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Assessing the Performance of a Novel Point-of-Care Qualitative Assay for Early Diagnosis of Acute Coronary Syndrome

Ronny Alcalai[a] Boris Varshisky[a] Ahmad Marhig[b] David Leibowitz[a] Larissa Kogan-Boguslavsky[a] Elisheva Dorfman[c] David Steiner[c] Emil Katz[c] Shaden Salameh[b] Chaim Lotan[a]

[a]Heart Institute, Hadassah Medical Center, Jerusalem, Israel; [b]Department of Emergency Medicine, Hadassah Medical Center, Mount Scopus, Jerusalem, Israel; [c]Novamed, Ltd., Jerusalem, Israel

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Troponin · Heart-type fatty acid-binding protein · Myocardial infarction · Diagnosis

Abstract
Background: Early and accurate diagnosis of acute coronary syndrome (ACS) is essential for initiating lifesaving interventions. In this article, the diagnostic performance of a novel point-of-care rapid assay (SensAheart©) is analyzed. This assay qualitatively determines the presence of 2 cardiac biomarkers troponin I and heart-type fatty acid-binding protein that are present soon after onset of myocardial injury. ***Methods:*** We conducted a prospective observational study of consecutive patients who presented to the emergency department with typical chest pain. Simultaneous high-sensitive cardiac troponin T (hs-cTnT) and SensAheart testing was performed upon hospital admission. Diagnostic accuracy was computed using SensAheart or hs-cTnT levels versus the final diagnosis defined as positive/negative. ***Results:*** Of 225 patients analyzed, a final diagnosis of ACS was established in 138 patients, 87 individuals diagnosed with nonischemic chest pain. In the overall population, as compared to hs-cTnT, the sensitivity of the initial SensAheart assay was significantly higher (80.4 vs. 63.8%, $p = 0.002$) whereas specificity was lower (78.6 vs. 95.4%, $p = 0.036$). The overall diagnostic accuracy of SensAheart assay was similar to the hs-cTnT (82.7% compared to 76.0%, $p = 0.08$). ***Conclusions:*** Upon first medical contact, the novel point-of-care rapid SensAheart assay shows a diagnostic performance similar to hs-cTnT. The combination of 2 cardiac biomarkers in the same kit allows for very early detection of myocardial damage. The SensAheart assay is a reliable and practical tool for ruling-in the diagnosis of ACS.

Introduction

Myocardial injury can be defined as the disruption of normal cardiac myocyte membrane integrity, resulting in release of intracellular constituents into the extracellular space and bloodstream, referred to as cardiac biomarkers [1–3]. These biomarkers include detectable levels of a variety of biologically active cytosolic and structural proteins, such as troponins, creatine kinase, myoglobin, heart-type fatty acid-binding protein (H-FABP), and lactate dehydrogenase [4, 5]. Such cardiac biomarkers serve as indicators of myocardial injury [1–5].

karger@karger.com
www.karger.com/crd

Ronny Alcalai
Cardiac Care Unit, Mt. Scopus
Hadassah Hebrew University Medical Center
PO Box 12000, Jerusalem 91120 (Israel)
ronny@hadassah.org.il

The causes of myocardial injury are numerous and include trauma, toxins, inflammation, increased wall stress, etc [6]. Myocardial infarction (MI) caused by an abrupt disruption of coronary blood flow (termed as acute coronary syndrome[ACS]) that results in imbalance between the supply and demand of oxygen and nutrients to the heart muscle is the most common cause of myocardial injury [7].

Early diagnosis of ACS is crucial for providing rapid intervention and treatment that can improve outcomes [3]. While an electrocardiogram (ECG) is the initial tool used for the diagnosis of ACS, its sensitivity for diagnosing ACS in patients presenting with ischemic-type chest pain without ST elevation is low. As such, cardiac biomarkers that serve as highly sensitive indicators of myocardial injury have become the principal tool for the diagnosis of ACS. Currently, cardiac troponins (T or I) are the only biomarkers recommended for the detection of myocardial injury and are integral to the diagnostic criteria for defining MI [8].

Another cardiac biomarker, H-FABP, is a low molecular-weight protein that behaves similarly to myoglobin in terms of its kinetics and release [9]. However, in contrast to myoglobin, there is more fatty acid-binding protein in heart than in skeletal muscle, potentially making it a more cardiac-specific test [10–12]. H-FABP appears in the blood within an hour of myocardial injury and its level peaks 5 h after the onset of a coronary event [13]. This is an earlier rise than troponin, which can only be detected within 3 h after such an event [14]. Nevertheless, assessing H-FABP levels as the sole marker for diagnosing an MI may not be accurate since it can be elevated in other conditions such as CVA [15].

Determining levels of a combination of the 2 markers, H-FABP and troponin, may serve as a useful diagnostic method for improved early diagnosis of ACS. This approach integrates the advantages of both biomarkers, with H-FABP serving as the initial marker to detect myocardial injury in the first hours after the onset of symptoms and troponin being a well-established marker for such events. The SensAheart© (Novamed, Ltd.) test device was developed as a rapid qualitative lateral flow immune chromatographic assay intended for the qualitative determination of the cardiac biomarkers H-FABP and troponin I in human whole blood. SensAheart detects both markers in a single immune test line. This combination increases the sensitivity and accuracy of myocardial injury detection, as compared to single marker-based assays available, since both biomarkers used in the SensAheart assay contribute to the intensity of the same band. Because of this additive effect, lower concentrations of each marker can generate a visible test line more readily detectable than possible with either individual marker alone. In this study, we assessed the diagnostic performance of the novel SensAheart assay at first medical contact compared to the high-sensitive cardiac troponin T (hs-cTnT).

Methods

Design

This is a prospective observational study designed to assess the diagnostic performance of the rapid point-of-care SensAheart assay as compared to the standard hs-cTnT-based test for the diagnosis of ACS. The institutional review board (0456-14-HMO) approved the trial, and all patients signed a written informed consent.

Population and Management

This study population comprised consecutive patients above 18 years admitted to the emergency department of Hadassah-Hebrew University Medical Centers during 2015–2018 with acute chest pain suggestive of ACS. Exclusion criteria included chronic renal failure (GFR <50), suspected muscle damage concurrent with the ischemic symptoms, sepsis, patients after chemotherapy, and patients with a pacemaker.

All patients underwent 12-lead ECG, although the ECG findings were not considered part of the inclusion or exclusion criteria. The management and treatment of patients were at the discretion of the attending treating physician, according to standard institutional protocols, and no change was made in management as part of this observational study.

Patients were divided into 2 subgroups according to the final diagnosis at discharge: ACS (with or without ST-segment elevation) and nonischemic chest pain (NICP). ACS diagnosis was based on current recommended guidelines for the diagnosis of ACS [3, 16], including ECG changes, biomarkers of myocardial necrosis, and coronary angiography results, if performed.

Necrosis of the myocardium was defined by hs-cTnT levels exceeding the lower reference limit of the kit if a typical kinetic with rise and fall was observed [8]. Coronary angiography was considered diagnostic for ACS if it revealed a culprit lesion. An expert cardiologist who was blinded to the SensAheart test results confirmed the final diagnosis. The diagnosis was based on the clinical, laboratory, and angiography findings, as listed above. NICP was defined for patients in whom ACS was excluded and who did not suffer from other acute medical conditions (both cardiac and noncardiac). Patients with other acute medical conditions such as infection, respiratory syndromes, myocarditis, heart failure, or cardiac arrhythmias not related to ACS were excluded from the final analysis.

Specimen Collection

Upon admission to the ER, 10 mL of blood were collected from each patient, of which 30 μL were used for the SensAheart assay, and the rest was sent to the laboratory for biochemical analysis. The SensAheart test procedure was as follows: 1 drop of whole blood (30 μL) was loaded onto the device surface. After the sample

was fully absorbed (about 10–20 s), 2 drops (~50 μL) of chasing buffer were applied to the cassette. Colored band(s) appeared within a few minutes (Fig. 1). Results were recorded after 15 min but not later than 20 min. A control band always appeared. If no such band was visible, the test was considered invalid. In this case, the assay was repeated with a new test cassette. When a colored band appeared in the test line, this was considered a positive result, whereas when no band appeared in the test line, this was considered a negative result. The intensities of the test and control bands are not normally equal, with the control band intensity usually being stronger than that of the test band. As such, the presence of a band in the test line was considered positive, regardless of its intensity (Fig. 1). The results of the SensAheart assay were documented but not taken into consideration for patient management.

Upon admission, all patients underwent a hs-cTnT assay (Roche Diagnostics, Mannheim, Germany). Additional measurements of hs-cTnT were performed as clinically indicated. The hs-cTnT assay was performed using electrochemiluminescence immunoassay technology on Elecsys and Cobas 6000 immunoassay analyzers (file:///C:/Users/ronny/Downloads/Roche%20Accelerated%20AMI%20Algorithm%20Brochure%20(1).pdf). The detection limit was 3 ng/L. The ninety-ninth percentile cutoff point was 14 ng/L, and the 10% coefficient of variation was 13 ng/L. The diagnostic hospital cutoff that was recommended by the hs-cTnT assay manufacturer (ROSHE) was 30 ng/L. According to the ESC/ACC consensus document [8], patients with AMI are defined by routine high-sensitive cardiac troponin values below 10% at the ninety-ninth percentile upper reference limit. In the final analysis, both the hospital cutoff (30 ng/L) and the guideline-recommended cutoff (14 ng/L) were used. Comparisons were made for both tests (i.e., SensAheart and hs-cTnT) for the samples taken only upon admission at first medical contact.

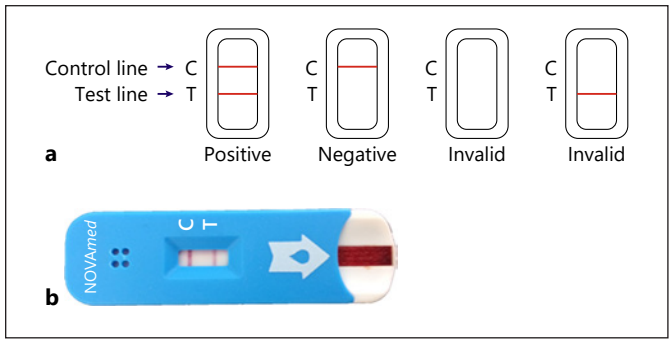
Statistics

Sample size calculation: based on ACS diagnostic, a one-group χ^2 test with a 0.05 two-sided significance level will have 90% power to detect the difference of at least 15% between the SensAheart test results and the hs-cTnT test results when the sample size is 75 for each of the 2 study methods [17].

All measured variables were tabulated by descriptive statistics. For categorical variables, summary tables were provided listing sample size and absolute and relative frequencies. For continuous variables, summary tables were provided listing sample size, arithmetic mean, standard deviation, median, and minimum and maximum values. Sensitivity and specificity analysis results were computed using 2 × 2 tables for outcomes of the SensAheart or hs-cTnT assay versus the final diagnosis and defined as positive or negative.

The following rates were calculated with corresponding 95% confidence intervals, using the following formulations: Sensitivity = (True Positive)/(True Positive + False Negative) × 100%; Specificity = (True Negative)/(True Negative + False Positive) × 100%; NPV = (True Negative)/(True Negative + False Negative) × 100%; Positive Predicated Value = (True Positive)/(True Positive + False Positive) × 100%.

Subgroup analysis was applied to SensAheart results versus the final diagnosis according to gender, cardiovascular disease, smoking status, diabetes, and other risk parameters (recoded as no risk parameters or any risk parameters). Data were analyzed using SAS, version 9.3 (SAS Institute, Cary, NC, USA).



Color version available online

Fig. 1. The SensAheart assay kit. **a** Schematic depiction of the SensAheart assay kit. Two distinct colored lines appear in the C and in T of the test cassette in the case of a positive result (left panel). One colored line appears in the C region in the case of a negative result (second left panel). Failure of the C line to appear reflects an invalid result (2 right panels). **b** A representative picture of the cassette showing typical positive results. C, control; T, test regions.

Results

Two hundred and fifty-five patients were screened during the study period. Thirty patients were excluded. Of these, 9 were excluded due to missing data, 9 did not meet the inclusion criteria, and 12 patients were eventually diagnosed with an acute nonischemic condition (Fig. 2).

Of 225 patients, 138 (61.3%) eventually were diagnosed with true ACS, 62 had STEMI, 71 had NSTEMI, and 5 patients were diagnosed as UAP. These 5 patients had in addition to suggestive clinical symptoms, a coronary angiogram showing a culprit lesion, but without elevation of hs-cTnT (cutoff 30 ng/L) throughout hospitalization. Eighty-seven (38.7%) had NICP, 4 of these patients had minor elevation of troponin without definite explanation including normal angiogram.

The baseline characteristics of both groups in the study population are presented in Table 1 and are typical of ACS patients. Whereas there was a higher percentage of males and smokers in the ACS group, as compared to patients with NICP, other clinical characteristics did not differ between the groups. Finally, patients with ACS presented with a significantly shorter time from symptom onset to admission, as compared to patients with NICP.

Analysis of the SensAheart and hs-cTnT test performances is presented in Table 2. When we used the hs-cTnT hospital cutoff of 30 ng/L, the initial SensAheart assay showed significantly higher sensitivity as compared to the initial hs-cTnT assay (80.4 vs. 63.8%, respectively; $p = 0.002$), yet also showed lower specificity (86.2 vs.

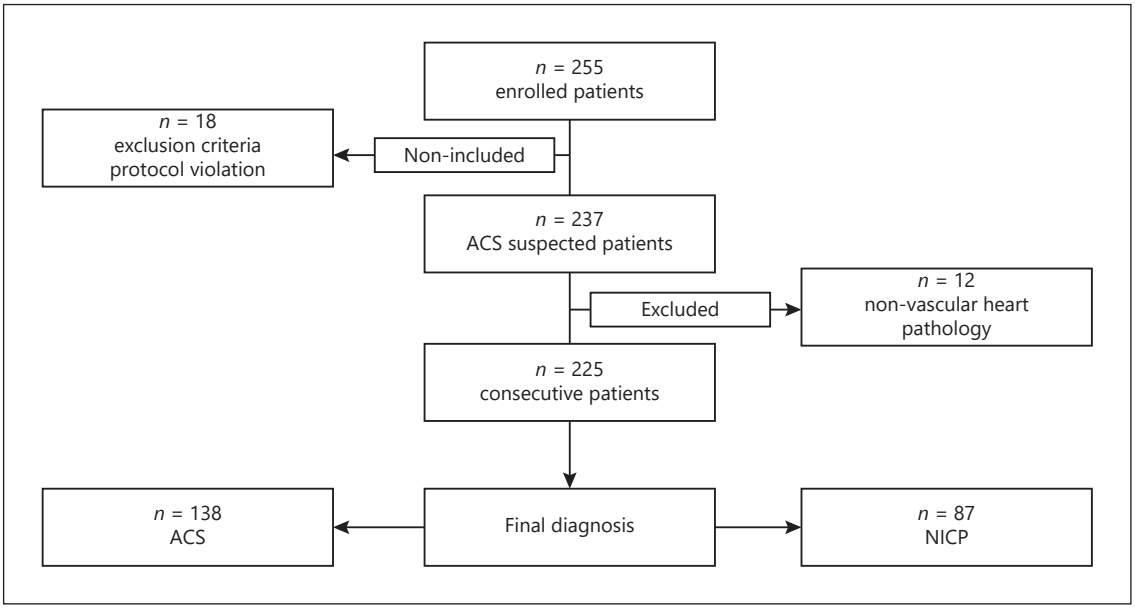


Fig. 2. Flowchart of the study design.

Table 1. Baseline characteristics of the study population according to the final diagnosis

	All 225	ACS 138 (61.3%)	NICP 87 (38.7%)	*p* value
Male gender, *N* (%)	175 (77.8)	116 (84.1)	59 (67.8)	0.004
Age, mean±SD	58.6±12.2	59.1±11.6	58±13.1	0.52
History of CAD, *N* (%)	67 (29.8)	37 (26.8)	30 (34.5)	0.22
Smoking, *N* (%)	102 (45.3)	71 (51.4)	31 (35.6)	0.01
Diabetes, *N* (%)	68 (30.2)	44 (31.9)	24 (27.6)	0.46
Hypertension, *N* (%)	136 (60.4)	79 (57.2)	57 (65.5)	0.24
Time from symptom onset to test, h, median (IQR)	6 (7)	4 (6)	10 (31)	<0.001

ACS, acute coronary syndrome; NICP, nonischemic chest pain; CAD, coronary artery disease; IQR, interquartile range.

95.4%, respectively; $p = 0.036$). There was a trend toward superior diagnostic accuracy of the initial SensAheart assay compared to the hs-cTnT-based assay (82.7 vs. 76.0%; $p = 0.079$). We also assessed the lower recommended cutoff hs-cTnT (14 ng/L). As expected, the sensitivity of the hs-cTnT assay was higher (76.1%), and the specificity was lower (80.5%) with this cutoff, yet both values were slightly lower than the sensitivity and specificity of the SensAheart assay (Table 2; p = ns). The overall accuracy of the initial SensAheart assay was comparable to the initial hs-cTnT assay (Table 2).

Since the release kinetics of cardiac biomarkers differ between STEMI and NSTEMI presentations, we performed the same analyses for patients who presented with ACS without ST-segment elevation. The results of this subpopulation were similar to the whole group with trend toward better sensitivity, lower specificity, and similar overall accuracy (see Table 3).

Adding the H-FABP marker to the device was intended to support early detection of myocardial injury due to early secretion as compared to troponin. To assess this potential advantage, we analyzed the subgroup of early arriving patients. This group consisted of 45 patients admitted up to 4 h from symptom onset. We excluded STEMI patients from this analysis since cardiac biomarkers are not part of the early diagnosis in these patients. Twen-

Table 2. Diagnostic performance of the SensAheart test and the high-sensitive troponin T assay, $N = 225$

	SensAheart	Hs-cTnT test (cutoff 30 ng/L)	*p* value*	Hs-cTnT test (cutoff 14 ng/L)	*p* value**
Sensitivity	80.4% (CI 73–86.2)	63.8% (CI 55.5–71.3)	0.002	76.1% (CI 68.3–82.5)	0.387
Specificity	86.2% (CI 77.3–92.1)	95.4% (CI 88.4–98.6)	0.036	80.5% (CI 70.8–87.5)	0.314
Positive predictive value	90.2% (CI 83.6–94.5)	95.6% (CI 89–98.6)	0.137	86.1% (CI 78.7–91.2)	0.322
Negative predictive value	73.5% (CI 64.2–81.2)	62.4% (CI 53.9–70.2)	0.073	68.0% (CI 58.4–76.2)	0.388
Diagnostic accuracy	82.7% (CI 77.5–87.1)	76.0% (CI 70.0–81.0)	0.079	77.8% (CI 71.9–82.7)	0.192

HS-TnT, high-sensitive troponin T; CI, confidence interval. * *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 30 ng/L. ** *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 14 ng/L.

Table 3. Diagnostic performance of the SensAheart test and the HS-TnT for patients with non-STE ACS, $N = 163$

	SensAheart	Hs-cTnT test (cutoff 30 ng/L)	*p* value*	Hs-cTnT test (cutoff 14 ng/L)	*p* value**
Sensitivity	75.0% (CI 63.7–84.2)	59.21% (CI 47.1–70.3)	0.070	68.4% (CI 56.7–78.6)	0.391
Specificity	86.2% (CI 77.1–92.7)	95.40% (CI 88.6–98.7)	0.020	80.2% (CI 70.2–88.0)	0.274
Positive predictive value	82.6% (CI 71.6–90.7)	91.9% (CI 80.4–97.7)	0.087	75.4% (CI 63.5–84.95)	0.277
Negative predictive value	79.8% (CI 70.2–87.4)	72.8% (CI 63.7–80.7)	0.279	74.2% (CI 64.1–82.7)	0.383
Diagnostic accuracy	81.0% (CI 74.1–86.7)	78.5% (CI 71.4–84.6)	0.575	74.2% (CI 66.8–80.7)	0.142

non-STE ACS, acute coronary syndrome without ST elevation; HS-TnT, high-sensitive troponin T; CI, confidence interval. * *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 30 ng/L. ** *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 14 ng/L).

Table 4. Diagnostic performance of the SensAheart test and the HS-TnT assay for patients with non-STE ACS presenting less than 4 h from symptom onset, $N = 45$

	SensAheart	Hs-cTnT test (cutoff 30 ng/L)	*p* value*	Hs-cTnT test (cutoff 14 ng/L)	*p* value**
Sensitivity	64.0% (CI 42.5–82.0)	32.0% (CI 14.9–53.5)	0.100	48.0% (CI 27.8–68.69)	0.328
Specificity	75.0% (CI 50.9–91.3)	90.0% (CI 68.3–98.8)	0.117	75.0% (CI 50.9–91.3)	1.000
Positive predictive value	76.2% (CI 52.8–91.8)	80.0% (CI 44.4–97.5)	0.748	70.6% (CI 44.0–89.7)	0.657
Negative predictive value	62.5% (CI 40.6–81.2)	51.4% (CI 34.0–68.6)	0.484	53.6% (CI 33.9–72.5)	0.573
Diagnostic accuracy	68.9% (CI 53.3–81.8)	57.8% (CI 42.1–72.3)	0.277	60.0% (CI 44.33–74.3)	0.380

non-STE ACS, acute coronary syndrome without ST elevation; HS-TnT, high-sensitive troponin T; CI, confidence interval. * *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 30 ng/L. ** *p* value for comparison between SensAheart and high-sensitive troponin T with cutoff of 14 ng/L).

ty-five (55.6%) were diagnosed with ACS, while 20 (44.4%) had NICP. Analysis of SensAheart and hs-cTnT test performances in this subpopulation of early arrivals is presented in Table 4. As in the general population, the SensAheart assay showed a trend to higher sensitivity compared to the hs-cTnT assay (64 vs. 32%, respectively; $p = 0.1$) but lower specificity (75 vs. 90%; $p = 0.12$) for ACS detection. The diagnostic accuracy of the SensAheart assay in this subpopulation was slightly better than the hs-cTnT assay (68.9 vs. 57.8%; $p = 0.28$).

To evaluate the credibility of the test in different populations, we further analyzed the performance of the assay

Table 5. Diagnostic performance of the SensAheart test – subgroup analysis

Subgroup	*N*	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Gender					
Females	50	86.4	82.1	79.2	88.5
Males	175	79.3	88.1	92.9	68.4
CAD background					
No	158	79.8	85.7	90.8	70.6
Yes	67	83.8	86.7	88.6	81.2
Smokers					
No	123	82.8	83.6	85.5	80.7
Yes	102	80.3	90.3	95.0	66.7
Diabetes					
No	157	80.2	85.5	89.0	74.6
Yes	68	84.1	87.5	92.5	75.0

CAD, coronary artery disease.

with different subgroups (Table 5). There were no significant variations between the different subgroups in terms of test performance. There were, however, minor differences, such as slightly better sensitivity and lower specificity with females and better specificity with smokers. The overall performances of the different subgroups were comparable to those of the general study population.

Discussion

Early diagnosis of myocardial injury due to coronary insufficiency in patients with chest pain is crucial for providing rapid aggressive treatment that can improve outcome. Since ECG displays limited diagnostic accuracy, diagnosis of ACS is mostly based on cardiac biomarkers [18]. Currently, cardiac troponins are the basis of the diagnostic workup due to their excellent sensitivity and specificity for the detection of myocardial injury [19]. Nevertheless, elevated levels of cardiac troponins can only be detected 3–6 h from the onset of myocardial injury [14], and the current tests based on this biomarker may lack sensitivity for patients presenting in the first hours after chest pain onset. The novel high-sensitive troponin assays were developed to overcome this gap; these tests can detect very low level of troponin allowing early diagnosis of myocardial injury within the first 3 h [8]. However, these tests are not available outside medical facilities with biochemistry laboratory services and are unavailable to a significant proportion of patients who prefer to postpone or avoid hospitalization despite symptoms indicative of ACS.

For these reasons, the SensAheart test, a new point-of-care device that detects both H-FABP and troponin I with the same simple test device was developed. Our results indicate that this additive effect results in higher sensitivity and possibly faster detection of myocardial injury compared to the widely used high-sensitive troponin T assay. Indeed, the sensitivity of the SensAheart test that was taken at first medical contact was 80.4%, as compared to 63.8% for the hs-cTnT-based test (cutoff 30 ng/L) taken at the same time.

The current universal definition of MI [8] calls for use of the ninety-ninth percentile as the troponin cutoff with a coefficient of variation of 10% at this concentration in order to overcome the gap in detecting myocardial injury until 12 h after onset of chest pain. This definition results in a lower troponin cutoff, thereby stimulating the development of high sensitivity assays [20, 21]. Accordingly, we compared the performance of the SensAheart assay with that of the initial hs-cTnT using the lower recommended cutoff (14 ng/L). The SensAheart assay showed slightly better sensitivity and specificity (Table 2). This indicates that a combination of cardiac troponin with a marker of different origin and kinetics enhanced test performance more than did lowering the cutoff, an action that may reduce specificity.

The advantage of the SensAheart test was more robust in patients presenting 4 h from the onset of chest pain. The initial hs-cTnT-based assay showed a low sensitivity of 32% in detecting ACS in such patients, while the SensAheart assay showed a sensitivity of 64%, superior to the hs-cTnT test. These results are comparable to those obtained with other early markers of myocardial injuries, such as myoglobin and copeptin [22, 23]. However, those markers are much less specific than a troponin-based assay [8] such as the SensAheart assay.

The overall diagnostic performance of a single SensAheart measurement was comparable to the initial hs-cTnT assay reading. Nevertheless, as SensAheart shows lower specificity and is not a quantitative assay, this assay is not meant to replace troponin in the final diagnosis of a coronary event. The SensAheart assay allows for earlier decision-making that is essential for identifying high-risk patients. Our results suggest that the diagnostic advantage of the SensAheart assay is mostly applicable to patients who present rapidly after symptom onset and for out-of-hospital settings.

The purpose of the present study was to assess accuracy of the novel SensAheart assay kit, and it was per-

formed on a relatively high-risk population with multiple cardiovascular risk factors and a high percentage of ECG changes, including ST-segment elevation. The setting and design of the study in a large tertiary referral center and inclusion of all suspected patients, regardless of ECG pattern, make the pool of the patients examined different from the common chest pain population, with more ACS positive patients. Due to this selected population, the negative predictive value (NPV) of the initial tests (using both SensAheart and hs-cTnT) was relatively low, as compared to other cohorts [24–27]. According to our findings, we cannot be certain that ACS can be ruled out by a single negative SensAheart test result. In the case of a negative result, further evaluation is warranted. It is likely that the NPV of the SensAheart assay in a low-risk population (i.e., with no risk factors and normal ECG) will be significantly higher and can be used for eliminating the possibility of ACS in low-risk patients. Nevertheless, this assumption should be validated in a different setting.

A review of the demographic and clinical characteristics of the study population reveals that it is representative and comparable to other general cohorts of high-risk chest pain populations [25, 28, 29]. Finally, subgroup analysis of this cohort demonstrated that the test was not skewed for any subgroup, with test performance and accuracy being maintained for all subgroups (Table 4).

Study Limitations

The number of patients enrolled in this study was relatively low; nevertheless, the findings reported were comparable to those obtained with larger cohorts. Statistical analysis revealed that the values measured were sufficient to permit valid comparison between the SensAheart and hs-cTnT assays. Since the study was performed in a hospital setting and included a relatively high-risk patient, the percentage of patients with MI was relatively high. As such, this distribution might limit the relevance of the results in populations with lower risk. The outcome selected for comparison (ACS vs. NICP) may be subject to error. Nevertheless, we used careful assessment of the patients' files by an independent observer to minimize mistakes in the final diagnosis.

Conclusions

The novel point-of-care SensAheart rapid assay, when taken at first medical contact, shows diagnostic performance comparable with the currently available high-sensitive troponin T assay, with better sensitivity and slightly lower specificity. The combination of 2 cardiac biomarkers used in the SensAheart assay, namely troponin I and H-FABP, allow for very early detection of myocardial injury. The SensAheart point-of-care assay, thus, appears to be a reliable and practical tool for determining an early diagnosis of ACS, particularly in patients who present early after symptom onset.

Statement of Ethics

This study complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

Elisheva Dorfman, David Steiner, and Emil Katz are employees of Novamed, Ltd. Boris Varshisky is a medical consultant for Novamed, Ltd. All other authors have no conflicts of interest to disclose.

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Novamed, Ltd. supplied the SensAheart kits for the study; no other external funding was used to support the study.

Author Contributions

R.A., B.V., A.M., L.K.B., D.S., E.K., C.L., and S.S. made substantial contributions to the conception and design of the work. B.V., A.H., and L.K.B. performed the blood tests for the participants. R.A., D.L., D.S., and E.K. contribute to the analysis and interpretation of data for the work. All authors contribute to the drafting of the manuscript or revising it critically for important intellectual content, approve the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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