

Impact of Point-of-care Testing in the Emergency Department Evaluation and Treatment of Patients with Suspected Acute Coronary Syndromes

Bertrand Renaud, MD, Patrick Maison, MD, Alfred Ngako, MD, Patrick Cunin, MD, Aline Santin, MD, Jérôme Hervé, MD, Mirna Salloum, MD, Marie-Jeanne Calmettes, MD, Cyril Boraud, MD, Virginie Lemiale, MD, Jean Claude Grégo, MD, Marie Debacker, MD, François Hémerly, MD, Eric Roupie, MD

Abstract

Objectives: To assess the impact of point-of-care testing (POCT) for troponin I (cTnI) measurement on the time to anti-ischemic therapy (TAIT) for patients with suspected non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS) presenting to the emergency department (ED).

Methods: This was an open-label, randomized, single-center trial conducted in a university-affiliated hospital. cTnI measurement of patients with suspicion of NSTEMI-ACS coming to the ED was randomly allocated to POCT or central hospital laboratory testing (CHLT). The authors compared patients' baseline characteristics, time to anti-ischemic therapy, and medical outcomes between the randomized groups, in all study participants and in high-risk NSTEMI-ACS (cTnI level ≥ 0.10 $\mu\text{g/mL}$), and in those with low suspicion ACS (no chest pain and no ST deviation).

Results: Of the 860 patients enrolled, 113 were high-risk NSTEMI-ACS patients, including 53 (46.9%) allocated to POCT and 60 (53.1%) to CHLT. POCT was associated with decreased time to anti-ischemic therapy of about three-quarters of an hour, which was due to a shorter time to physician notification of cTnI level, in both all and subgroup participants. In contrast, neither ED length of stay nor medical outcomes differed between study groups.

Conclusions: Point-of-care testing for cTnI measurement might be clinically relevant for ED patients with a suspicion of NSTEMI-ACS, particularly for high-risk patients with a low suspicion of ACS.

ACADEMIC EMERGENCY MEDICINE 2008; 15:216–224 © 2008 by the Society for Academic Emergency Medicine

Keywords: point-of-care systems, coronary artery disease, myocardial infarction, emergency medicine, troponin, randomized controlled trials

Rapid diagnosis of patients with high-risk non-ST elevation acute coronary syndromes (NSTEMI-ACSs) may be critical, as recent findings suggest that adverse outcomes increase with increasing time to coronary angiography and related treatment.^{1–3} The key components of risk stratification are patient symptoms,

Structure des Urgences (BR, AN, AS, JH, MS, MJC, CB, VL, JCG, MD, ER), Service de Pharmacologie Clinique, Unité de Recherche Clinique (PM, PC), and Département d'Informatique Hospitalier (PMSI et Recherche Clinique) (FH), AP-HP, Albert-Chenevier-Henri Mondor, Créteil, France; Faculté de Médecine, Université Paris 12 (BR, PM, AN, PC, AS, JH, MS, MJC, CB, VL, JCG, MD, FH, ER), Créteil (APHP), France.

Received October 18, 2007; revisions received November 24 and November 26, 2007; accepted November 28, 2007.

Dr. Renaud has been supported by the "Département de la Formation Continue des Médecins de l'Assistance Publique des Hôpitaux de Paris (AP-HP)," by l'A.R.M.U.R. (Association de Recherche en Médecine d'Urgence, France), by SQUARE (Association pour la QUALité, la Recherche et l'Enseignement à l'Hôpital Saint-Joseph (Paris)), and by GlaxoSmithKline France.

Potential conflict of interest: Reagents for the troponin I assay on the point-of care device (Stratus-SC) were supplied by Dade Behring, Marburg, Germany.

The corresponding author certifies, on behalf of all authors, that Dade Behring had no role, either directly or through a third party, in gathering or preparation of data or in the writing of the manuscript.

Clinical Trial Registration number: ISRCTN92275378; <http://www.controlled-trials.com/ISRCTN92275378>.

Address correspondence: Dr. Bertrand Renaud, MD; e-mail: bertrand.renaud@hmn.aphp.fr. Reprints will not be available.

physical and electrocardiogram (ECG) findings, and biomarkers of cardiac injury.⁴ Because many patients with ACS in the emergency department (ED) are “low suspicion” (i.e., have neither chest pain nor a diagnostic ECG, as defined by high-risk findings such as ischemic ST-segment elevation, depression, T-wave inversion), biomarkers can help physicians to identify ACS and to stratify risk.⁵⁻⁹ Because biomarkers are assessed in a central hospital laboratory outside the ED, they are often the time-limiting step in diagnosis of ACS.^{4,8,10,11}

Cardiac-specific troponins reliably allow early identification of patients with acute myocardial infarction and are of critical prognostic value, especially troponin I (cTnI).¹² Moreover, the diagnosis of acute myocardial infarction depends on troponin testing in up to 50% of patients when the ECG is nondiagnostic.^{12,13} For the purposes of this report, we define patients as “high risk” if they have an elevated troponin; these patients must receive timely anti-ischemic therapy and are candidates for early invasive care.^{3,14-20}

Point-of-care testing (POCT) has become popular to hasten the availability of laboratory test results.²¹ Faster results are of special interest in the ED to reduce the time to treatment.²²⁻²⁴ However, the impact of POCT on daily practice is poorly documented, particularly for ED patients with suspicion of NSTEMI-ACS.²⁵ We hypothesized that POCT for cTnI measurement in the ED would hasten care, particularly for patients without chest pain or a diagnostic ECG. Our study aim was to compare time to anti-ischemic treatment (TAIT) and medical outcomes for patients with a suspicion of NSTEMI-ACS by place of cTnI testing: POCT at the ED versus central hospital laboratory testing (CHLT).

METHODS

Study Design

We conducted an open-label, randomized controlled trial of adults with suspicion of ACS presenting to our ED. Patients enrolled in this study were randomly allocated to either POCT or CHLT for measuring cTnI level. Blood samples were the unit of randomization. Randomization in blocks of 20 was done with computer generated codes prior to start of the study by our hospital clinical research unit (PM, PC), which was not involved in data collection or patient care. Allocations were concealed in consecutively numbered, sealed, opaque envelopes, safely stocked in the ED. The institution's review board for the protection of human subjects approved the study protocol and patient informed consent procedures. The trial is registered under number ISRCTN92275378 (<http://www.controlled-trials.com/ISRCTN92275378>).

Study Setting and Population

With approximately 43,000 patients annually, our 14-physician ED is affiliated with the Hospital Henri Mondor, a French university and tertiary-care 900-bed hospital located in the Paris area, serving a population of 800,000 individuals, and is equipped to perform percutaneous coronary reperfusion therapy.

Patients who came to the ED on weekdays (convenience sampling) between November 2002 and April

2004, with a suspicion of ACS, were eligible for enrollment. Symptoms prompting the suspicion of ACS included chest pain, dyspnea, epigastric pain, nausea-vomiting, neck or arm discomfort, fatigue, fall, syncope, and dizziness.^{4,7,16} Symptoms refer to the main complaints that included persistent symptoms and symptoms that lasted 24 hours before ED arrival. Board-certified emergency physicians (EPs) attended all patients around the clock, and the attending physician made the symptoms-based decision to order cTnI testing.

Inclusion criteria for study patients were 1) age ≥ 18 years, 2) suspicion of ACS, and 3) order to measure cTnI. To meet Inclusion Criterion 2, a patient was required to present with one of the complaints listed above and either a cTnI level of $\geq 0.1 \mu\text{g/L}$ or at least two of the following: age 60 years or older, at least three cardiovascular risk factors, personal history of coronary artery disease, chest pain, or ECG changes indicating ischemia (ST-segment depression in two continuous leads, T-wave inversion > 3 mm, or transient ST-segment elevation). After giving informed consent for study participation, eligible patients were enrolled by attending EPs who then disclosed the allocated group.

Exclusion criteria were refusal or inability to provide informed consent or previous enrollment in the study. Because patients with ST elevation ACS (typical chest pain and persistent [> 20 min] ST-segment elevation [> 0.1 mV in limb leads or 0.2 mV in precordial leads]) did not represent a diagnostic challenge compared to NSTEMI-ACS and were candidates for urgent reperfusion procedure, they were excluded from the current analysis.²⁶ We defined two subgroups for analysis: “high-risk patients” (those with elevated cTnI) and “low-suspicion” ACS (neither chest pain nor a diagnostic ECG).

Study Protocol

Emergency physicians collected data through standardized patient interviews and medical record review during the ED evaluation. Data included 1) demographic data (i.e., age and gender); 2) clinical data (source of referral, presenting complaints, cardiovascular risk factors), personal and familial history of atherosclerosis, hypertension, hyperlipemia, diabetes mellitus, smoking history, body mass index $\geq 25 \text{ kg/m}^2$; 3) ECG abnormalities, thrombolysis in myocardial infarction (TIMI) score, and laboratory creatinine and cTnI; and 4) disposition (i.e., hospitalization, site of care).^{4,13} Demographic data, presenting complaints, and cardiovascular risk factors were collected directly from patients' or a relative's interview. The source of the referral, ECG abnormalities, laboratory measures, and disposition were ascertained from the medical record.

Therapeutic data collected included whether anti-ischemic treatment (AIT) was ordered before cTnI results were available and, if so, whether the AIT was modified as a result of the cTnI. AIT refers to medication given in the ED to decrease acute myocardial ischemia, including antithrombin therapy (unfractionated heparin [UH] or low-molecular-weight heparin [LMWH]), platelet activation inhibitors (e.g., aspirin,

ticlopidine, clopidogrel), nitrates, and beta-blocking agents.

The study procedures occurred as follows: 1) cTnI measurement order; 2) enrollment and baseline data collection; 3) collection of blood sample; 4) POCT or CHLT of cTnI according to randomization; 5) request by physician for cTnI test result and, if necessary, order of a second cTnI measurement; 6) determination of therapeutic regimen and disposition; and 7) follow-up of procedures and medical outcomes. Each physician in charge of a patient was allowed to start AIT whenever necessary. This could happen before cTnI was ordered in the case of a perceived high-risk patient with NSTEMI-ACS or after becoming aware of the patient's cTnI.

On a daily basis, two independent physicians (PC, PM) not involved in patients' care, and two EPs in charge of study monitoring (AN, BR), reviewed the data collected for overall consistency, with a particular focus on the time of data collection. Discrepancies between patients' computer-based medical records that automatically write in memory the times of patient care at the ED (including arrival, first medical contact, cTnI availability, and treatment decision and disposition) were resolved by discussion with attend-

ing physicians and nurses. To assess whether treating physicians altered the randomization allocation, we compared the rank of subsequent numbered envelopes disclosure to the rank of patients' ED arrival time.

Measures

The primary study outcome measure was TAIT, as defined by time from presentation to time when any of the predefined AITs were ordered. Secondary study outcomes were the time from presentation to physician notification of cTnI level and the time from presentation to inpatient bed assignment (i.e., ED length of stay [LOS]).

For designated high-risk patients (NSTEMI-ACS and cTnI level $\geq 0.1 \mu\text{g/L}$), performance of coronary angiography and reperfusion and 30- and 90-day mortality were assessed by two research assistants who were blinded to patients' allocation group, by standardized review of medical records and, whenever necessary, telephone interviews with the patient, a relative, or the family practitioner.

cTnI Level Measurement. Each patient's cTnI was measured after randomization allocation. Our hospital

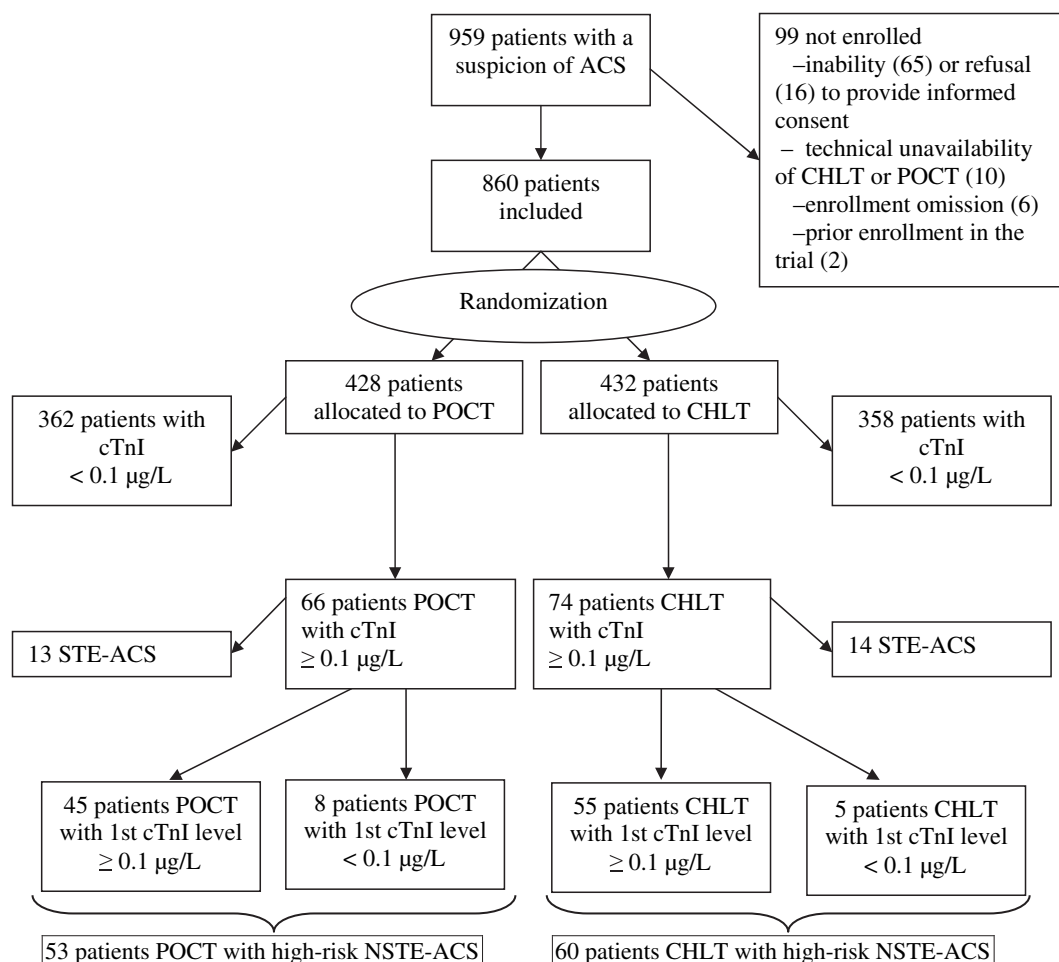


Figure 1. Study participants flow. ACS = acute coronary syndrome; CHLT = central hospital laboratory testing; cTnI = troponin I; NSTEMI-ACS = non-ST-segment elevation ACS; POCT = point-of-care testing; STE-ACS = ST-segment elevation ACS.

central laboratory staff took responsibility for cTnI measurement and for CHLT and POCT quality control per French quality standards for medical laboratories.²⁷ Based on the analytic performance of the Stratus CS system (Stratus CS test systems, Dade Behring, Marburg, Germany) and on consensus statements by the joint European Society of Cardiology/American College of Cardiology (ESC/ACC), all patients with cTnI $\geq 0.10 \mu\text{g/L}$ were considered positive.^{28,29}

Point-of-care Testing. We used a whole-blood rapid-assay device (Stratus CS), which is a fluorometric enzyme immunoassay analyzer for quantitative determination of cTnI. The device analyzes closed routine sample tubes containing anticoagulated whole blood and gives results within 15 minutes.²⁹ The Stratus CS cTnI assay is appropriate for clinical use as it is diagnostically equivalent to CHLT (good correlation to CHLT and precision of a highly sensitive troponin

Table 1
Baseline Patients Characteristics

| Characteristics* | Overall | | Patients with cTnI $\geq 0.1 \mu\text{g/L}$ | |
|--|------------------|----------------|---|------------------|
| | POCT (n = 419) | CHLT (n = 414) | POCT (n = 53) | CHLT (n = 60) |
| Demographic characteristics | | | | |
| Median age (IQR) | 62 (49–75) | 64 (50–77) | 67 (63–71) | 68 (64–73) |
| Male gender (%) | 62.0 | 58.4 | 71.7 | 60.0 |
| Source of referral (%) | | | | |
| Out-of-hospital emergency care services | 11.1 | 10.1 | 13.2 | 17.0 |
| Ambulance | 17.1 | 22.6 | 20.7 | 23.7 |
| Personal | 56.8 | 51.6 | 50.9 | 45.8 |
| Other | 14.9 | 15.7 | 15.1 | 13.6 |
| Cardiovascular risk factors (%) | | | | |
| Body mass index $\geq 25 \text{ kg/m}^2$ | 58.7 | 58.6 | 50.0 | 51.8 |
| Hypertension | 48.8 | 49.1 | 62.3 | 60.0 |
| Diabetes mellitus | 20.7 | 21.4 | 22.6 | 30.0 |
| Hyperlipidemia | 32.6 | 35.8 | 43.4 | 31.7 |
| Smoking history | 52.2 | 48.0 | 54.7 | 50.0 |
| Familial history of atherosclerosis | 25.1 | 27.1 | 28.3 | 21.7 |
| Personal history of atherosclerosis | 46.7 | 48.1 | 37.7 | 35.0 |
| Presenting complaint (%) | | | | |
| Chest pain | 57.7 | 55.6 | 54.7 | 66.7 |
| Typical chest pain | 25.1 | 25.3 | 43.4 | 46.7 |
| Typical left arm pain | 13.2 | 16.4 | 26.4 | 25.0 |
| General malaise | 18.9 | 23.8 | 7.5 | 25.0 |
| Dyspnea | 32.3 | 32.6 | 47.2 | 35.0 |
| Epigastric pain | 8.1 | 8.4 | 3.8 | 15.0 |
| ECG features (%) | | | | |
| ST-segment depression or transient elevation | 10.0 | 14.1 | 11.3 | 21.7 |
| T-wave inversion | 24.5 | 30.8 | 34.0 | 50.0 |
| Pathologic Q-wave | 15.1 | 10.4 | 13.2 | 11.7 |
| Left bundle branch block | 13.8 | 16.2 | 5.7 | 8.5 |
| Arrhythmia | 10.0 | 11.2 | 1.9 | 8.3 |
| Biologic measures | | | | |
| Renal failure* (%) | 4.7 | 5.8 | 11.8 | 17.5 |
| cTnI measure ($\mu\text{g/L}$), Median (IQR) | 0.02 (0.01–0.04) | 0.01 (0–0.05) | 0.24 (0.14–1.00) | 0.44 (0.18–2.10) |
| Second cTnI measure† ($\mu\text{g/L}$), Median (IQR) | 0.02 (0.01–0.05) | 0.01 (0–0.04) | 0.13 (0.11–0.16) | 0.14 (0.14–0.29) |
| Thrombolysis in myocardial infarction score (%) | | | | |
| 1 | 18.9 | 17.6 | 9.4 | 10.0 |
| 2 | 28.3 | 30.7 | 32.1 | 41.7 |
| 3 | 31.1 | 27.2 | 28.3 | 16.7 |
| 4 | 16.7 | 16.4 | 22.6 | 15.0 |
| 5–6 | 4.9 | 8.2 | 7.5 | 16.7 |

CHLT = central hospital laboratory testing; cTnI = troponin I; ECG = electrocardiogram; IQR = interquartile range; POCT = point-of-care testing.

*Renal failure denoted patients with creatinine level $\geq 120 \mu\text{mol/L}$ or creatinine clearance estimated by the Cockcroft formula $< 30 \text{ mL/min}$ when available.

†195 patients underwent a second cTnI measurement.

Table 2
Comparisons of Time Lags in Minutes (Median and Interquartile Range [IQR]) between Patients Allocated to the Point-of-care Testing (POCT) or to the Central Hospital Laboratory Testing (CHLT) for Cardiac Troponin

| Characteristics | Overall | | p-Value |
|---|----------------|---------------|---------|
| | POCT (n = 419) | CHLT n = 414) | |
| Time (minutes), median (IQR) | | | |
| From presentation to blood sample collection | 75 (70–80) | 65 (60–70) | 0.005 |
| From blood collection to physician notification of first cTnI | 38 (35–42) | 109 (104–115) | <0.001 |
| From Presentation to AIT | 151 (139–162) | 198 (187–210) | <0.001 |
| Length of stay at ED (min), median (IQR) | 309 (204–411) | 307 (229–401) | 0.99 |

Low-suspicion ACS referred to patients presenting no chest pain and non-ST-deviation NSTEMI-ACS with elevated cTnI. cTnI = troponin I; ED = emergency department; IQR = interquartile range; NSTEMI-ACS = non-ST-segment elevation acute coronary syndrome; AIT = anti-ischemic treatment.

method [a coefficient of variation of < 10% at the 99th percentile of the reference population].^{30,31}

ED nurses were trained by Dade Behring staff prior to the study enrollment period and performed all point of care cTnI measurements. In an attempt to defeat a potential Hawthorne effect, nurses were asked not to deliver the cTnI result until a request was obtained from the attending physician.

Central Hospital Laboratory Testing. CHLT of cTnI was performed on the Dimension RxL-HM analyzer (Dade Behring), a one-step enzyme immunoassay based on two cTnI-specific monoclonal antibodies that gives a result in about 17 minutes.³²

Data Analysis

The sample size estimate was chosen to detect a difference of 15 minutes in TAIT between the study subgroups of patients with cTnI $\geq 0.1 \mu\text{g/L}$, which were expected to include 15% of the entire study cohort. We assumed a power of 80%, statistical significance level of 5%, and mean TAIT of 90 minutes with standard deviation of 30 minutes, resulting in an estimated sample size of 64 patients in each high-risk subgroup that required 420 patients to be included in each study group.

Comparisons between groups were performed using the t-tests or Wilcoxon rank-test for continuous variables and chi-square or Fisher's exact test for categorical variables. All analyses were performed using Stata Version 8.0 (Stata Corp., College Station, TX).

RESULTS

Of the 959 patients screened from November 2002 to April 2004, a total of 833 were enrolled, of whom 419 (50.3%) were randomly allocated to the POCT group and 414 (49.7%) to the CHLT group (Figure 1). There were 53 (12.6%) high-risk patients in the POCT group and 60 (14.5%) in the CHLT group. Among those high-risk patients, 55 patients had a low suspicion of ACS, 27 (6.4%) in the POCT group and 28 (6.8%) in the CHLT group.

Troponin I was elevated in 113 (13.1%) patients (53 [46.9%] in the POCT group and 60 [53.1%] in the

CHLT group; Table 1). Ninety-nine (87.6%) patients were classified positive on the first cTnI test, and 14 (12.4%) more were positive on the second test. Of those, 85 (75.2%) patients were treated with platelet activation inhibitors (aspirin alone in 70.8%), 40 (35.4%) with UH, 28 (24.8%) with LMWH, 40 (35.4%) with nitrates, and 4 (3.5%) with beta-blocking agents at ED. Treatment was started in 54 (47.8%) patients before physician knowledge of cTnI: 35 (64.8%) of these patients reported chest pain and 30 (55.6%) had ECG abnormalities suggestive of acute ischemia. AIT given before cTnI knowledge included aspirin, 33 of 54 (61.1%); nitrates, 25 of 54 (46.3%); UH, 20 of 54 (37.0%); and LMWH, 12 of 54 (22.2%).

The median time from patient arrival in the ED to blood sample collection was 10 minutes longer in the POCT group than in the CHLT group for the 833 patients with a suspicion of NSTEMI-ACS, but this difference in times was smaller in the study subgroups (Table 2). The median time from blood sample collection to physician notification of cTnI was shorter in the POCT group than in the CHLT group. As a result, TAIT was shorter for POCT patients than for CHLT patients, and this was even more pronounced for the two study subgroups. Excluding those high-risk patients who only had an elevated troponin on the second sample (first troponin normal), the results were similar (TAIT, 102, interquartile range [IQR] = 84–148 vs. 166, IQR = 123–216) for POCT and CHLT, respectively [$p < 0.001$]. Median LOS in the ED did not significantly differ in any of the three POCT-CHLT comparisons.

Patients with elevated cTnI level usually became inpatients (94.7%); 78 (69.0%) were initially admitted to a cardiac or medical intensive care unit (Table 3), and 3 patients refused hospitalization against medical advice. Procedures did not differ by study group: 52 (46.0%) patients had a coronary angiography during the index hospitalization, of whom 5 (4.4%) had immediate coronary angiography (ICA), 20 (17.7%) had transluminal coronary angioplasty, and 15 (13.3%) had a coronary artery bypass graft. The 5 patients with ICA reported typical chest pain on arrival. Two (1.8%) patients, both from the POCT group, died within 30 days after ED arrival. Their initial cTnI levels were 0.1 and 0.42 $\mu\text{g/L}$.

| NSTE-ACS Elevated cTnI | | | Low-suspicion ACS | | |
|------------------------|---------------|---------|-------------------|---------------|---------|
| POCT (n = 53) | CHLT (n = 60) | p-Value | POCT (n = 27) | CHLT (n = 28) | p-Value |
| 70 (54–87) | 67 (52–82) | 0.77 | 57 (39–110) | 61 (27–112) | 0.98 |
| 36 (28–43) | 101 (90–113) | <0.01 | 27 (15–60) | 120 (76–137) | <0.01 |
| 145 (117–173) | 192 (163–221) | <0.01 | 120 (92–248) | 198 (156–244) | 0.03 |
| 275 (161–422) | 199 (122–353) | 0.15 | 226 (163–469) | 201 (115–428) | 0.43 |

Table 3
Treatment and Medical Outcomes of Patients with NSTE-ACS and cTnI ≥ 0.1 µg/L

| | POCT (n = 53) | CHLT (n = 60) | p-Value |
|--|---------------|---------------|---------|
| Anti-ischemic treatment at the ED (%) | | | |
| Overall | 84.9 | 85.0 | 0.99 |
| Specific treatment prior to physician notification | 41.5 | 53.3 | 0.21 |
| Antiplatelet therapy (%) | | | |
| Overall | 77.4 | 73.3 | 0.62 |
| Prior to physician notification | 24.5 | 33.3 | 0.30 |
| Unfractionated heparin (%) | | | |
| Overall | 30.2 | 40.0 | 0.23 |
| Prior to physician notification | 13.2 | 21.7 | 0.24 |
| Low-molecular-weight heparin (%) | | | |
| Overall | 30.2 | 20.0 | 0.21 |
| Prior to physician notification | 11.3 | 10.0 | 0.82 |
| Nitrates (%) | | | |
| Overall | 43.4 | 28.3 | 0.09 |
| Prior to physician notification | 18.9 | 25.0 | 0.43 |
| Beta-blocking agents (%) | | | |
| Overall | 5.7 | 1.7 | 0.34 |
| Prior to physician notification | 0 | 0 | – |
| Procedures (%) | | | |
| Coronary angiography | 47.2 | 45.0 | 0.64 |
| Immediate coronary angiography | 1.9 | 6.7 | 0.22 |
| Transluminal coronary angioplasty | 17.0 | 18.3 | 0.42 |
| Aortocoronary bypass | 11.3 | 15.0 | 0.57 |
| Outcome (%) | | | |
| Inpatient treatment | 96.2 | 93.3 | 0.68 |
| Hospitalization in cardiology wards | 69.8 | 68.3 | 0.86 |
| Admission in CCU or ICU | 67.9 | 70.0 | 0.81 |
| 30-day mortality* | 3.8 | 0.0 | 0.21 |
| 90-day mortality* | 11.5 | 8.3 | 0.57 |

CCU = coronary care unit; CHLT = central hospital laboratory testing; cTnI = troponin I; ICU = intensive care unit; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; POCT = point-of-care testing.
*Outcomes were missing for mortality at 30 days (n = 1) and mortality at 90 days (n = 1) in the CHLT group.

By the 90-day follow-up, overall 11 (9.8%) patients had died; their median cTnI level was 1.1 µg/L (IQR = 0.24–2.51 µg/L) vs. 0.29 µg/L (IQR = 0.17–1.2 µg/L) in survivors (p = 0.34). Neither 30-day mortality nor 90-day patient mortality rates differed between study groups.

DISCUSSION

In this trial of adults arriving at the ED with suspicion of NSTE-ACS, we found that POCT was associated with a faster decision-making process than CHLT was. POCT was associated with a shorter TAIT (median 151 min, IQR = 139–162 min) compared to CHLT (median 198 min, IQR 187–210 min). Therefore, the diagnosis of myocardial infarction could be made slightly earlier in the subset of patients with vague symptoms (Figure 2).

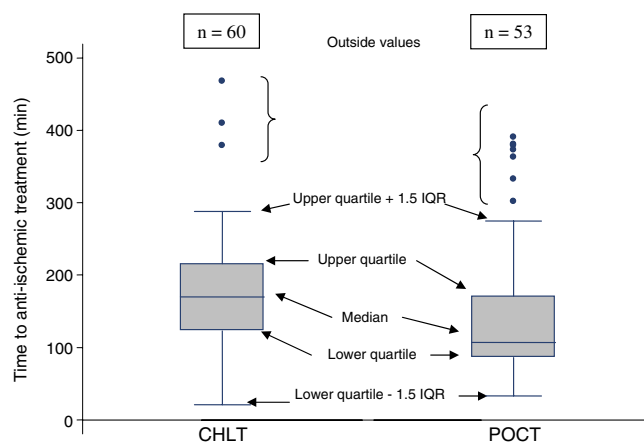


Figure 2. Time to anti-ischemic therapy (TAIT) of the 113 patients with non-ST-segment elevation acute coronary syndrome and elevated troponin I (cTnI; ≥ 0.1 µg/L) allocated to point-of-care testing (POCT) compared to those allocated to central hospital laboratory testing (CHLT) for patients with NSTE-ACS and elevated cTnI. Boxes are delimited by the upper limit (75th percentile) and by the lower limit (25th percentile) of the interquartile range (IQR). The line inside boxes figures the median value of the TAIT. Adjacent lines figure the upper (upper quartile + 1.5 IQR) and the lower (lower quartile – 1.5 IQR) adjacent values, and dots represent outside values.

As there is increasing evidence supporting early invasive therapy for patients with high-risk NSTEMI-ACS, we believe that a time saving of 45 minutes has clinical relevance in the ED.^{2,3,7,33} Nonetheless, our findings underscore the limited impact of POCT for shortening ED LOS.

Consistent with other reports, numerous study patients (45.1%) did not have typical chest pain.^{7,34} Presenting complaints differed somewhat, particularly within the study subgroups. Consistent with current European guidelines, AIT was often started in the ED in both groups.^{4,10,35} However, AIT was initiated in 52.2% of high-risk patients after cTnI level knowledge, and this rate was somewhat higher in the POCT group. Accordingly, ICA was less likely performed on POCT patients. The reliability of cTnI levels obtained on the POCT device has been repeatedly demonstrated.^{23,24,36} Therefore, the differences in early onset of AIT and in ICA performance between study groups likely reflects the higher rate of POCT patients arriving with vague symptoms and nonsuggestive ECG findings, as has been associated with the underuse of invasive procedures.^{7,35} Most high-risk patients were admitted to coronary care or intensive care units and 46.0% subsequently underwent coronary angiography followed by revascularization procedure. This underscores the coronary artery disease severity and the risk of adverse outcomes associated with delayed treatment of high-risk patients, who are often undertreated and are at greater risk of death.^{7,33,37,38}

Point-of-care testing resulted in shortening the TAIT, particularly for 38.9% of high-risk patients with a low suspicion of ACS. For nontroponin testing, previous studies have not always shown a significant benefit of implementing POCT in the ED.^{21,39-42} By studying only patients with suspicion of NSTEMI-ACS, for whom treatment decision or bed request may be delayed until the cTnI result is known, we were able to show a difference in TAIT.^{23,43}

Nevertheless, despite hastening decision-making, we did not demonstrate a significant difference in the study group average LOS in the ED. This suggests that POCT is only part of the whole-system approach that is required to improve timeliness of care.²¹⁻²³ Indeed, many other factors determine the duration of ED visits, such as the absence of centralized bed assignment in our hospital. Apart from chance variation, we could not explain the unexpected trend toward a longer LOS for the POCT group. Nonetheless, even if EPs cannot entirely control delays from the onset of symptoms to hospital admission, reducing in-hospital care delays can reduce both morbidity and mortality. Depending on the institution, a shorter time to diagnosis might also affect time to bed request or unit assignment.^{22,44}

LIMITATIONS

We were not able to enroll patients throughout the entire week, which may have introduced a selection bias. Physicians and nurses could not be blinded to patient assignment, which may have influenced their attitudes or recording of their decision-making times. To decrease the chance of this bias, data collection was

reviewed by nonstudy physicians for overall consistency with a particular focus on the time of data collection. Our study was not powered to detect differences in mortality, particularly regarding high-risk patients, although time saving itself has proven to be a relevant endpoint.^{33,44,45} The quite low and late AIT use, particularly for high-risk patients, may have artificially increased the proportion of patients for whom the cTnI level was the time-limiting step in the diagnosis of low suspicion ACS.^{22,46} Because timeliness of care is tightly linked to routine practices, and the impact of POCT may vary across institutions, and because our findings were obtained from a single center trial, our results might not be generalizable to other EDs. Finally, inasmuch as the crude cost of POCT for cTnI was higher than CHLT, and the fact that we did not collect the working time spent by nurses to perform the procedure, additional studies should address the cost-effectiveness of POCT for cTnI measurement in the ED.^{47,48}

CONCLUSIONS

Point-of-care testing decreased the time to the initial delivery of AIT for ED patients with suspicion of NSTEMI-ACS, both overall and in the high-risk group. This benefit may be particularly relevant for NSTEMI-ACS patients with low suspicion, for which time to diagnosis is shortened. This decreased time to delivery of therapy did not significantly impact ED LOS and outcomes in this small study.

The authors thank Prof. Christian Brun-Buisson and Dr. Dave Van Pelt for their critical review of the manuscript.

References

1. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA*. 2000; 284:60-7.
2. Tricoci P, Lokhnygina Y, Berdan LG, et al. Time to coronary angiography and outcomes among patients with high-risk non ST-segment elevation acute coronary syndromes. Results from the SYNERGY Trial. *Circulation*. 2007; 116:2669-77.
3. Neumann FJ, Kastrati A, Pogatsa-Murray G, et al. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. *JAMA*. 2003; 290:1593-9.
4. Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. *Eur Heart J*. 2007; 28:1598-660.
5. Canto JG, Fincher C, Kiefe CI, et al. Atypical presentations among Medicare beneficiaries with unstable angina pectoris. *Am J Cardiol*. 2002; 90:248-53.
6. Culic V, Eterovic D, Miric D, Silic N. Symptom presentation of acute myocardial infarction: influence

- of sex, age, and risk factors. *Am Heart J.* 2002; 144:1012–7.
7. Brieger D, Eagle KA, Goodman SG, et al. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest.* 2004; 126:461–9.
 8. Gibler WB, Cannon CP, Blomkalns AL, et al. Practical implementation of the guidelines for unstable angina/non-ST-segment elevation myocardial infarction in the emergency department: a scientific statement from the American Heart Association Council on Clinical Cardiology (Subcommittee on Acute Cardiac Care), Council on Cardiovascular Nursing, and Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration with the Society of Chest Pain Centers. *Circulation.* 2005; 111:2699–710.
 9. Apple FS, Ler R, Chung AY, Berger MJ, Murakami MM. Point-of-care i-STAT cardiac troponin I for assessment of patients with symptoms suggestive of acute coronary syndrome. *Clin Chem.* 2006; 52:322–5.
 10. Bertrand ME, Simoons ML, Fox KA, et al. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J.* 2002; 23:1809–40.
 11. Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. *Clin Chem.* 1999; 45:1104–21.
 12. Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. *N Engl J Med.* 1997; 337:1648–53.
 13. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA.* 2000; 284:835–42.
 14. Bhatt DL, Roe MT, Peterson ED, et al. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. *JAMA.* 2004; 292:2096–104.
 15. Bach RG, Cannon CP, Weintraub WS, et al. The effect of routine, early invasive management on outcome for elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med.* 2004; 141:186–95.
 16. Alexander KP, Newby LK, Cannon CP, et al. Acute coronary care in the elderly, part I: Non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation.* 2007; 115:2549–69.
 17. Mehta SR, Cannon CP, Fox KA, et al. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA.* 2005; 293:2908–17.
 18. de Winter RJ, Windhausen F, Cornel JH, et al. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med.* 2005; 353:1095–104.
 19. Erhardt L, Herlitz J, Bossaert L, et al. Task force on the management of chest pain. *Eur Heart J.* 2002; 23:1153–76.
 20. Harrington RA, Becker RC, Ezekowitz M, et al. Antithrombotic therapy for coronary artery disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004; 126(3 Suppl): 513S–548S.
 21. Kendall J, Reeves B, Clancy M. Point of care testing: randomised controlled trial of clinical outcome. *BMJ.* 1998; 316:1052–7.
 22. Singer AJ, Ardise J, Gulla J, Cangro J. Point-of-care testing reduces length of stay in emergency department chest pain patients. *Ann Emerg Med.* 2005; 45:587–91.
 23. Leman P, Guthrie D, Simpson R, Little F. Improving access to diagnostics: an evaluation of a satellite laboratory service in the emergency department. *Emerg Med J.* 2004; 21:452–6.
 24. Wu AH. Point of care testing for conventional cardiac markers. *Point of Care: J Near-Patient Test Technol.* 2006; 5:20–4.
 25. McCord J, Nowak RM, McCullough PA, et al. Ninety-minute exclusion of acute myocardial infarction by use of quantitative point-of-care testing of myoglobin and troponin I. *Circulation.* 2001; 104:1483–8.
 26. Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J.* 2003; 24:28–66.
 27. Pascal P, Beyerle F. [Quality standards for medical laboratories]. *Pathol Biol (Paris).* 2006; 54:317–24.
 28. The Joint European Society of Cardiology/American College of Cardiology. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *Eur Heart J.* 2000; 21:1502–13.
 29. Heeschen C, Goldmann BU, Langenbrink L, Matschuck G, Hamm CW. Evaluation of a rapid whole blood ELISA for quantification of troponin I in patients with acute chest pain. *Clin Chem.* 1999; 45:1789–96.
 30. Christenson RH, Cervelli DR, Bauer RS, Gordon M. Stratus CS cardiac troponin I method: performance characteristics including imprecision at low concentrations. *Clin Biochem.* 2004; 37:679–83.
 31. Beneteau-Burnat B, Baudin B, Vaubourdolle M. Evaluation of Stratus CS stat fluorimetric analyser for measurement of cardiac markers Troponin I (cTnl), creatine kinase MB (CK-MB), and myoglobin. *J Clin Lab Anal.* 2001; 15:314–8.
 32. Hafner G, Peetz D, Dati F, et al. Analytical and clinical evaluation of troponin I determination on dimension RXL-HM. *Clin Chem Lab Med.* 2000; 38:355–61.

33. Spacek R, Widimsky P, Straka Z, et al. Value of first day angiography/angioplasty in evolving non-ST segment elevation myocardial infarction: an open multicenter randomized trial. The VINO Study. *Eur Heart J*. 2002; 23:230–8.
34. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol*. 2002; 90:358–63.
35. Hasdai D, Behar S, Wallentin L, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J*. 2002; 23:1190–201.
36. Delaney B, Wilson S, Fitzmaurice D, Hyde C, Hobbs R. Near-patient tests in primary care: setting the standards for evaluation. *J Health Serv Res Policy*. 2000; 5:37–41.
37. Coronado BE, Pope JH, Griffith JL, Beshansky JR, Selker HP. Clinical features, triage, and outcome of patients presenting to the ED with suspected acute coronary syndromes but without pain: a multicenter study. *Am J Emerg Med*. 2004; 22:568–74.
38. Canto JG, Shlipak MG, Rogers WJ, et al. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA*. 2000; 283:3223–9.
39. Parvin CA, Lo SF, Deuser SM, Weaver LG, Lewis LM, Scott MG. Impact of point-of-care testing on patients' length of stay in a large emergency department. *Clin Chem*. 1996; 42:711–7.
40. Fleisher M, Schwartz MK. Automated approaches to rapid-response testing. A comparative evaluation of point-of-care and centralized laboratory testing. *Am J Clin Pathol*. 1995; 4 Suppl(1):S18–25.
41. Saxena S, Wong ET. Does the emergency department need a dedicated stat laboratory? Continuous quality improvement as a management tool for the clinical laboratory. *Am J Clin Pathol*. 1993; 100:606–10.
42. Collinson PO, John C, Lynch S, et al. A prospective randomized controlled trial of point-of-care testing on the coronary care unit. *Ann Clin Biochem*. 2004; 41(Pt 5):397–404.
43. Brogan GX Jr, Bock JL. Cardiac marker point-of-care testing in the emergency department and cardiac care unit. *Clin Chem*. 1998; 44(8 Pt 2):1865–9.
44. Newby K. Clinical outcomes according to time to treatment. *Clin Cardiol*. 1997; 20(11 Suppl 3):III11–5.
45. Ryan JW, Peterson ED, Chen AY, et al. Optimal timing of intervention in non-ST-segment elevation acute coronary syndromes: insights from the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) Registry. *Circulation*. 2005; 112:3049–57.
46. Christenson J, Innes G, McKnight D, et al. A clinical prediction rule for early discharge of patients with chest pain. *Ann Emerg Med*. 2006; 47:1–10.
47. Apple FS, Chung AY, Kogut ME, Bubany S, Murakami MM. Decreased patient charges following implementation of point-of-care cardiac troponin monitoring in acute coronary syndrome patients in a community hospital cardiology unit. *Clin Chim Acta*. 2006; 370:191–5.
48. Collinson PO. Testing for cardiac markers at the point of care. *Clin Lab Med*. 2001; 21:351–62.