Vinogradova N. G.[1], Berestovskaya V. S.[2], Blankova Z. N.[3], Vavilova T. V.[2], Gomyranova N. V.[3], Masenko V. P.[3], Mareev V. Yu.[4], Skvortsov A. A.[3], Sorokina N. A.[5], Tereshchenko S. N.[3]

[1] Lobachevsky National Research State University of Nizhny Novgorod, Nizhny Novgorod, Russia

[2] Almazov National Medical Research Center, St. Petersburg, Russia

[3] Chazov National Medical Research Center of Cardiology, Moscow, Russia

[4] Lomonosov Medical Research and Educational Center of the Lomonosov Moscow State University, Moscow, Russia

[5] Regional Clinical Hospital #1, Tyumen, Russia

Laboratory Aspects of Using the Results of NT-proBNP Concentration Immunochemical Determination in the Management of Patients With Heart Failure: Support for Clinical Decision-Making

The burden of heart failure (HF) has been increasing worldwide in recent decades. Early diagnosis of HF based on the outpatient measurement of natriuretic peptide (NP) concentration will allow timely initiation of the treatment and reducing the incidence of adverse outcomes in HF. Unfortunately, the frequency of NP testing remains low worldwide. At the online expert meeting held on March 15, 2024, the features of the N-terminal pro-brain natriuretic peptide (NT-proBNP) test (Elecsys proBNP by Roche) were discussed along with the interpretation of test results and presentation of results in laboratory reports. The experts addressed the features of the Elecsys proBNP test in patients with suspected HF in various clinical scenarios (chronic and acute HF). The limits of clinical decision for the NT-proBNP test were established depending on the clinical scenario. Changes in the Elecsys proBNP test results depending on the comorbidities were addressed. The experts suggested ways to optimize the format of the Elecsys proBNP test result reports in the Russian Federation, which will accelerate the implementation of the test in clinical practice and optimize the management of HF patients.

Keywords Natriuretic peptide; NT-proBNP; Elecsys proBNP test; chronic heart failure; hospitalization; decompensated chronic heart failure

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Corresponding author Vinogradova N. G. E-mail: vinogradovang@yandex.ru

Introduction

The prevalence of heart failure (HF) has been rising globally over the past few decades, largely due to an aging population and the improved survival of patients with cardiovascular and cardiometabolic diseases and conditions that are known to cause chronic heart failure (chronic HF) [1–4]. Despite the implementation of efficient disease management approaches, the prognosis for patients with HF remains poor [5, 6].

Nevertheless, in recent years, drugs and approaches that are effective in preventing HF and hospitalizations for HF have been developed and introduced into clinical practice [7, 8]. In light of these circumstances, the importance of early detection of HF cannot be overstated. Timely treatment is crucial to maximize the active period of quality life for patients and to prevent hospitalizations and other complications associated with HF.

The early detection of chronic HF necessitates a comprehensive approach that incorporates both clinical examinations and laboratory tests, as detailed in the clinical guidelines established by the world's leading cardiology communities [3, 9, 10].

The measurement of natriuretic peptide (NP) is of significant importance in the diagnosis of HF, as this test is essential for the exclusion or confirmation of the condition. Furthermore, the N-terminal pro-brain natriuretic peptide (NT-proBNP) is the primary laboratory diagnostic test for the assessment of HF in a range of clinical settings and scenarios. The utilization of NT-proBNP has been designated with the highest class of recommendation (IA) for the diagnosis and prognosis of chronic HF and acute decompensated heart failure (ADHF). The incorporation of NP determination into the standards of medical care and the accessibility of this

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Central illustration. Laboratory aspects of using NT-proBNP immunoassay results in the management of patients with chronic heart failure: the support of clinical decision making

Expert consensus on generation of the standardized report of the results of the NT-proBNP test, conducted using the Elecsys proBNP II assay (Roche) The report should include the following elements:
A patient-specific reference value for NT-proBNP, determined on the basis of sex and age
NT-proBNP < 125 pg/mg is the threshold for ruling out chronic HF.
NT-proBNP < 300 pg/mg is the threshold for ruling out acute HF.
NT-proBNP < 375 pg/mg is the threshold for ruling out chronic HF in the presence of atrial fibrillation or atrial flutter.
A note indicating that the reference values are provided with consideration of age and sex, and that the interpretation of the results should be conducted by a qualified physician in conjunction with the patient's medical history, clinical data, and the results of other diagnostic tests.

Anticipated results of the NT-proBNP assay according to sex and age[2]

Age, years	Male, NT-proBNP, pg/mL				Female, NT-proBNP, pg/mL			
	Median	95 th percentile	97,5 th percentile	99 th percentile	Median	95 th percentile	97,5 th percentile	99 th percentile
35–44	18.9	90.8	115	137	59.9	202	237	311
45–54	23.5	121	173	273	63.8	226	284	395
55–64	47.4	262	386	920	81.8	284	352	417
65–74	89.3	486	879	2346	133	470	623	784
All	35.6	238	344	703	78.6	304	389	509

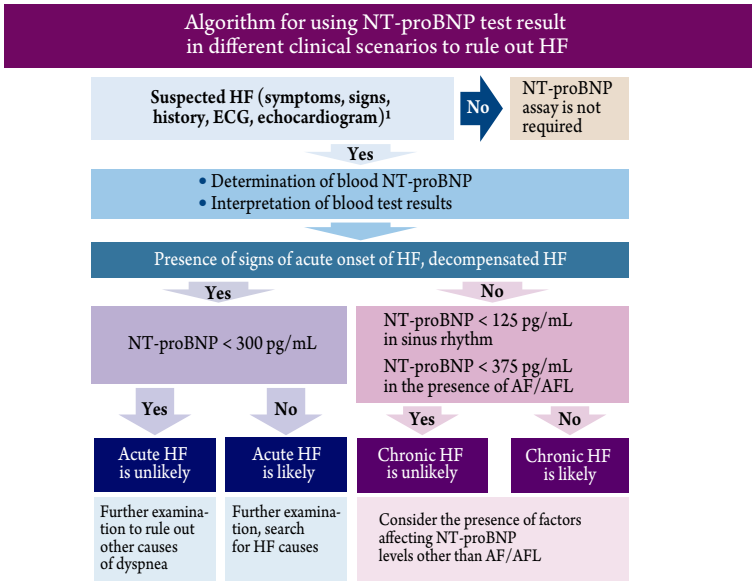
NT-proBNP thresholds confirming the diagnosis of ADHF in patients with severe dyspnea[2]

Age, years	Optimal cut-off value, pg/mL	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
<50 years	450	97	93	76	99	94
50–75 years	900	90	82	83	88	85
>75 years	1800	85	73	92	55	83

Note: NT-proBNP, N-terminal pro-brain natriuretic peptide; ADHF, acute decompensated heart failure; PPV, positive predictive value; NPV, negative predictive value; AFL, atrial flutter; AF, atrial fibrillation; HF heart failure; CUT-OFF V, CUT-OFF -VALUE CHF, chronic heart failure.

[1] – In accordance with the most recent clinical guidelines set forth by the Ministry of Health of the Russian Federation (2020)

[2] – In accordance with the instructions for the Elecsys proBNP II assay (Roche)



test permit differential diagnosis and monitoring of HF therapy with its use [3, 4, 9].

The most challenging scenarios for interpreting the results of NT-proBNP determination are those of diagnosing de novo HF in the outpatient setting. The utilization of diverse forms of issuing the NT-proBNP test results and result reporting and the extensive range of clinical decision limits for outpatients may potentially lead clinicians to question the value of the test. The absence of a unified methodology for the presentation of information within test result reports, which is essential for the accurate interpretation of NT-proBNP values, may diminish the clinical efficacy of the test, facilitate the occurrence of diagnostic errors and the associated adverse events [11, 12].

In this regard, it is imperative to establish a professional standard for the inclusion of information in NT-proBNP test reports in laboratories across the Russian Federation (RF).

On March 15, 2024, the expert committee session was held in order to evaluate the current practices of issuing NT-proBNP test results and report formats in laboratories across the Russian Federation and establishing guidelines for a unified format of NT-proBNP test result reporting (Elecsys proBNP) in medical laboratories performing laboratory tests for outpatient clinics. The objective was to enhance clinical decision-making support and optimize the management of patients with chronic HF in the Russian Federation.

The expert committee met to deliberate upon the following matters:

- Diagnostic characteristics and peculiarities of NT-proBNP test application in real-world clinical practice.
- Analysis of the presentation of NT-proBNP test results (in terms of report formats) in the Russian Federation and in international practice and determination of their compliance with clinical guidelines and consensuses on the application of NT-proBNP tests period
- Support for clinical decision making based on NT-proBNP results in the diagnosis of HF. Rationale for the test application in the context of different clinical scenarios.

- Aspects of the use of immunochemical determinations of NT-proBNP levels in outpatient management of patients with chronic HF and chronic HF patients with comorbidities.

Diagnostic characteristics and peculiarities of NT-proBNP test application in real-world clinical practice

The suggestion that natriuretic peptides should be used to exclude heart failure was first included in the European Society of Cardiology (ESC) guidelines in 1995 [13]. In 2021, the world's leading experts in the field proposed a universal definition of HF. This definition emphasizes the importance of measuring NPs to exclude HF and highlights the possibility of using NT-proBNP for earlier and more accurate diagnosis of HF, which could potentially improve patient outcomes [4, 14].

The current Russian clinical guidelines recommend the use of the NP test for the diagnosis of HF. Furthermore, the NP test is a mandatory diagnostic tool for HF with left ventricular ejection fraction (LVEF) greater than 40% (class of recommendations A, level of evidence 2) [9].

It is important to note that the NT-proBNP test is included in the standard of medical care for patients with HF at both outpatient and inpatient stages of medical care in the Russian Federation [15]. Follow-up monitoring of patients with HF in the Russian Federation necessitates the outpatient administration of the NP test at least once every two years [16].

Notwithstanding the NP test's status as a priority diagnostic instrument in clinical guidelines and standards, the utilization and interpretation of NT-proBNP levels in real-world clinical practice remain suboptimal. As a result, the likelihood of an early diagnosis of chronic HF and the subsequent administration of recommended treatment is reduced [14]. In both rural and urban areas, including in high-income countries, the underutilization of the test in routine outpatient and inpatient practice persists for a number of reasons contingent on the specific health system in a particular region or country [17, 18]. Furthermore, the underutilization of the NP test may be attributed to the fact that the clinical decision threshold for NT-proBNP is subject to variation based on the patient's disease profile and clinical context, which can render the test challenging to interpret [14]. In order to utilize the NP test and arrive at an accurate diagnosis, it is essential to interpret the result correctly, taking into account all the characteristics of the laboratory test [19].

In 2003, the Food and Drug Administration (FDA) approved the Elecsys proBNP (Roche) test for risk stratification in patients with acute coronary syndrome (ACS) or congestive (HF). Additionally, the test has been approved as an adjunctive tool for assessing the increased risk of cardiovascular events and mortality in patients at risk of HF with stable coronary heart disease. In the FDA notification for the indicated method (Elecsys proBNP test), the expected values/reference range/clinical decision threshold are stated as follows: < 125 pg/mL for patients younger than 75 years of age and < 450 pg/mL for patients 75 years of age and older [20].

A multitude of subsequent studies have broadened the range of applications for the Elecsys proBNP test, encompassing the following conditions: diagnosis in suspected chronic HF, assessment of chronic HF severity, monitoring of therapy in patients with LV dysfunction, risk stratification in patients with ACS and chronic HF, and assessment of cardiovascular risk in patients with the diagnosis of type 2 diabetes mellitus (DM) and the optimization of cardioprotective therapy in patients with type 2 DM and no history of established cardiovascular disease (CVD), as well as the identification of individuals at high risk of developing atrial fibrillation (AF) among the elderly [19].

In addition to the features of the Elecsys proBNP test presented in the manual, numerous studies have been conducted in recent years to determine the role of the test in the diagnosis of acute heart failure (AHF) [21]. At the same time, separate grades of test results were created for the emergency setting, which was also reflected in the Russian and international clinical guidelines [3, 9, 19].

Thus, when using the NT-proBNP test in real-world clinical practice, it is necessary to take into account the clinical characteristics of the patient (sex, age, comorbidities) and the conditions of medical care in which the test is performed (outpatient or inpatient setting, including emergency care) in order to maximize the effectiveness of the test results.

Presentation of NT-proBNP test results (in terms of report formats) in the Russian Federation and in international practice

The value of laboratory services in informing clinical decision-making is contingent upon the quality of the laboratory itself and the subsequent utilization of test results. Diagnostic errors may result from an inaccurate perception and underestimation of the characteristics of the laboratory test, an erroneous evaluation of the test result without sufficient consideration of diagnostic probabilities and uncertainties, and the specific characteristics of the information presented and the format in which the laboratory test result is issued [11, 22]. It is noteworthy that the laboratory test

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may be conducted when a patient presents for testing independently, without a referral. [23]. However, patients are not always adequately informed to comprehend or identify a clinical condition and may thus be directed by comments in the laboratory report [23].

The section of the laboratory report designated as a «reference range» is of significant importance for an accurate interpretation of the NP test result. A comparison of patient-specific test results with the established reference range can assist the physician in identifying potential conditions or diseases. In interpreting the result of the test, it is essential to consider the following:

- There are no universally accepted reference ranges for laboratory tests due to the inherent differences in equipment and methodology employed by different manufacturers. It is therefore essential that physicians are aware of the methodologies employed in a given laboratory for the determination of NT-proBNP. In the event of any queries pertaining to methodology, it is recommended that they be directed to reliable sources of information, such as those provided on the International Federation of Clinical Chemistry and Laboratory Medicine website [24].
- The threshold approach to clinical decision-making is predicated on the discriminant quantification of a test for the purpose of medical decision-making. A clinical decision threshold (CDT) is an examination finding that indicates an elevated risk of adverse clinical outcomes or the presence of a specific condition. CDT or rule-in/rule-out criteria for specific clinical situations are established based on the results of clinical trials and are included in clinical guidelines. These guidelines typically include the indication of specific classes of recommendations and levels of evidence for different clinical scenarios [25]. In a laboratory result report, the rule-in/rule-out criteria may be provided in the reference range section and/or included as a comment, with no additional information provided regarding the clinical decision threshold. It is important to note that CDTs are not equivalent to reference ranges.

There is currently no regulation governing the presentation of NT-proBNP test results in the Russian Federation. Standardization of the format of laboratory test reports, especially at the outpatient stage of medical care, is a key element of continuity of clinical information in different medical organizations in the Russian Federation.

The utilization of diverse forms of issuing the NT-proBNP test results and result reporting and the extensive range of clinical decision limits for outpatients may potentially lead clinicians to question the value of the test, which in turn influences underutilization of the test [11, 12].

Familiarization with open foreign and Russian electronic resources allowed us to identify the following formats of information presentation for interpretation of NT-proBNP test results (as HF symptoms gradually progress), performed using Roche electrochemiluminescent technology:

The «Reference ranges» section includes exclusion criteria of < 125 pg/mL for patients younger than 75 years of age and < 450 pg/mL for patients 75 years of age and older [26, 27];

The «Reference ranges» section includes values obtained in the population depending on sex and age, with concentrations < 125 pg/mL to exclude HF [28, 29].

It should be kept in mind that the «Clinical trial data. Expected values» section of the Elecsys proBNP II test manual (Roche) includes expected values/reference ranges, i.e., values obtained in the population depending on sex and age in individuals without documented CVD. Age-related increases in NT-proBNP are observed in clinically healthy individuals, reflecting the rising prevalence of risk factors [19]. It is important to note that these values do not reflect the rule-in and rule-out criteria for different clinical scenarios related to HF or other diseases, thus, they cannot be considered as CDTs.

The following expected values are reported for the Elecsys proBNP test based on NT-proBNP levels in 4,266 subjects of the Gutenberg Health Study aged 35 to 74 years. The descriptive statistics for NT-proBNP levels (pg/mL) in the reference group are presented in Table 1 [19].

Support for clinical decision making based on NT-proBNP results in the diagnosis of HF

As the NT-proBNP test is applicable in a variety of clinical scenarios, the literature reports rule-in/rule-out criteria or CDTs, based on multiple studies, for each clinical scenario separately. For instance, the NT-proBNP values < 125 pg/mL exclude, with a high level of evidence, the presence of cardiac dysfunction in patients presenting with symptoms suggestive of CHRONIC HF and a gradual progression of the disease. This threshold has been demonstrated to be a reliable diagnostic tool on numerous occasions [14, 30], applicable to a diverse range of age groups [31] and patients with risk factors [32]. Furthermore, studies have demonstrated that when excluding CHRONIC HF, the application of an age-specific threshold for NT-proBNP (125 pg/mL for patients younger than 75 years and 450 pg/mL for patients aged 75 years or older) does not enhance the

Table 1. Anticipated results of the NT-proBNP assay

Age, years	Male, NT-proBNP, pg/mL				Female, NT-proBNP, pg/mL			
	median	95th percentile	97.5th percentile	99th percentile	median	95th percentile	97.5th percentile	99th percentile
35–44	18.9	90.8	115	137	59.9	202	237	311
45–54	23.5	121	173	273	63.8	226	284	395
55–64	47.4	262	386	920	81.8	284	352	417
65–74	89.3	486	879	2346	133	470	623	784
Total	35.6	238	344	703	78.6	304	389	509

NT-proBNP, N-terminal pro-brain natriuretic peptide.

efficacy of HF diagnosis [33]. Conversely, a threshold of 400 pg/mL for all patients markedly diminishes the probability of an accurate diagnosis [34]. Given the high sensitivity of the test for the exclusion of chronic HF, the negative prognostic values of NT-proBNP reach 95–100%. Concomitantly, NT-proBNP values ≥ 125 pg/mL are linked with an elevated risk of cardiac complications and may serve as an indicator of cardiac dysfunction. In the context of the Elecsys proBNP II test (Roche), it is important to consider that the positive predictive value of NT-proBNP for the confirmation of chronic HF ranges from 30% to 60%. This figure is dependent on the specific characteristics of the study cohort. The results of the test may vary depending on a number of factors, including sex, age, race, the presence or absence of chronic HF, AF, obesity, chronic kidney disease (CKD), and potentially other comorbidities [35–39].

The clinical value of NT-proBNP levels ≥ 125 pg/mL in the early diagnosis of chronic HF has been demonstrated on numerous occasions. Furthermore, these levels can predict the presence of HF or conditions associated with a high risk of developing chronic HF [32]. It is important to note that this CDT aligns with the gradual development of HF. In European and Russian guidelines, the thresholds for exclusion of CHRONIC HF, importantly, in progressive disease are < 125 pg/mL for NT-proBNP and < 35 pg/mL for B-type natriuretic peptide (BNP) [3, 9].

In the clinical scenario of HF in acute onset of the disease, the use of appropriate CDT is essential for the diagnosis of AHF. The reliability of using a rule-out criterion of <300 pg/mL to exclude the diagnosis of ADHF has been demonstrated in studies that have included the determination of NT-proBNP in patients with an acute onset of dyspnea. The negative predictive value of this criterion is 97–98% [21, 40–43].

It is therefore recommended that CDT be used in patients with suspected ADHF at NT-proBNP levels below 300 pg/mL in order to reliably rule out the diagnosis ADHF, as set forth in the current European and Russian clinical guidelines [3, 9].

Additional individual cases of CDT are presented in the results of the ICON-RELOADED study (N-Terminal Pro-B-Type Natriuretic Peptide in the Emergency Department) for patients presenting with acute dyspnea. The study identified definitive NT-proBNP thresholds for the diagnosis of ADHF in patients presenting with acute dyspnea. These thresholds were categorized according to age groups and are presented in Table 2 [21]. The data in question are included in the Elecsys proBNP test manual and in the current clinical guidelines for HF, where they are presented in the section on ADHF diagnosis [9, 19].

The CDTs presented above for the NT-proBNP test in the diagnosis of ADHF are provided in the European Society of Cardiology (ESC) 2023 position paper on the diagnosis of AHF in the emergency department. The document explicitly indicates that the values vary depending on the patient profile and clinical context. Therefore, they should be interpreted with caution, in order to ensure that an accurate diagnosis can be made.

Table 2. NT-proBNP thresholds confirming the diagnosis of ADHF in patients with severe dyspnea

Age	Optimal cut-off value, pg/mL	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
< 50 years	450	97	93	76	99	94
50–75 years	900	90	82	83	88	85
> 75 years	1800	85	73	92	55	83

NT-proBNP, N-terminal pro-brain natriuretic peptide; ADHF, acute decompensated heart failure; PPV, positive predictive value; NPV, negative predictive value.

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The paper, however, indicates that the aforementioned CDTs for ADHF do not necessitate adjustments based on sex, body mass index (BMI), renal function, LVEF, or the presence of AF. Furthermore, the ESC experts provide CDT for the NT-proBNP test for ADHF > 5000 pg/mL, irrespective of age or other parameters. They propose that this threshold significantly increases the likelihood of ADHF [14].

Aspects of the use of immunochemical determinations of NT-proBNP levels in outpatient management of patients with CHRONIC HF and comorbidities

In addition to the aforementioned reference levels and CDTs for diagnosing HF, a substantial amount of supplementary information has been gathered from papers investigating the role of the NT-proBNP test in cardiovascular diseases and comorbidities. The most notable alterations in NT-proBNP levels have been documented in patients with obesity, CKD and AF, with the potential for these conditions to exert multidirectional effects [39].

The presence of obesity as a concomitant condition of chronic HF has been demonstrated to affect the results of the NP test. There is an inverse relationship between obesity, as defined by an elevated BMI, and NP, as demonstrated in several studies. Consequently, the application of the NP test in the diagnosis of chronic HF in overweight and obese patients remains a significant challenge. It has been suggested that reducing the thresholds for NP or employing a correction for high BMI may improve the accuracy of HF diagnosis in obese individuals. In view of the growing prevalence of obesity worldwide and the emergence of dyspnea and reduced exercise tolerance alongside a notable increase in body weight, which can closely resemble the clinical presentation of HF, the utilization of the NT-proBNP test is becoming increasingly pertinent [44]. It is important to note, that low NP levels in this category of patients may be misleading. It is therefore essential to consider that NP levels are lower in obese patients with chronic HF than in normal-weight patients with the same condition [37]. It cannot be stated with confidence that this is true for the AHF scenario, as some large hospital practice studies have not identified a correlation between NT-proBNP concentration and BMI [45].

A reduction in renal function also serves as a modifier of serum NT-proBNP concentration. This is observed to be higher in patients with CHRONIC HF and CKD compared to those with HF alone [46]. The PRIDE study, which included patients with a wide range of estimated glomerular filtration rates (GFR) from 15 mL/min/1.73 m^2 to 252 mL/min/1.73 m^2, demonstrated that kidney failure was associated with an increased risk of congestive HF. Moreover, the deterioration of renal function was accompanied by structural and functional abnormalities of the heart, as determined by echocardiography. It was demonstrated that NT-proBNP and GFR were inversely and independently correlated, with NT-proBNP exceeding 450 pg/mL in patients under the age of 50 and 900 pg/mL in those aged 50 and above had an 85% sensitivity and an 88% specificity for diagnosing AHF among patients with GFR > 60 mL/min/1.73 m^2. A cut-off point of NT-proBNP of 1200 pg/mL for patients with an GFR < 60 mL/min/1.73 m^2 was identified as yielding a sensitivity and specificity of 89% and 72%, respectively, for the test [47]. Therefore, when eGFR is observed to decrease, an increase in CDT is observed for the diagnosis of AHF combined with CKD. Nevertheless, experts posit that when age-adjusted NT-proBNP thresholds are utilized, further adjustment of NT-proBNP levels is unwarranted for the confirmation of AHF, given the substantial correlation between age and impaired renal function [46].

In accordance with the findings of experts in the field, in cases of V HF accompanied by CKD, despite the potential elevation in NT-proBNP levels resulting from impaired clearance and myocardial stress and damage, the correction of CDTs is not typically necessary, as the correlation between NT-proBNP levels and prognosis remains consistent across the entire range of eGFR [46, 48].

The interpretation of NT-proBNP results represents a significant challenge in the diagnosis of HF in patients with AF. It has been demonstrated that the presence of AF is associated with a significant elevation of NP levels compared to patients with sinus rhythm, even in the absence of HF. This may have implications for CDTs in the diagnosis of CHRONIC HF in patients with AF [49].

A meta-analysis of screening studies demonstrated a correlation between NP and cardiac rhythm disturbances. The mean values of NP in patients with AF exceed those of NT-proBNP in patients with sinus rhythm by a factor of 3 to 3.5 [50]. Based on these findings, it is proposed that a threefold value observed in patients without rhythm disturbance be used as a preliminary indicator for the confirmation of chronic HF in the presence of AF, or CDT of 375 pg/mL for this disease [49]. Similarly, the same CDT is proposed for use in atrial flutter [14]. In the 2021 ESC guidelines for the exclusion of HF in patients with AF, it is proposed that a NT-proBNP value below 365 pg/mL be used. This value was chosen as a consensus value and differs slightly from the CDT presented above [3].

As previously stated, the clinical scenario of the diagnosis of AHF does not necessitate the adjustment of the CDTs for NT-proBNP to account for factors such as obesity, eGHF, AF, and other comorbidities. In the context of excluding chronic HF in an outpatient setting, the experts propose a modification of the CDTs based on the presence of comorbidities. The following proposed modifications for comorbidities are based on expert opinion rather than robust evidence. As additional information becomes available, these modifications should be refined.

An increase of 35% in the NT-proBNP CDT is recommended for patients with eGFR < 30 mL/min/1.73 m^2, a 25% increase for those with eGFR 30 to 45 mL/min/1.73 m^2, and a 15% increase for those with eGFR 45 to 60 mL/min/1.73 m^2. In individuals with a BMI between 30 and 35 kg/m^2, the threshold value of NT-proBNP should be reduced by 25%. For those with a BMI between 35 and 40 kg/m^2, the reduction should be 30%, and for those with a BMI greater than 40 kg/m^2, the reduction should be 40%. In instances of AF or atrial flutter, the NT-proBNP CDT should be augmented by 50% in the event that the ventricular rate is ≤90 beats per minute (bpm) at the time of blood collection, as determined preferably by electrocardiography. Alternatively, if the ventricular rate is > 90 bpm, the NT-proBNP CDT should be increased by 100% [14].

Currently, the majority of laboratories performing outpatient NT-proBNP testing are unable to incorporate patient clinical data into the test report, such as obesity, presence of AF or atrial flutter at the time of blood collection, ventricular rate, and impaired renal function at the time of testing.

It is conceivable that with the advent of a unified medical and laboratory information system in the Russian Federation, which could include data from all providers of medical services, it may become feasible to evaluate the NT-proBNP test in terms of comorbidities.

The Expert Committee held a discussion and open vote on the issues related to the preparation of the Elecsys proBNP test result report in the Russian Federation, taking into account current clinical practice.

- Rule-out criteria for HF based on the Elecsys proBNP test results.
- Rule-in criteria for HF based on the Elecsys proBNP test results.
- The incorporation of reference values into the Elecsys proBNP test results report format.
- The Elecsys proBNP test report format in the Russian Federation.

Conclusion

According to available research, more than 45% of the conditions that contribute to the risk of adverse events are preventable. An accurate interpretation of the Elecsys proBNP test is essential for the prevention of adverse events associated with the provision of medical care to patients with heart failure. In contemporary healthcare, the concept of safety management encompasses not only the safety monitoring of medical technologies, but also the reduction of the impact of systemic factors that form the basis of adverse events [12].

The studies presented in the publication were conducted using the Elecsys proBNP test (Roche), which enables the verification of this method's compliance with the criteria set forth in clinical guidelines for heart failure, both in cases of gradual and acute onset of the disease.

The presented features of the Elecsys proBNP II (Roche) test application facilitate the early diagnosis of chronic HF in at-risk populations and enable outpatient monitoring during the course of HF management. It should be noted that the results of the test may vary depending on a number of factors, including sex, age, the presence of AF, obesity, CKD, and other conditions.

It is currently feasible to utilize this diagnostic tool to ascertain the absence of both acute HF in the inpatient setting and chronic HF in the outpatient setting. It is recommended that the clinical decision thresholds for NT-proBNP (125 pg/mg and 300 pg/mg for chronic and acute HF, respectively) be included in the test result report. In light of the intricate nature of comorbidity assessment in outpatient settings and the dearth of evidence to support modifying the clinical decision threshold for rule-in in the diagnosis of chronic HF associated with comorbidities, it is recommended to abandon the clinical decision threshold for ruling out of chronic V. However, given the substantial influence of AG and atrial flutter on the levels of NPs, it is recommended that the clinical decision threshold for ruling out chronic HF in patients with this comorbidity (NT-proBNP below 375 pg/mL) be included in the test result report.

In accordance with the stipulations set forth in GOST and Order of the Ministry of Health of the Russian Federation No. 464n On Approval of the Rules of Laboratory Research dated May 18, 2021, it is imperative that the test report include the reference values for NT-proBNP determined in consideration of the patient's sex and age [23, 51].

Thus, a consensus has been reached among experts on the presented issues, as well as a standardized account of the results of the NT-proBNP test, conducted using the Elecsys proBNP II test (Roche). This report should include the following parameters:

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Пороговые значения для поддержки клинического решения при диагностике сердечной недостаточности с использованием NT-proBNP

(согласованное мнение экспертов)[1]

Высокая чувствительность и специфичность иммунохимического метода определения NT-proBNP в крови обеспечивают его использование в качестве объективного диагностического маркера при развитии симптомов или признаков сердечной недостаточности.

Использование NT-proBNP имеет наивысший класс рекомендаций для диагностики и прогноза хронической сердечной недостаточности и острой декомпенсации сердечной недостаточности[2,3]. Включение определения концентрации НУП в стандарты оказания медицинской помощи и доступность исследования позволяет проводить с его помощью дифференциальную диагностику и мониторинг терапии сердечной недостаточности[4].

Интерпретация результатов определения NT-proBNP требует персонифицированного подхода с учетом клинического профиля пациента и различий в клинических сценариях[7].

Клинический сценарий 1

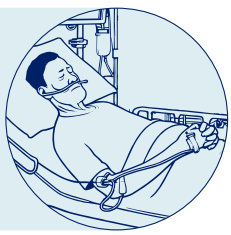
Концентрация NT-proBNP для исключения сердечной недостаточности *de novo* в амбулаторных условиях[5,6].

Критерий исключения	< 125 пг/мл	Возраст	Все категории

Клинический сценарий 2

Концентрация NT-proBNP для исключения сердечной недостаточности при наличии фибрилляции предсердий или трепетания предсердий[7].

Критерий исключения	< 375 пг/мл	Возраст	Все категории



Клинический сценарий 3

Концентрация NT-proBNP для исключения сердечной недостаточности в стационаре, включая отделение интенсивной терапии[5].

Критерий исключения	< 300 пг/мл	Возраст	Все категории

Своевременная диагностика сердечной недостаточности создает условия для своевременного старта лечения, что позволяет максимально продлить активный период жизни пациентов и минимизировать осложнения заболевания.

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ООО «Рош Диагностика Рус»
115114, Россия, Москва, ул. Летниковская д. 2, стр. 2., тел: + 7 (495) 229-69-99, diagnostics.roche.com, www.roche.com

Для медицинских специалистов
MC-RU-01249

- A patient-specific reference value for NT-proBNP, determined on the basis of sex and age.
- NT-proBNP < 125 pg/mg is the threshold for ruling out chronic HF.
- NT-proBNP < 300 pg/mg is the threshold for ruling out acute HF.
- T-proBNP < 375 pg/mg is the threshold for ruling out chronic HF in the presence of AF or atrial flutter.
- Furthermore, the report should include a note indicating that the reference values are provided with consideration of age and sex, and that the interpretation of the results should be conducted by a qualified physician in conjunction with the patient's medical history, clinical data, and the results of other diagnostic tests.

In order to facilitate clinical decision-making based on the presented information, an algorithm was developed to utilize the NT-proBNP test result in various clinical scenarios to rule out HF (Figure 1).

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Conflict of interest

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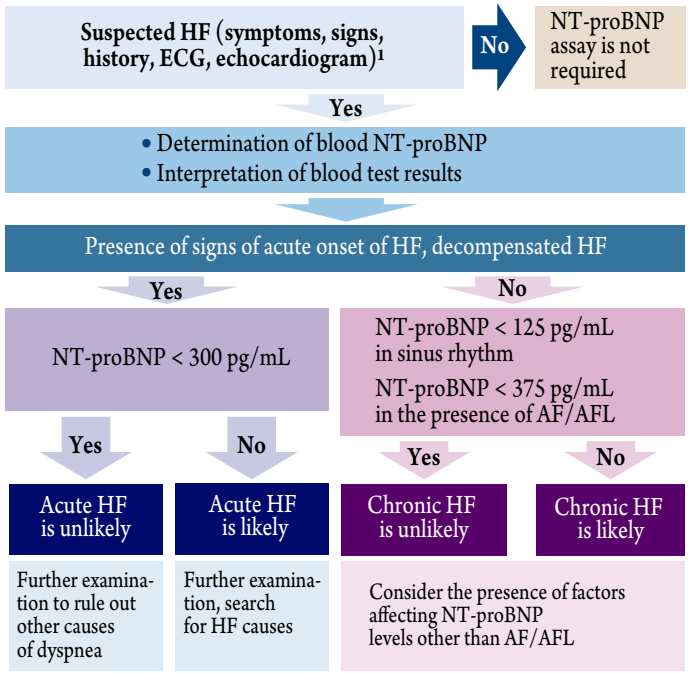
Figure 1. Algorithm for using NT-proBNP test result in different clinical scenarios to rule out HF



[1] In accordance with the most recent clinical guidelines set forth by the Ministry of Health of the Russian Federation (2020) [9].
CH, heart failure; AFL, atrial flutter; AF, open atrial fibrillation.

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