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Case Report

Multimarker panel in patients admitted to emergency department: A comparison with reference methods

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Abstract

Objectives: Point of care testing and multimarker panels are rapidly expanding in emergency departments. We determined the reliability of Short-of-Breath SOB® panel in patients admitted for acute dyspnea and/or chest pain.

Design and methods: SOB® D-dimer, BNP, cTnI, CK-MB and myoglobin assays were compared with references in 97 outpatients.

Results: The correlation between SOB® and references methods was acceptable, but with limited precision and accuracy.

Conclusions: Diagnostic performances and cut-off values should be further validated before clinicians replace traditional cardio-respiratory biomarkers by the new SOB® panel.

Keywords: Multimarker; BNP; Troponin; Dyspnea; Chest pain; Emergency triage

Introduction

Dyspnea and thoracic pain are frequently seen in patients admitted in emergency departments (ED) [1,2]. These symptoms represent a challenging differential diagnosis. The rule-out process is costly and time consuming, so that protocols based on biomarkers are emerging for a prompt exclusion of a cardiac disease or pulmonary embolism. Point-of-care testing (POCT) currently represent one of the most rapidly expanding areas in clinical diagnostics [3]. In particular, POCT are in agreement with published guidelines recommending a 30-minute turn-around time for cardiac markers in patients evaluated for possible acute coronary syndrome [4,5]. Moreover, POCT has the potential for decreasing therapeutic turnaround time, increasing clinical efficiency, and improving medical and economic outcomes [3]. Recent studies focused on the clinical interest of combined POC markers included in multimarker panels for a better prognostic evaluation of cardiac diseases [6]. Nevertheless, the current debate on the clinical interest of point-of-care and multimarker approaches is far from being closed [7]. Shortness Of Breath panel SOB® (Biosite, San Diego, CA, USA), which is a POCT allowing the concomitant determination of D-dimer level and 4 cardiac markers (BNP, cTnI, CK-MB and myoglobin), seems interesting for the rapid exclusion diagnosis of pulmonary embolism (PE), congestive heart failure (CHF) and coronary artery disease (CAD).

Therefore, the aim of our study was to evaluate the SOB® panel and to assess its reliability in patients presenting in ED with dyspnea and/or atypical thoracic pain.

Materials and methods

Study population consisted of 97 consecutive patients admitted to ED with dyspnea and/or chest pain. Patients were

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classified in 5 major diagnoses groups by clinicians unaware of SOB® panel results, according to the final medical chart following the ED stay or the hospitalization: CHF, CAD, PE, pulmonary diseases (PD) and patients without cardiopulmonary disorders (No). CHF was diagnosed on the basis of clinical signs (pulmonary congestion, jugular venous distension, S3, peripheral oedema), chest radiography, echocardiography and/or radionuclide angiography. All CHF patients had an ejection fraction less than 40%. CAD was defined by a well documented ECG (ST-segment elevation and/or depression ≥ 1 mm); significant coronary stenosis confirmed by angiography and progressive increase in blood cTnI concentrations occurring in the 24 h after admission. PE was established by lung scintigraphy and/or spiral CT scan according to current recommendations [8]. PD consisted in chronic obstructive pulmonary disease (mean forced expiration volume/vital capacity 66% or less of the predicted value) and/or pneumonia (diagnosed from chest X-ray). Patients without overt cardiopulmonary disorders were classified as dyspnea due to anxiety, psychological stress, gastroesophageal reflux disease and allergy reaction. The protocol was approved by the local Institutional Review Board.

Blood was collected at admission in heparinized, EDTA and citrated tubes. Whole blood from one EDTA tube was directly used for SOB® testing. After centrifugation within 1 h, plasmas from other tubes were assayed in the central laboratory. Reference methods for biomarkers measurement have been chosen according to their validation in clinical management studies and were VIDAS® D-dimer ELISA test (Biomerieux), BNP immunoassay (Beckman coulter; Biosite reagents) and Access 2® (Beckman Coulter) for cTnI, CK-MB and myoglobin.

Statistical analysis

Concordance between methods was estimated by kappa coefficient. Passing and Bablok regression analysis was performed and correlation coefficients determined by Pearson's test. Reliability was assessed by Bland and Altman plot. Statistical analyses were performed with MedCalc package (MedCalc Software, Belgium). A p value <0.05 was considered as significant.

Results

The study included 97 patients. Biomakers profiles at admission are shown in Table 1

SOB® D-dimer assay correlated significantly with Vidas D-dimer assay ($r=0.89$, 95% CI: 0.84 to 0.93, $p<0.0001$) and concordance was very good ($K=0.83$). Passing and Bablok regression analysis yielded a slope 0.95 (95% confidence interval: 0.87 to 1.03) and an intercept of −128 ng/mL (95% CI: −248 to −65) (Fig. 1A). Bland–Altman analysis showed a mean difference of 419 ng/mL, surrounded by a limit of agreement extending from −2829 to 1992 ng/mL (Fig. 1C).

SOB® BNP correlated significantly with Access 2 BNP method ($r=0.88$, 95% CI: 0.82 to 0.92, $p<0.0001$) and the concordance was good ($K=0.77$). Passing and Bablok regression analysis shown in Fig. 1B reported a slope of 1.24 (95% CI: 1.15 to 1.35) and an intercept of −25.93 pg/mL (95% CI: 42.75 to −16.23). Bland–Altman analysis showed a mean difference of 29.5 pg/mL, surrounded by a limit of agreement extending from −349 to 408 pg/mL (Fig. 1D).

SOB® cTnI correlated significantly with the Access 2 cTnI assay ($r=0.76$, 95% CI: 0.66 to 0.84, $p<0.0001$) but concordance was only moderate ($K=0.51$) and important absolute differences for concentrations were observed.

SOB® CK-MB and myoglobin correlated significantly with Access 2 assays ($r=0.85$, 95% CI: 0.78 to 0.90, $p<0.0001$; and $r=0.86$, 95% CI: 0.80–0.91, $p<0.0001$, respectively). The concordance was moderate for CK-MB ($K=0.43$) and good for myoglobin ($K=0.68$). Bland–Altman analysis showed a mean difference of −1.1 ng/mL, for CK-MB and a mean difference of 52 ng/mL for myoglobin.

The sensitivity, specificity, negative predictive value, positive predictive value and likelihood ratios of the SOB® parameters for the clinical outcomes are summarized in Table 2.

Discussion

The SOB® panel, which offers simultaneous rapid bedside analysis for five biomarkers on whole blood, has been compared with traditional and validated methods. Our results showed that SOB® assays correlated with the references, but

Table 1
Patients biomarkers profiles at admission as a function of the final diagnosis

	n (male/female)	Age, yrs	Creatininemia mg/dL	SOB D-dimer ng/mL	SOB BNP pg/mL	SOB cTnI ng/mL	SOB CK-MB ng/mL	SOB Myoglobin ng/mL
No	30 (24/12)	69 (36–95)	1.0±0.1	583 (100–4330)	37 (10–156)	0.04 (0.04–0.05)	1.6 (1.0–4.7)	72 (19–398)
PD	17 (11/6)	73 (30–86)	1.0±0.1	1245 (100–5000)	82 (41–332)	0.05 (0.04–0.71)	2.0 (1.0–7.9)	116 (46–500)
PE	21 (7/14)	67 (31–87)	1.0±0.1	2862 (656–5000)	100 (9–681)	0.06 (0.04–0.56)	1.8 (1.0–18.7)	85 (32–340)
CAD	10 (6/4)	72 (51–86)	1.2±0.2	430 (100–5000)	140 (40–601)	0.25 (0.04–18.30)	4.7 (1.2–57.8)	105 (31–258)
CHF	19 (13/6)	79 (62–91)	1.3±0.9	740 (100–4430)	600 (339–1205)	0.05 (0.04–0.39)	2.0 (1.0–28.1)	100 (28–500)
Whole cohort	97 (55/42)	71 (30–95)	1.1±0.3	954 (100–5000)	105 (5–2040)	0.06 (0.04–18.30)	2.0 (1.0–57.8)	90 (19–500)

No = no cardiopulmonary disorders; PD = pulmonary disorders; PE = pulmonary embolism; CAD = coronary artery disease; CHF = congestive heart failure. Results for age are presented as mean (range) and for creatininemia as mean ± standard deviation. Results for D-dimer, BNP, cTnI, CK-MB and myoglobin are presented as geometrical means and range.