 and 2).

Trained nurses and research nurses in the CCU collected consent forms and baseline data. All other missing data were collected retrospectively from patients' medical records by two authors (MSL, MMS). Data on readmissions were collected through patients' medical records, and data on 1-year mortality was obtained from the Central Population Registry. Follow-up for mortality was therefore 100% complete.

Endpoints

The primary endpoint was a diagnosis of ACS at index admission as adjudicated by two independent cardiologists (MMS, RS) who had access to all clinical and laboratory information including hs-TnT, however, blinded to the result of Protocol 1. Adjudication was performed after completion of the study.

Myocardial infarction (MI) was adjudicated according to the third universal definition of MI in which the diagnosis is based on cardiac troponins (cTn) > 99% upper reference limit (URL; 14 ng/L in the current assay) plus a significant rising or falling pattern of cTn in a clinical context suggestive of cardiac ischemia (19). According to the ESC consensus paper, a 20% rise or fall was considered significant in case of the first hs-TnT being > 14 ng/L, and an absolute change of 7 ng/L (plus at least 1 value of hs-TnT > 14 ng/L) was considered significant in case of the first hs-TnT being ≤ 14 ng/L (20).

Unstable angina (UA) was adjudicated in patients not fulfilling criteria for a diagnosis of MI, but with other parameters strongly favoring progressive/unstable cardiac ischemia, such as: ischemic changes in the electrocardiogram (ECG), classical ischemic pain progressing or not responding to treatment, a coronary angiography (CA)