Evaluation of the Alere NT-proBNP Test for Point of Care Testing

Banafsheh Seyyed Khezri, Lena Carlsson, and Anders Larsson*

Department of Medical Sciences, Section of Clinical Chemistry, Uppsala University, Uppsala, Sweden

Background: The object of the study was to evaluate the Alere point of care NT-proBNP assay as a suitable alternative to the central laboratory method to provide short test turnaround times in primary care. **Method:** Blood NT-proBNP results obtained with the Alere assay ($n = 100$) were compared with serum NT-proBNP results analyzed by a Cobas 8000 analyzer (Roche Diagnostics, Mannheim, Germany). **Results:** There was a good agreement between the two NT-proBNP methods when used as a rule-out

test for heart failure (HF) and the cut-off value <300 ng/L. A total of 47 samples gave values <300 ng/L with both methods and 51 samples gave values >300 with both methods. Thus, there was an agreement for 98% of the samples. **Conclusions:** The study shows that the Alere NT-proBNP assay could be used in primary care permitting rapid NT-proBNP testing to rule out HF. *J. Clin. Lab. Anal.* 30:290–292, 2016. © 2015 Wiley Periodicals, Inc.

Key words: NT-proBNP; method evaluation; point of care test; primary care

INTRODUCTION

Heart failure (HF) is a growing public health problem. It is a major health problem for the patient and it is costly for the society and the costs continue to escalate throughout the industrialized world. The prevalence will most likely continue to increase as the prevalence increases with age. Today more than 10% of patients over 70 years of age suffer from HF. Untreated, approximately 60–70% of the patients have died within 5 years (1,2). It is thus important to diagnose HF patients early and start treatment. Many of the HF symptoms are nonspecific and could be due to a number of other conditions (3).

Patients with symptoms that could be due to HF are often encountered in primary care and NT-proBNP is often used as a rule-out test for HF (4,5). Today, the test is performed at the hospital laboratory and the samples have to be transported to the laboratory for the analysis. The test results are thus rarely available at the initial consultation. If NT-proBNP tests were available as point of care (POC) tests at the primary care center, this would most likely reduce the time to diagnosis and initiation of treatment of HF patients. The release of NT-proBNP into the circulation is a response to excessive stretching of the heart muscle cells and thus reflects decompensation of the heart. A negative NT-proBNP can be used to rule out HF while an elevated NT-proBNP value is a strong indicator of HF (6–8). The aim of this study was to evaluate the new Alere Triage POC NT-proBNP test and compare the

results of the assay with the NT-proBNP test results from the centralized laboratory.

MATERIALS AND METHODS

Study Population

The samples used were from routine requests at the Department of Clinical Chemistry and Pharmacology, Uppsala University Hospital, Uppsala. The laboratory information system was used to identify simultaneous requests for both NT-proBNP and full-blood cell counts. The K₂-EDTA tubes (BD Vacutainer tube 354664, Becton Dickinson, Franklin Lakes, NJ) from the cell counter were retrieved and used for POC testing of blood NT-proBNP at Samariterhemmet primary care center, Uppsala. The POC assay was performed with whole blood. The centralized NT-proBNP testing was performed with SST tubes

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*Correspondence to: Anders Larsson, Department of Medical Sciences, Section of Clinical Chemistry, Uppsala University, Akademiska sjukhuset, Entrance 61, 3rd Floor, SE-751 85 Uppsala, Sweden. E-mail: anders.larsson@akademiska.se

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(BD Vacutainer tube 366588). The local ethical committee (01-367) approved the collection of samples. The work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

NT-proBNP Assays

Serum NT-proBNP was measured at the Department of Clinical Chemistry, Uppsala University Hospital, by a Roche Cobas 8000, using the e602 module (Roche Diagnostics, Mannheim, Germany) according to the specifications of the manufacturer. The instrument had a total coefficient of variation (CV) of 0.9% at 107 ng/l and 1.3% at 2,060 ng/l. NT-proBNP was measured in whole blood with the Alere Triage analyzer (Alere, San Diego, CA) according to the recommendations of the manufacturer.

Statistical Analysis

The correlation between the methods was evaluated with Deming regression analysis using Method Validator (Metz, France). CV was calculated using Excel 2007 (Microsoft, Seattle, WA). Values below 20 ng/l (the lower detection limit for the Triage analyzer) were set to 20 ng/l in the Deming regression analysis and values >10,000 with the Roche method were excluded in the Deming plot.

RESULTS

CV for the Alere Triage Analyzer

A total of 15 measurements during 5 days for each of the two NT-proBNP levels were used to calculate the total CV. The total CV at 143 ng/l was 9.9% and the total CV at 2,297 ng/L was 6.0%.

Correlation Between the Two NT-proBNP Methods

The equation for the Deming correlation between the two methods was $\text{NT-proBNP}_{\text{Alere}} = 1.04 \times \text{NT-proBNP}_{\text{Roche}} + 23.3$; $r = 0.94$ (Fig. 1). The 0.95 confidence interval (CI) for the slope was 0.75–1.33 and for the intercept –194.3–240.9. The mean difference ($\text{NT-proBNP}_{\text{Alere}} - \text{NT-proBNP}_{\text{Roche}}$) between the two methods was 70.5 ng/l (0.95 CI –77.9–219). No antigen excess problems were observed with the Alere method with NT-proBNP results up to 70,000 ng/l according to the Roche method.

Agreement Between the two NT-proBNP Methods as Rule-Out Test for HF (Cut-Off Value 300 ng/l)

A total of 47 samples gave values <300 ng/l with both methods and 51 samples gave values >300 with both methods (Table 1). There was, thus, an agreement for 98%

Fig. 1. Deming regression plot presenting individual patient results measured with Roche (x-axis) and (y-axis) NT-proBNP assays.

TABLE 1. Distribution of Test Results <300 and >300 ng/l With the Two NT-proBNP Methods ($n = 100$)

	Alere <300 ng/l	Alere >300 ng/l
Roche <300 ng/l	47	1
Roche >300 ng/l	1	51

of the samples. Two samples showed divergent results: sample 1: 36 (Roche) and 349 (Alere), and sample 2: 325 (Roche) and 257 (Alere).

DISCUSSION

The echocardiograph is considered as the best test to diagnose HF (9, 10). Echocardiographs are however often negative due to the nonspecific signs of HF, which causes many referrals of patients without HF. The use of NT-proBNP as initial rule-out test for HF reduces the number of negative echocardiographs and thus reduces costs (8, 11).

Many of the patients seeking primary care are elderly and have symptoms that could be due to HF. Our primary care serves a population of approximately 300,000 inhabitants and we have approximately 7,000 NT-proBNP test requests per year from primary care. In comparison with a POC test, the centralized laboratory NT-proBNP test is associated with longer test turnaround times (TAT). The actual assay times are similar, but the transportation of the samples to the hospital is the main reason for the

longer test TAT. It is thus not possible to get a test result from the central laboratory during the initial consultation. The doctor thus has to contact the patient about the test result after the consultation, usually by phone. These calls are time consuming and thus costly. Consultations by phone is most likely less effective than regular consultations especially considering that HF is mainly a disease of elderly and many of them have hearing disorders. A POC NT-proBNP assay could thus be useful in primary care. A POC test could provide test results during the initial consultation and would thus reduce the time to diagnosis and initiation of treatment.

We have evaluated the performance of the Alere NT-proBNP assay on the Triage analyzer. The method had a CV <10% at the two levels tested and showed a good agreement with the Roche method used at the central laboratory. Further, the analyzer has advantages in being relatively small and easy to handle for the operator. The effect of hematocrit was not evaluated in this study. It cannot be ruled out that very high or low hematocrit could have an impact on the results and we would suggest that in such cases the test should be performed on plasma samples. In conclusion, the POC Alere NT-proBNP assay is a suitable alternative to the central laboratory method and would provide test results with short TAT.

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