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Utility of Point-of-Care Diagnosis of Chronic Heart Failure Using an Express Test for Semi-Quantitative Determination of NT-proBNP Levels

Aim	To evaluate the accuracy of a rapid test for semi-quantitative determination of NT-proBNP levels in the diagnosis of CHF in comparison with quantitative assessment; to study the strength of the association of the results of this NT-proBNP test with indicators of the CHF severity.
Material and methods	The concentration of NT-proBNP was determined in 44 patients at bedside both semi-quantitatively using an express test (BioTest, Novosibirsk) and quantitatively in a laboratory. In 11 patients, the severity of CHF was assessed with the CHF Clinical Status Scale (CSS). Echocardiography was performed in all patients.
Results	The sensitivity of the quantitative and semi-quantitative tests coincided and was 95%. The specificity of the quantitative test was 100% in our study, whereas the semi-quantitative test showed a specificity of 92%. The negative predictive value of either test was 96%. The diagnostic accuracy was 98% and 93%, respectively. In patients with significantly high NT-proBNP concentrations, the semi-quantitative test demonstrated a reduced ability to verify values above 1800 pg/ml; in patients with threshold concentrations, the semi-quantitative test showed an increased subthreshold sensitivity. Increases in the NT-proBNP concentration correlated with the severity of CHF according to the stage of the disease.
Conclusion	Due to the sufficiently high sensitivity, specificity, ease of use, and speed of obtaining results, the rapid test for semi-quantitative measuring NT-proBNP is promising for outpatient screening bedside diagnosis of CHF and in the emergency room to confirm or exclude CHF. When determining the dynamics of NT-proBNP during the treatment of CHF, the use of the semi-quantitative rapid test with visual assessment of the results may produce an error compared to the quantitative assessment, which will probably not allow tracking the effect of therapy or predicting exacerbation of the disease.

Keywords	Chronic heart failure; NT-proBNP; rapid test; diagnosis
For citations	Iosifov A.V., Shtegman O.A. Utility of Point-of-Care Diagnosis of Chronic Heart Failure Using an Express Test for Semi-Quantitative Determination of NT-proBNP Levels. Kardiologiia. 2024;64(7):27–30. [Russian: Иосифов А.В., Штегман О.А. Применимость прикроватной диагностики хронической сердечной недостаточности с помощью экспресс-теста для полуколичественного определения уровня NT-proBNP. Кардиология. 2024;64(7):27–30].

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Chronic heart failure (CHF) is one of the leading causes of death worldwide. According to the EPOCH-CHF study, the prevalence of CHF in Russia has increased by one-third in 20 years to 8.2% [1]. Nearly 30% of CHF patients die within 2 years of a decompensation episode, and one in ten patients die even when followed by a CHF expert and given the best possible therapy [2]. In recent years, there have been notable advancements in the management of CHF. Timely and appropriate therapy has been demonstrated to not only restore left ventricular ejection fraction, but also to improve the prognosis of patients [3, 4]. In view of the above, the significance of early identification of CHF, the administration of the best possible treatment, and the monitoring of its efficacy become paramount. The gold standard for diagnosing CHF syndrome is the measurement of the levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) [5]. Concurrently, there is a lack of express diagnostic tests for NT-proBNP levels in clinical settings. These tests must undergo miniaturization and validation [6].

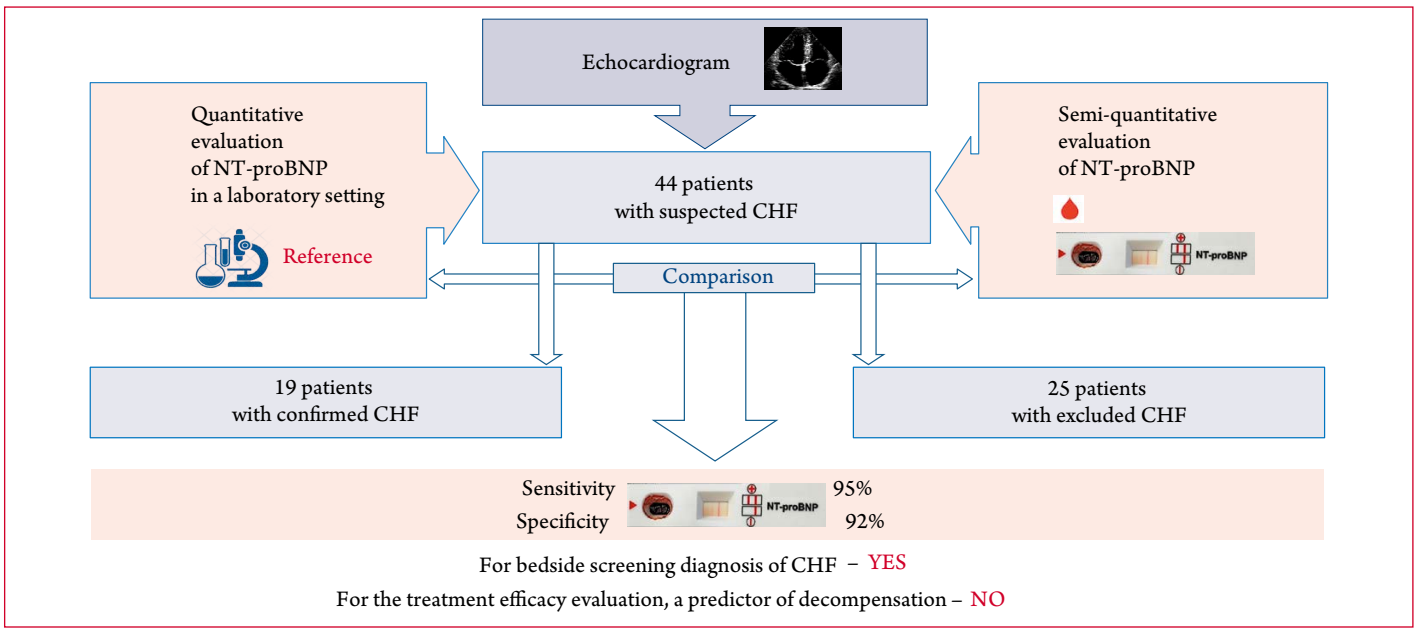
Objective

The objective of the study was to evaluate the accuracy of the express test for semi-quantitative determination of NT-proBNP level in the diagnosis of CHF in comparison with quantitative assessment, and to study the strength of the correlation between the results of NT-proBNP determination using this test and the indicators of CHF severity.

Material and Methods

ИThe study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki. All patients provided written informed consent prior to

Central illustration. Utility of Point-of-Care Diagnosis of Chronic Heart Failure Using an Express Test for Semi-Quantitative Determination of NT-proBNP Levels



participation in the study. Due to the limited number of patients included in the study, it was classified as a pilot study. A semi-quantitative evaluation of NT-proBNP levels was conducted using an express test (NPO BioTest, Novosibirsk) and a quantitative evaluation in a laboratory setting using the COBAS 601 electrochemiluminescent module in 44 patients. The semi-quantitative test enabled the visual distinction, in comparison with the attached scale, of a negative result, indicated by the absence of the second strip after 30 minutes, and a weakly positive result (ranging from 125 to 450 pg/mL), a positive result (between 450 and 900 pg/mL), a strongly positive result (between 900 and 1800 pg/mL), and a maximum result (above 1800 pg/mL). The results of the semi-quantitative analysis were recorded in scores ranging from 0 to 4. Of the total number of patients included in the study cohort, 19 were hospitalized at the Krasnoyarsk Interdistrict Clinical Emergency Hospital, named after N. S. Karpovich, due to acute decompensated heart failure, classified as a minimum of NYHA class III. They were assigned to Group 1. The severity of CHF was evaluated using the SHOCS score. The remaining 25 individuals who did not exhibit any signs of CHF were included in Group 2. To ascertain the presence or absence of CHF, all patients underwent echocardiography, during which the following parameters were assessed: left ventricular ejection fraction (LVEF), respiratory excursion of the inferior vena cava, and pulmonary artery systolic pressure (PASP). In Group 1, the median LVEF was 34 (29–43) %, with median PASP of 55 (52-70) mm Hg. Insufficient respiratory excursion of the inferior vena cava was observed in 9 patients (62%) of Group 1. Two patients in this group exhibited preserved systolic function, with a PASP of 45 mm Hg and 70 mm Hg, respectively. All patients in Group 2 exhibited LVEF more than 50%, inferior vena cava collapse greater than 50% during inspiration, and a PASP less than 30 mm Hg. The results of NT-proBNP level determination were compared with the presence of cardiac diseases, sex and age, and body mass index (BMI).

The statistical analysis of the data was conducted using the licensed software suite STATISTICA 12.0 (STATSOFT, USA). The absolute values are presented as the medians and the 25% and 75% percentiles (Me (25%; 75%)), and the differences between the indices were evaluated using the Mann-Whitney test for independent samples. The Pearson test of agreement was employed for the purpose of comparing relative values. A p-value of less than 0.05 was considered to be statistically significant. The sensitivity, specificity, positive predictive value, and negative predictive value of the semi-quantitative test were calculated.

Results and Discussion

A comparison was conducted between the sex and age, and somatometric indices of the patients in the two groups. The results of the NT-proBNP level measurements were compared (Table 1).

The mean age of patients in Group 1 (patients with CHF) was significantly higher, and there were more male patients. No significant differences in BMI were observed.

The sensitivity of the quantitative and semi-quantitative tests was identical, at 95% (18 cases of CHF out of 19 were confirmed). The specificity of the quantitative test was 100% in our study, while the semi-quantitative test demonstrated a specificity of 92% due to the presence of two false positive results (Figure 1).

ISSN 0022-9040. Kardiologiia. 2024;64(7). DOI: 10.18087/cardio.2024.7.n2647

Table 1. Patient characteristics based on the presence of CHF

Parameter	Patients with CHF (n = 19)	Patients without CHF (n = 25)	P
Age, years	66 (59; 77)	44 (35; 52)	< 0.001
Male patients, %	58	36	> 0.05
Height, m	1.7 (1.65; 1.76)	1.7 (1.65; 1.76)	> 0.05
Weight, kg	80 (70; 90)	77 (65; 80)	> 0.05
BMI, kg/m^2	27.7 (23.9; 31.1)	25.8 (22.1; 27.9)	> 0.05
Pre-existing cardiovascular disease, %	100	12	< 0.001
Quantitative level of	3330 (384; 10800)	63 (22; 81)	<0,001
NT-proBNP, pg/mL	3330 (384; 10800)	63 (22; 81)	< 0.001
Semi-quantitative level of			
NT-proBNP, score	3 (2; 3)	0	< 0.001

BMI, body mass index; CHF, chronic heart failure; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Figure 1. Frequency of detection of NT-proBNP elevations greater than 125 pg/mL by quantitative and semi-quantitative (express assay) evaluation of NT-proBNP levels

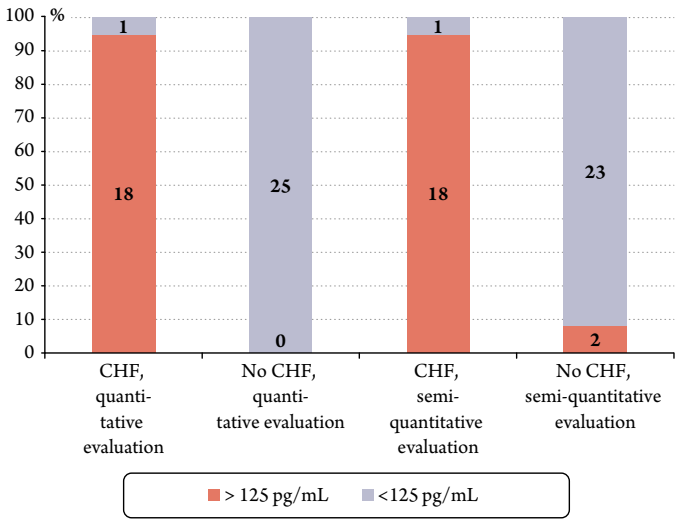


Table 2. Correlation coefficients of NT-proBNP with age and CHF severity

Parameter	Quantitative evaluation of NT-proBNP	P	Semi-quantitative evaluation of NT-proBNP	P
Age	0.69	< 0.001	0.77	< 0.001
BMI	0.47	0.0013	0.45	0.0022
CHF stage	0.68	< 0.001	0.60	< 0.001
SHOCS score	0.28	> 0.05	0.31	> 0.05

BMI, body mass index; CHF, chronic heart failure; SHOCS, Symptomatic Hospital and Outpatient Clinical Score.

The positive predictive value of the quantitative test was 100%, and the semi-quantitative test demonstrated a positive predictive value of 90%. The negative predictive value for both measurement options was 96%. The diagnostic accuracy was 98% and 93%, respectively.

In 9 instances, the range of NT-proBNP elevation as determined by the semi-quantitative test was found to be lower than that determined by quantitative analysis in the laboratory. In all instances, the quantified NT-proBNP levels exceeded 3000 pg/mL. The two false-positive results of the semi-quantitative test indicated a range of 125–450 pg/mL and corresponded to 98 and 100 pg/mL, respectively. These findings indicate an elevated subthreshold sensitivity of the semi-quantitative test, accompanied by an underestimated capacity to verify values exceeding 1800 pg/mL.

The correlation between NT-proBNP levels and the presence and severity of CHF by stage and the SHOCS score, as well as with sex and BMI, was evaluated (Table 2). Among patients with CHF, BMI was observed to be slightly higher, which may explain the significant positive correlation between the levels of NT-proBNP and this index. A large-scale population-based study demonstrated a negative correlation between BMI and NT-proBNP levels, with this correlation becoming more pronounced with increasing BMI [7]. In our study, however, there were no patients with severe obesity (maximum BMI was 33 kg/m^2). Patients with edema exhibited a higher BMI, which likely accounts for the discrepancy between our data and the findings of large-scale population-based studies. Additionally, it is essential to consider the observed trend of decreasing body weight with the progression of CHF in the context of severe multiorgan metabolic disorders.

The severity of CHF was assessed by SHOCS score only in 11 patients, which does not provide sufficient evidence to conclude with certainty that there is no correlation between this index and the levels of NT-proBNP. The stage of CHF was evaluated in all patients. Consequently, a correlation of moderate strength was identified. It seems probable that the strength of this correlation was affected by the treatment received by the patients with CHF.

A meta-analysis of studies examining the bedside examination of natriuretic peptides [8] demonstrated a beneficial impact of this diagnostic technology on cardiovascular events in ambulatory patients. This is attributed to the prompt treatment of CHF and the effective correction of the treatment. Bedside testing technologies exhibit a slight reduction in accuracy when compared to traditional laboratory diagnostic methods. However, they offer a notable advantage in terms of rapid result acquisition [9]. In recent years, bedside testing technologies have represented a significant advancement in the management of patients with CHF [6]. Practicing physicians worldwide require prompt and cost-effective diagnostic

solutions to ascertain the presence of life-threatening cardiovascular pathology in patients [10].

The advent of an inexpensive, domestically manufactured express test that does not necessitate the use of specialized devices is a highly encouraging development with significant potential for integration into routine clinical practice. However, this study has a number of limitations that should be taken into account. The study did not include patients with initial manifestations of heart failure. Furthermore, the applicability of the test by age, BMI, and concomitant diseases is not yet clear, and further research is required in this area.

Conclusions

The semi-quantitative express test for NT-proBNP demonstrated a sensitivity and specificity of 95% and 92%, respectively. The positive predictive value and negative predictive value of the semi-quantitative express test for NT-proBNP were 90% and 96%, respectively. The diagnostic accuracy was 93%. In the future, express tests for semi-quantitative determination of NT-proBNP levels may be employed for the purpose of bedside screening diagnosis of CHF in patients during outpatient visits and during admission to hospitals in order to confirm or exclude the presence of CHF.

In order to ascertain the alterations in NT-proBNP levels throughout the course of CHF therapy, the utilization of the semi-quantitative express test with a visual assessment of the results may prove to be inaccurate in comparison to a quantitative assessment, which will likely prevent from monitoring the therapeutic effect or predicting an exacerbation of the disease.

Acknowledgements

Semi-quantitative rapid tests for assessing the concentration of NT-proBNP were provided free of charge by NPO BioTest (Novosibirsk).

No conflict of interest is reported.

The article was received on 30/01/2024

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ISSN 0022-9040. Kardiologiia. 2024;64(7). DOI: 10.18087/cardio.2024.7.n2647