

Letter to the Editor

Concetta Prontera, Silvia Masotti, Maria Franzini, Michele Emdin, Claudio Passino, Gian Carlo Zucchelli and Aldo Clerico*

Comparison between BNP values measured in capillary blood samples with a POCT method and those measured in plasma venous samples with an automated platform

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To the Editor,

Brain natriuretic peptide (BNP) assay is recommended as the first line biomarker for diagnosis, prognosis and management of patients with heart failure (HF) [1, 2]. A recent pilot study reported that BNP assay at home, using a novel finger-stick technology, may be useful for early detection of decompensation, driving quick adjustments of treatment regimen, and decreasing repeated hospitalization of HF patients [3]. However, at the present time, there are no published data demonstrating that BNP values measured in capillary blood samples are comparable to those measured in venous plasma samples with fully automated BNP immunoassay methods. Therefore, the aim of the present study is to compare some analytical characteristics and clinical results found with the Heart Check Alere Test Strip

(Alere Technologies Limited, Stirling, Scotland) for the BNP assay in finger-stick blood samples to those observed with the automated Alere Triage BNP BCIS method, using the automated UniCel DxI 800 platform (Beckman Coulter, Inc, Fullerton, CA, USA).

The Alere Heart Check Test Strip is a point of care testing (POCT) immunoassay to be used with the Alere Heart Check Meter for the measurement of BNP using fresh capillary whole blood [4]. Following insertion of the test strip into the meter, a drop of finger-stick blood is applied to the test strip, and the meter analyzes the sample and determines the BNP concentration, which can be transmitted through a wireless connection mechanism to a target location. The immunoassay is a direct, one-step sandwich immunoassay, which uses a biotinylated anti-BNP monoclonal antibody bound to streptavidin coated magnetic solid phase particles [4]. The range of the BNP assay is 10–4955 ng/L with a limit of blank of 8.7 ng/L [4].

The POCT method reproducibility (n=10) was evaluated with two control EDTA samples, provided as calibrators by the manufacturer. The first control sample showed a mean value of 185.5±25.1 ng/L (CV 13.6%) and the second one 1722.1±291.9 ng/L (CV of 16.9%); these data are well in agreement to those reported by the manufacturer [4]. Moreover, two EDTA plasma samples of HF patients, repeatedly assayed, using two different lots of calibrators, showed a reproducibility of 7.1% (93.3±6.7 ng/L, n=21) and 16.4% (1163.3±190.7 ng/L, n=15), respectively.

The BNP values observed with this POCT method were compared with those measured with the Alere Triage BNP BCIS method using the automated UniCell DxI 800 platform [5]. We measured 88 fresh finger-stick samples of capillary whole blood and EDTA plasma samples of healthy adult subjects and patients diagnosed with systolic HF. We also measured two plasma control samples collected from patients with HF and eight control samples

*Corresponding author: Prof. Aldo Clerico, MD, Department of Laboratory Medicine, Fondazione CNR-Regione Toscana G. Monasterio, Scuola Superiore Sant'Anna, Via Moruzzi 1, 56126 Pisa, Italy, Phone: +39 0585 493569, Fax: +39 0585 493601, E-mail: clerico@ftgm.it; and Scuola Superiore Sant'Anna, Pisa, Italy
Concetta Prontera, Michele Emdin and Claudio Passino: Fondazione CNR-Regione Toscana G. Monasterio, Pisa, Italy
Silvia Masotti and Maria Franzini: Scuola Superiore Sant'Anna, Pisa, Italy
Gian Carlo Zucchelli: QualiMedLab Spin-Off dell'Istituto di Fisiologia Clinica del CNR, Pisa, Italy

distributed in the multicenter CardioOrmoCheck study with both methods (Table 1). The CardioOrmoCheck study is a proficiency testing study for the measurement of BNP and NT-proBNP, organized in Italy since 2005, as previously reported in detail [6–8]. The Passing-Bablok plot between the 98 BNP values measured with the DxI 800 platform (considered as the reference method) are reported in Figure 1A. Moreover, a very close linear regression was observed using the log-transformed BNP values measured by these two methods (POCT method = $0.135 + 0.956 \log\text{-DxI}$ platform, $R=0.956$, $n=98$). The mean (\pm SD) percent difference between the values found with the two methods $[(\text{POCT}-\text{DxI})/\text{DxI} \times 100]$ was of $14.9 \pm 40.5\%$ ($p=0.0404$ by Wilcoxon-signed rank test for bias between methods). Finally, the Bland-Altman plot suggests that there is only a trend ($p=0.0543$) for the presence of a proportional bias between these two methods (Figure 1B).

The mean ratio between the values measured with the POCT method and the DxI platform in the two EDTA plasma samples of HF patients and the eight plasma control samples were not significantly different to the mean ratio found in the remaining 88 capillary blood samples (1.134 ± 0.405 vs. 1.283 ± 0.508 , $p=0.4181$ by Mann-Whitney U-test).

In conclusion, our data suggest that it is possible to measure BNP in fresh finger-stick samples of capillary whole blood with an acceptable reproducibility, and within 10–20 min to obtain results close correlated to those measured by the automated platform in plasma blood samples collected from a vein. The measurement of BNP in fresh finger-stick samples of capillary whole blood with this POCT method is in particular indicated for the management of HF patients at home and for the BNP assay in neonates and children.

Table 1 BNP values (ng/L) measured with the POCT method in the authors' laboratory and those found by laboratory participant to the external quality assessment scheme CardioOrmoCheck using the automated DxI platform in eight control samples distributed in the 2014 cycle.

Control sample	POCT method, ng/L	Automated platform, ng/L	Ratio
41a	264.5	172.3	1.54
41b	161.5	129.6	1.25
42a	194.0	179.3	1.08
42b	183.0	138.3	1.32
43a	203.5	208.8	0.98
43b	155.0	141.6	1.09
44a	172.0	171.7	1.00
44b	179.0	185.6	0.96
Mean \pm SD	189.1 \pm 34.4	165.9 \pm 27.1	1.15 \pm 0.20

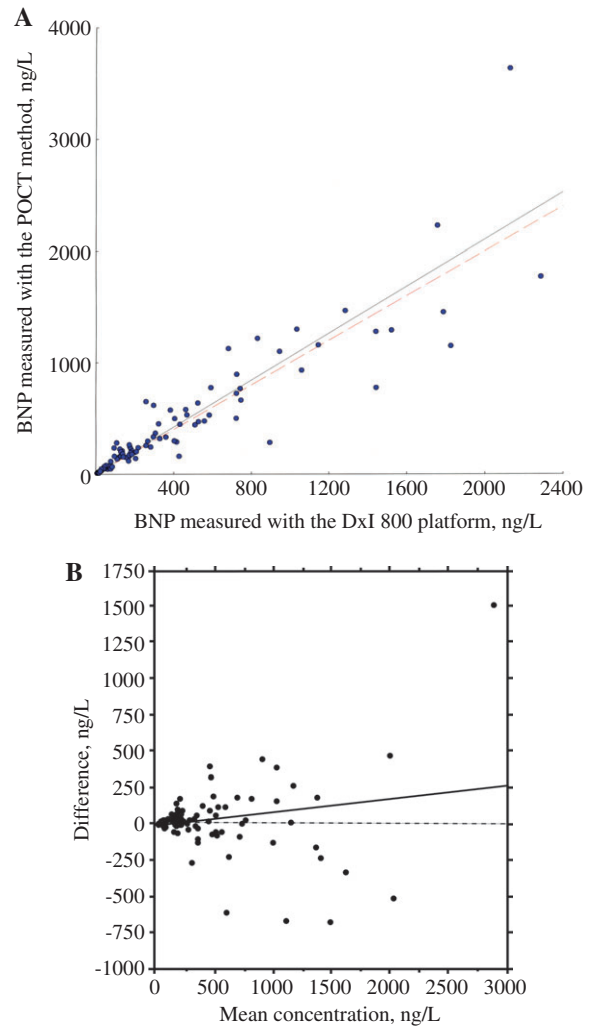


Figure 1 Passing-Bablok and Bland-Altman plots. (A) Passing-Bablok agreement test between the BNP values measured with the DxI 800 platform (X-axis, considered as the reference method) and the POCT method in 98 samples collected from healthy subjects and patients with heart failure. The slope of linear regression was 1.051 (confidence 95% range 0.961–1.154) and the intercept 3.87 ng/L (range –3.49 to 11.41 ng/L). The dotted line indicates the identity relationship ($Y=X$). (B) Bland-Altman plot reporting in the X-axis the mean of BNP values measured by the POCT method and DxI platform, while in the Y-axis the difference between the value measured by POCT method and DxI platform, respectively. The linear regression found between the values of X and Y variables is also indicated by a continuous line [$Y(\text{difference}) = -17.593 + 0.089X(\text{mean})$; $p=0.0543$].

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References

1. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al.; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;62:e147–239.
2. Emdin E, Clerico A, Clemenza F, Galvani M, Latini R, Masson S, et al. Consensus document. Recommendations for the clinical use of cardiac natriuretic peptides. *J Cardiovasc Med (Ital Heart J)* 2005;6:430–46.
3. Maisel A, Barnard D, Jaski B, Frivold G, Marais J, Azer M, et al. Primary results of the HABIT Trial (Heart failure assessment with BNP in the home). *J Am Coll Cardiol* 2013;61:1726–35.
4. Heart Check BNP Test Strip product insert. 00377 SPEC-0492 Rev. 1 2011 Alere Technologies Ltd., Stirling, Scotland.
5. Prontera C, Storti S, Emdin M, Passino C, Zyw L, Zucchelli GC, et al. Comparison of a fully automated immunoassay with a point-of-care testing method for B-type natriuretic peptide. *Clin Chem* 2005;51:1274–6.
6. Prontera C, Zaninotto M, Giovannini S, Zucchelli GC, Pilo A, Sciacovelli L, et al. Proficiency testing project for brain natriuretic peptide (BNP) and the N-terminal part of the propeptide of BNP (NT-proBNP) immunoassays: the CardioOrmoCheck study. *Clin Chem Lab Med* 2009;47:762–8.
7. Clerico A, Zaninotto M, Prontera C, Giovannini S, Ndreu R, Franzini M, et al. Study Group on Cardiovascular Risk Biomarkers of the Italian Society of Clinical Biochemistry. State of the art of BNP and NT-proBNP immunoassays: the CardioOrmoCheck study. *Clin Chim Acta* 2012;414:112–9.
8. Franzini M, Masotti S, Prontera C, Ripoli A, Passino C, Giovannini S, et al. Systematic differences between BNP immunoassays: comparison of methods using standard protocols and quality control materials. *Clin Chim Acta* 2013;424:287–91.