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Original article

Low LDL Levels are Associated with the Absence of Dyspnea in Patients with Chronic Heart Failure

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Abstract: *Objective* — The goal of our study was to identify biochemical criteria among those most commonly used in general clinical practice for dyspnea in chronic heart failure (CHF).
Methods — The study included 594 patients with confirmed CHF. We measured biochemical parameters (levels of creatinine, glucose, low-density lipoprotein [LDL], and C-reactive protein [CRP]) and performed the six-minute walk test (6MWT) before and after disease-modifying therapy (DMT) over the period of 12 months: angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor-neprilysin inhibitors (ARNIs), beta blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 (SGLT2) inhibitors. The association of biochemical markers with the presence of dyspnea in patients with CHF was evaluated through correlation analysis and a decision tree.
Results — We established that the most closely associated biochemical maker with dyspnea in patients with CHF is the LDL level with cutoff values of 3.245 and 3.266 mmol/L before and after DMT, respectively. High specificity of LDL was demonstrated for recognizing the absence of dyspnea, but critically low sensitivity for the presence Shortness of breath.
Conclusion — Low LDL level is associated with an absence of dyspnea in patients with CHF against the background of DMT.

Keywords: chronic heart failure, disease-modifying therapy, dyspnea, biochemical parameters, six-minute walk test.

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Introduction

Chronic heart failure (CHF) is still a leading cause of morbidity and mortality worldwide. It significantly reduces the quality of life in patients and contributes to increased healthcare costs [1-2]. Living in low-density regions of Russia is characterized by poor access to cardiac care, along with climatic, geographical, and social limitations, as well as additional functional loads that increase the risk of developing cardiovascular diseases (CVDs). The effectiveness of cardiac care in low-density regions remains insufficient and is largely determined by medical, social, technological, and infrastructural factors. These factors substantially complicate the management of patients with CHF. That is why improving the organization of specialized medical care in such settings is particularly urgent [3-5].

In recent years, clinical guidelines for the management of patients with CHF underwent noteworthy changes. Currently, the introduction of disease-modifying therapy (DMT) is of particular importance. DMT involves the use of four main groups of pharmaceutical drugs: angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor-neprilysin inhibitors (ARNIs), beta blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 (SGLT2) inhibitors [6-13].

One of the key factors in the successful management of CHF is the availability of practical, accessible, and reliable criteria for assessing the patient's status. In this regard, symptoms that can be assessed by a primary care physician, a paramedic, or even by a patient himself or herself, are of particular importance. Dyspnea is one of the most common symptoms for which patients seek medical attention. However, the shortness of breath is observed not only in CVDs but also in other pathological conditions, such as obesity, bronchopulmonary diseases, anemia, etc. This significantly confounds differential diagnosis. According to a meta-analysis by J. Mant et al., dyspnea is the only symptom with a high sensitivity (up to 89%), albeit a relatively low specificity (up to 51%) [14]. Regular monitoring of symptoms, including assessment of dyspnea, is an important element of effective management of patients with CHF. According to a meta-analysis by S.C. Inglis et al., structured telephone support and telemonitoring facilitate remote monitoring of the patient's clinical condition and an early detection of decompensation signs, which increases his or her involvement in self-management [15]. Remote methods of monitoring the condition and key parameters are especially relevant in resource-limited settings and remote areas, since they ensure timely diagnosis of deterioration in the patient's condition and access to specialized care, thereby improving the quality and duration of life in patients with CHF.

In addition to clinical symptoms, regular monitoring of laboratory parameters can improve the accuracy of decompensation risk assessment in patients with CHF. According to the 2024 study by T. Fröhling et al., biochemical markers in blood demonstrated a statistically significant relationship with the clinical status and prognosis of the disease [16]. E.g., patients with decompensated CHF showed increased levels of biomarkers: soluble urokinase plasminogen activator receptor (suPAR), heart-type fatty acid-binding protein (H-FABP), vascular cell adhesion molecule 1 (VCAM-1), and growth/differentiation factor 15 (GDF-15). The highest increase in concentration was observed for H-FABP (2.2-fold), while suPAR, VCAM-1, and GDF-15, exhibited 1.6- or 1.7-fold increase vs. patients with compensated CHF [16]. It is worth noting that traditional biomarkers retain important clinical significance: according to the recommendations of the European Society of Cardiology (ESC), measuring the level of natriuretic peptides is recommended for the diagnosis of CHF and assessment of its course [17]. Additional opportunities for prognostic assessment are provided by a multi-biomarker approach, including the measurement of B-type natriuretic peptide (BNP), cardiac troponin I (cTnI) and high-sensitivity C-reactive protein (hs-CRP). As shown in the 2010 study of M.N. Zairis et al., the risk of sudden cardiac death within 31 days gradually increases with the increase in the number of biomarkers with elevated concentrations, which emphasizes their additional value for risk stratification in patients with decompensated CHF [18]. A promising direction in the diagnosis and prognosis of CHF with preserved ejection fraction (CHFpEF) is the study of metabolomic markers of amino acid metabolism. According to M.F. Petruhnova et al. (2024), threonine levels can be employed as an additional diagnostic and prognostic criterion in CHFpEF, reflecting the involvement of amino acid metabolism in the pathogenesis of the disease [19]. Although none of the known biomarkers is able to fully reflect the complex pathophysiology of CHF, their use largely ensures an objective and reproducible assessment of the patient's condition, as well as facilitates the early diagnosis of acute decompensated heart failure (ADHF) and monitoring the effectiveness of DMT [20].

Despite significant progress in the study of novel biomarkers associated with CHF, the issue of the diagnostic and prognostic value of conventional blood biochemical parameters remains imperative. These include the lipid profile, creatinine and glucose levels, etc., which continue to be used to assess the metabolic status of patients and identify concomitant disorders. It is known that a reduction in the rate of creatinine excretion in urine is associated with a more severe grade of heart failure and an increased risk of adverse outcomes, chronic kidney disease and the severity of CHF [21]. However, during the treatment of ADHF, changes in serum creatinine levels demonstrate a paradoxical relationship with clinical outcomes: its increase is not accompanied by an aggravated prognosis, while a diminution in concentration is associated with a higher frequency of adverse events [22]. In addition to protein metabolism and creatinine excretion disorders, carbohydrate metabolism parameters play a significant role in the pathogenesis and prognosis of CHF. Studies also demonstrate a close relationship between glucose levels and the risk of CHF decompensation. In particular, in the group of patients with high cardiovascular risk, each increase in fasting glucose concentration by 1 mmol/L was associated with a 1.1-fold increase in the risk of hospitalization for CHF; moreover, this relationship persisted even after multivariate adjustment [23].

Changes in the blood lipid profile are of high importance in the pathogenesis and prognosis of CHF. The relationship between lipid profile parameters and the risk of CHF decompensation remains a subject of debate. It was revealed that in patients with ADHF, lower cholesterol levels paradoxically correlated with aggravated outcomes, which challenges traditional concepts about the effect of lipids on cardiovascular risk [24]. The established *'cholesterol paradox'* in patients with CHF indicates the need for a better in-depth analysis of the metabolic changes accompanying disease progression. Numerous data indicate that changes in the lipid profile in CHF reflect the severity of the disease rather than being its cause. Specifically, declined high-density lipoprotein (HDL-C) levels are associated with deteriorated renal function and more pronounced myocardial dysfunction, suggesting that lipid abnormalities can be considered a marker of disease severity and a poor prognosis [25]. Despite numerous studies, the role of commonly used biochemical parameters in general practice in the pathogenesis of CHF requires further clarification. However, trying to reveal their associations with dyspnea as a noninvasive criterion for CHF, while assessing patient's status, appears fully appropriate.

The *objective* of our study was to examine the association of the most commonly used biochemical parameters in general clinical practice (LDL, creatinine, glucose) with dyspnea in patients with CHF against the background of DMT.

Material and Methods

Ethical approval

This non-interventional clinical trial was approved by the Ethics Committee of Saratov State Medical University (Protocol No. 2 of April 10, 2023).

Table 1. Clinical characteristics of patients with CHF

Parameter	*Before DMT*	*After DMT*
n=594		
Age, years (M±SD)	63±5	
Men, n (%)	244 (41.1)	
Women, n (%)	350 (58.9)	
Smoking		
Smokers, n (%)	59 (9.9)	36 (6.1)
Nonsmokers, n (%)	535 (90.1)	558 (93.9)
Presence of dyspnea		
Present, n (%)	160 (26.9)	151 (25.4)
Absent, n (%)	434 (73.1)	443 (74.6)
SBP, mmHg (M±SD)	152±23	124±7
DBP, mmHg (M±SD)	84±16	72±6
Heart rate, bpm (M±SD)	86±12	65±6
Body mass index, kg/m^2, n (%)		
>30	198 (33.3)	156 (26.3)
25-30	270 (45.5)	264 (44.4)
≤25	126 (21.2)	174 (29.3)
Body mass index, kg/m2 (M±SD)	28.9±4.6	27.5±4.2
Sinus rhythm, n (%)	370 (62.3)	410 (69)
Atrial fibrillation/flutter, n (%)	224 (37.7)	184 (31)
Hypertension, n (%)	472 (79.5)	
Dyslipidemia, n (%)	356 (59.9)	302 (50.8)
Type 2 diabetes mellitus, n (%)	188 (31.6)	
Coronary artery disease, n (%)	428 (72.1)	
Prior myocardial infarction, n (%)	268 (45.1)	
Prior percutaneous coronary intervention, n (%)	176 (29.6)	
Prior coronary artery bypass grafting, n (%)	14 (14.1)	

SBP, systolic blood pressure; DBP, diastolic blood pressure.

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Table 2. Descriptive statistics for six-minute walk test and various biochemical parameters before and after disease-modifying therapy (DMT) (N=594)

Parameter	*Timepoint*	*Mean*	*Median*	*SD*	*SE*	*W (385)*	*t (385)*	*p-level*
6MWT, m	before DMT	328	340	92.1	4.7	0	-	<0.001
	after DMT	361	378	89.9	4.6			
Creatinine, µmol/L	before DMT	87.3	84.3	19.3	1	63,995	-	<0.001
	after DMT	77.3	76.0	14.6	0.8			
Glucose, mmol/L	before DMT	5.5	5.5	0.7	0.039	-	16.9	<0.01
	after DMT	4.8	4.7	0.6	0.035			
LDL, mmol/L	before DMT	2.9	2.9	1	0.1	-	10.8	<0.001
	after DMT	2.4	2.4	0.4	0			
CRP, mg/L	before DMT	3.6	3.6	1.2	0.1	61,007	-	<0.001
	after DMT	2	2.1	0.6	0			

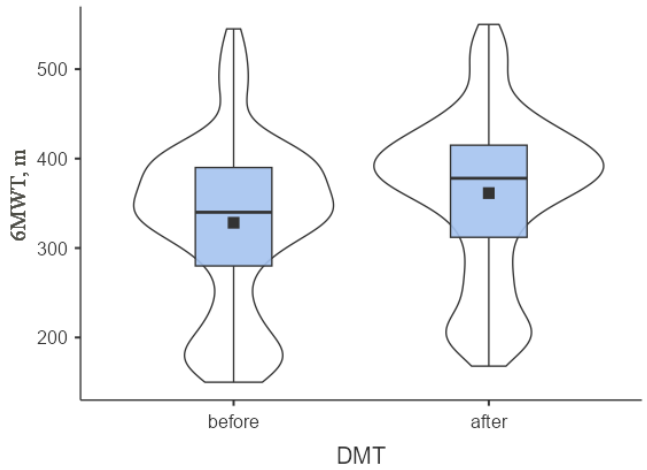

Figure 1. Violin plots of six-minute walk test (6MWT) results before and after disease-modifying therapy (DMT).

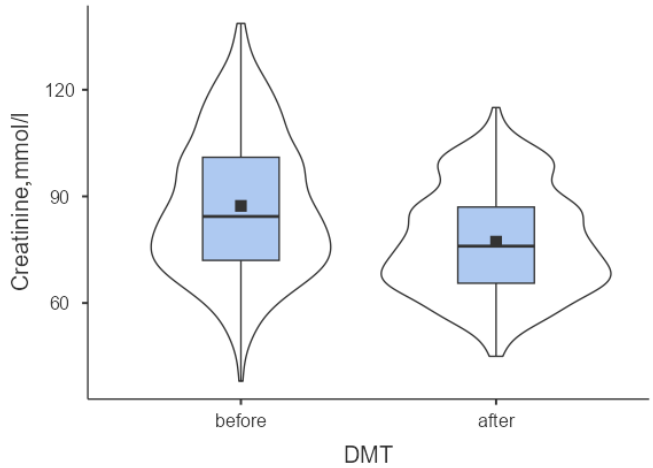

Figure 2. Violin plots of creatinine levels before and after disease-modifying therapy (DMT).

Study design

The study was conducted from April 2023 through October 2024.

Inclusion criteria:

1) Patients living in 7 small towns and corresponding rural areas of the Saratov Oblast (Dukhovnitsky, Volsky, Tatishchevsky, Lysogorsky, Petrovsky, Engelssky, and Baltaysky Districts);

2) Confirmed CHF in accordance with the Russian clinical guidelines [7];

3) Age ranging 18-80 years.

Exclusion criteria:

1) Pregnancy;

2) Cognitive impairment (28 or more pts. on the Mini-Mental State Examination (MMSE);

3) Oncological diseases;

4) Patients with chronic obstructive pulmonary disease (COPD) and asthma;

5) Other ongoing pharmacotherapy (statins, anticoagulants, antiplatelet agents).

We measured the following parameters: six-minute walk test (6MWT) results; levels of creatinine, glucose, LDL, and CRP before and after DMT (two data collection instances) in the same group of patients over the period of 12 months. We standardized doses, manufacturers, and monitored the regularity of medication intake in accordance with Russian clinical guidelines [7].

Study subjects

The study included 594 patients with confirmed CHF in accordance with the clinical guidelines of the Russian Federation: CHF with reduced left ventricular (LV) ejection fraction (CHFrEF ≤40%); CHF with moderately reduced LV ejection fraction (CHFrEF ranging 41-49%); CHF with preserved LV ejection fraction (CHFpEF ≥50% [7]; the mean age of the participants of 63±5 years. All respondents had preserved cognitive functions based on the MMSE score. The clinical characteristics of the patients with CHF are presented in *Table 1*.

Biochemical parameters

The following biochemical parameters were measured: creatinine (µmol/L), glucose (mmol/L), LDL (mmol/L), and CRP (mg/L). Reagents from Mindray Biomedical Electronics Co., Ltd. (Shenzhen, China) were used.

Six-minute walk test

We performed 6MWT twice: initially (before the prescription of DMT) and after the optimal treatment strategy was implemented. A physician administered 6MWT in the morning hours before the patient took any cardiac medications and made sure that he or she did not smoke at least 2 hrs. before the test. A registration form was completed before and after the test, indicating blood pressure and heart rate.

During the 6MWT, we assessed the patient's exercise tolerance based on the distance walked, which corresponds to New York Heart Association (NYHA) of functional classes [26]: FC I (no limitation, 426-550 m); FC II (slight limitation, 300-425 m); FC III (marked limitation, 150-299 m); FC IV (severe limitation, up to 150 m).

Hence, during the 6MWT, the distance walked by the patient was assessed and the decision tree was created to predict dyspnea based on clinical parameters.

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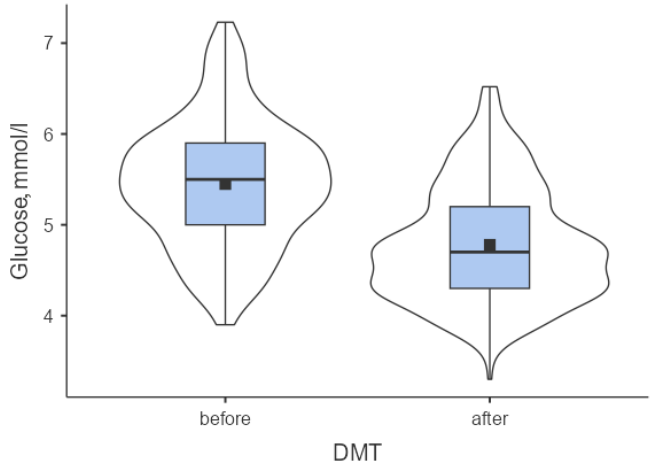

Figure 3. Violin plots of glucose levels before and after disease-modifying therapy (DMT).

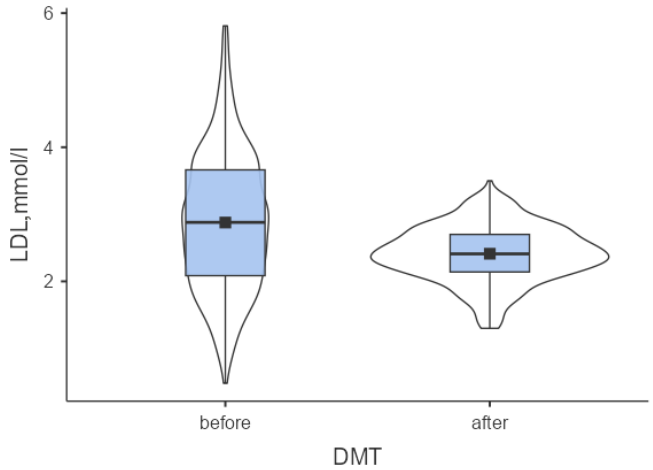

Figure 4. Violin plots of low-density lipoprotein (LDL) levels before and after disease-modifying therapy (DMT).

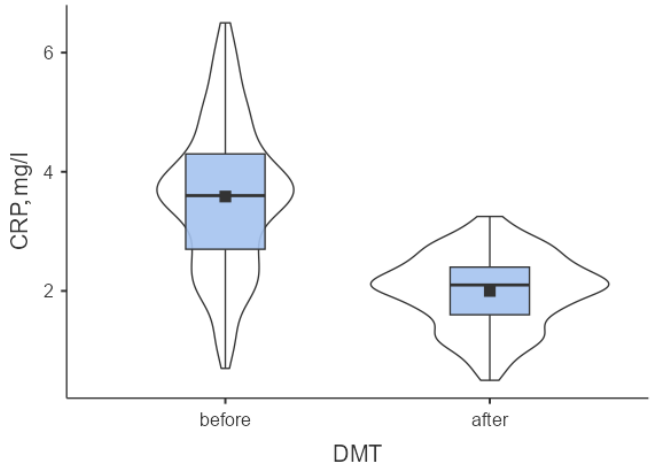

Figure 5. Violin plots of C-reactive protein (CRP) levels before and after disease-modifying therapy (DMT).

Table 3. Correlation matrix for six-minute walk test (6MWT) and biochemical parameters in patients before disease-modifying therapy

	6MWT, m	*Creatinine, µmol/L*	*CRP, mg/L*	*Glucose, mmol/L*	*LDL, mmol/L*
6MWT, m	–				
Creatinine, µmol/L	-0.064	–			
CRP, mg/L	-0.163***	0.278***	–		
Glucose, mmol/L	-0.110**	0.220***	0.201***	–	
LDL, mmol/L	-0.078	0.114**	0.154***	-0.023	–

* p<0.05, ** p<0.01, *** p<0.001.

Table 4. Correlation matrix for six-minute walk test (6MWT) and biochemical parameters in patients after disease-modifying therapy

	6MWT, m	*Creatinine, µmol/L*	*CRP, mg/L*	*Glucose, mmol/L*	*LDL, mmol/L*
6MWT, m	—				
Creatinine, µmol/L	-0.071	—			
CRP, mg/L	-0.158***	0.272***	—		
Glucose, mmol/L	-0.115**	0.215***	0.198***	—	
LDL, mmol/L	-0.082	0.118**	0.148***	-0.031	—

* p<0.05, ** p<0.01, *** p<0.001.

Statistical processing of collected data

The following descriptive statistics were calculated for all quantitative variables: mean (M), median (Me), standard deviation (SD), and standard error of the mean (SE). Violin plots were used as a supplementary method for visualizing differences.

The normality of the distribution of quantitative physiological variables in the comparison groups was tested using the Shapiro-Wilk test, which ensured the choice of appropriate statistical methods. Based on the results of Shapiro-Wilk test, the values of 6MWT (W=0.965, p<0.001), creatinine (W=0.986, p=0.001), and CRP (W=0.975, p<0.001) did not comply with a normal distribution, while glucose (W=0.993, p=0.183) and LDL (W=0.995, p=0.395) values were normally distributed. The Wilcoxon signed-rank test was employed to assess changes in 6 MWT distance, along with creatinine and CRP levels, while a parametric Student's t-test was utilized to analyze changes in glucose and LDL concentrations. Correlation analysis of the relationships between the variables was conducted using the Spearman's rank correlation coefficient.

Descriptive statistics, correlation analysis, and difference tests were performed using Jamovi version 2.6.44.

To assess the feasibility and accuracy of predicting dyspnea based on biochemical parameters, a decision tree machine learning method was employed. The method utilized Python programming language using the Google Colab cloud service. Before constructing the decision tree, all necessary libraries for data analysis, model building, evaluation and visualization were included, such as NumPy, Pandas, Scikit-Learn, Matplotlib, and Seaborn. Data collected before and after DMT were analyzed in terms of four parameters: levels of creatinine (µmol/L), CRP (mg/L), glucose (mmol/L), and LDL (mmol/l), vs. the target variable (*Dyspnea*) reflecting the presence or absence of dyspnea. Initially, the data were divided into training set and test set at a ratio of 85% to 15%, with stratification by the target feature to maintain the ratio of classes. To account for possible class imbalance, weights for each class were calculated using the balanced function in Scikit-Learn. When constructing decision tree models that accounted for class imbalance (the presence or absence of dyspnea), we used optimal parameter values characterizing the branching depth of a decision tree within the levels.

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After selecting the optimal depth, the decision trees were trained on the labeled training data set, while their quality was assessed on the test set. The evaluation included constructing a confusion matrix, which was visualized using a heat map.

The confusion matrix clearly demonstrates the number of correct and incorrect classifications of respondents based on the presence or absence of dyspnea. The vertical axis indicates the true classes (the actual presence or absence of dyspnea), whereas the horizontal axis indicates the classes predicted by the model. Thus, each cell of the matrix reflects the number of study patients in the corresponding combination of actual and predicted states. The upper left element of the matrix corresponds to true negative (TN) classification, when the model correctly identified the absence of dyspnea. The upper right element represents false positive (FP) results, that is situations in which the model incorrectly predicted the presence of dyspnea in respondents who did not have it. The lower left element reflects false negative (FN) classification, i.e. situations in which the model did not detect dyspnea in respondents who actually had it. The lower right element represents true positive (TP) results, when the model correctly identified the presence of dyspnea.

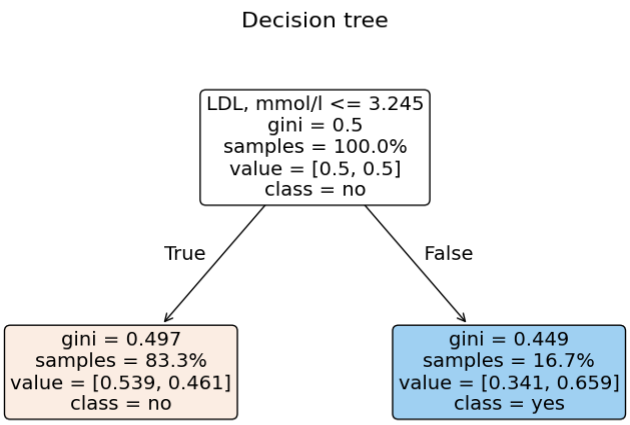

Figure 6. Decision tree for predicting dyspnea based on LDL levels in patients before disease-modifying therapy.

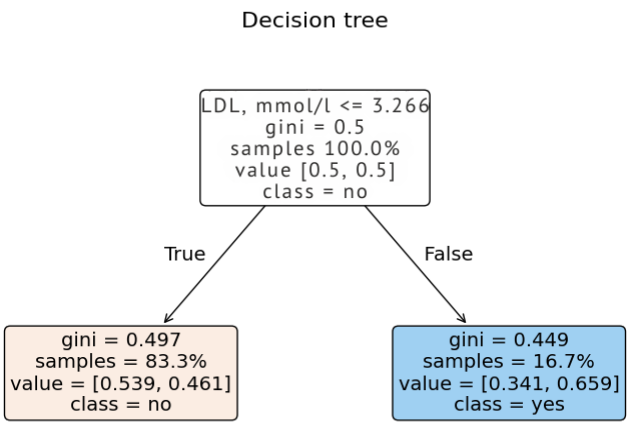

Figure 7. Decision tree for predicting dyspnea based on LDL levels in patients after DMT.

Table 5. Assessment of the model quality for predicting dyspnea in patients before disease-modifying therapy

	precision	*recall*	*f1-score*	*support*
no	0.73	0.91	0.81	66
yes	0.25	0.08	0.12	24
accuracy			0.69	90
macro avg	0.49	0.50	0.47	90
weighted avg	0.60	0.69	0.63	90

Table 6. Assessment of the model quality for predicting dyspnea in patients after disease-modifying therapy

	precision	*recall*	*f1-score*	*support*
no	0.84	0.93	0.88	75
yes	0.29	0.13	0.18	15
accuracy			0.80	90
macro avg	0.57	0.53	0.53	90
weighted avg	0.75	0.80	0.76	90

precision – the proportion of TP results among all objects classified by the model as belonging to a given class; recall – the proportion of correctly recognized objects of a given class among all those actually belonging to this class; f1-score – the harmonic mean between precision and recall, support – the number of observations (objects) for each class, accuracy – the overall accuracy of the model (the proportion of correctly classified objects among all), macro avg – the means for all classes ignoring class imbalance (each class has the same weight), weighted avg – the means for all classes taking into account class imbalance (the weight of each class is proportional to the number of objects).

Results

The median and mean values imply that after DMT, respondents demonstrated statistically significantly better results on the 6MWT, as well as lower levels of creatinine, glucose, LDL, and CRP vs. pretreatment data (*Table* 2). The distribution of values is shown in *Figures* 1-5 in the form of violin plots.

We conducted a correlation analysis of the studied parameters, viz., the manifestation of dyspnea based on 6MWT results, and levels of creatinine, CRP, glucose and LDL. The results exhibited a weak inverse correlation between 6MWT results and CRP concentration, as well as a very weak inverse correlation with glucose levels in patients before and after DMT (*Tables* 3 and 4).

decision tree depth (that was determined during hyperparameter selection) was one level, which means that adding additional branches does not improve the predictive performance on the validation subsamples. On the contrary, risk of overfitting is increasing. Hence, the decision tree took the form of a single-level classifier with a single splitting node. Contingent on the decision tree construction results, solely the LDL parameter with a threshold of 3.245 (3.266) mmol/L was informative for discriminating based on the presence of dyspnea, while the other parameters did not substantially improve the quality of the model. If in a patient with CHF, LDL≤3.245 before DMT or ≤3.266 after DMT, the patient is unlikely to experience dyspnea. If LDL>3.245 (3.266), the patient is likely to experience dyspnea as a criterion for ongoing CHF decompensation (*Figures* 6 and 7).

Analysis of the classification report – revealed higher precision and recall values for the *no* class, which characterizes the absence of dyspnea and presence of compensated CHF. Analysis of the dyspnea prediction quality and confusion matrix was conducted based on the patients' biochemical parameter values before DMT (n_1=594) and after it (n_2=594) (*Tables* 5 and 6).

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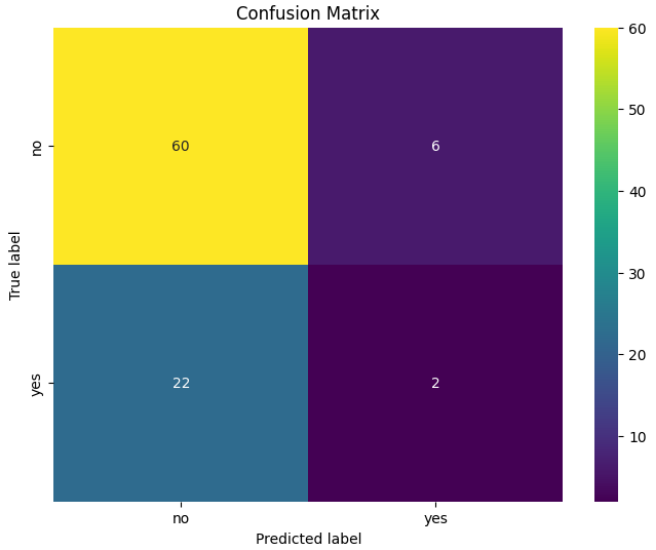

Figure 8. Confusion matrix for predicting CHF decompensation in patients before disease-modifying therapy.

The confusion matrix clearly demonstrates the number of correct and incorrect classifications of respondents for the presence of dyspnea. TN results are cases where the model correctly identified the absence of dyspnea (60 subjects), while TP results are cases where the model correctly predicted the presence of dyspnea (2 subjects). FP results (the model incorrectly predicted dyspnea in patients without it) accounted for 6 study participants, while FN results (the model did not detect dyspnea, even though it was present) were characteristic for 22 patients. The test sample included 90 test subjects (15% of the total sample), which allowed evaluating the model accuracy (decision tree).

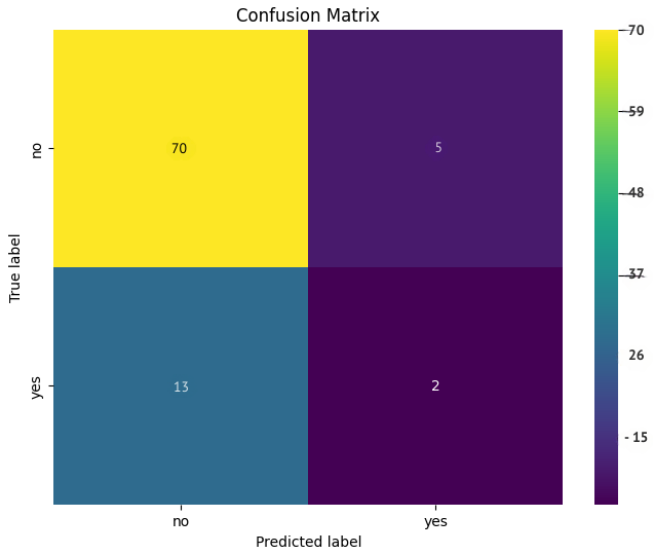

Figure 9. Confusion matrix for predicting CHF decompensation in patients after disease-modifying therapy.

The confusion matrix clearly demonstrates the number of correct and incorrect classifications of respondents for the presence of dyspnea. TN results are cases where the model correctly identified the absence of dyspnea (70 subjects), while TP results are cases where the model correctly predicted the presence of dyspnea (2 subjects). FP results (the model incorrectly predicted dyspnea in patients without it) accounted for 5 patients, while FN results (the model failed to detect dyspnea even though it was present) were characteristic for 13 subjects. The test sample included 90 subjects (15% of the total sample), which allowed evaluating the model accuracy (decision tree).

An analysis of the confusion matrices suggests that omission and FP errors are the least common when identifying the absence of dyspnea (*Figures 8* and 9). The test sample included 90 participants (i.e., 15% of the entire sample). The model demonstrates the highest proportion of correct classifications for cases of absence of dyspnea (TN=60). However, the model sensitivity for detecting the presence of dyspnea is extremely low (TP=2 with FN=22). Thus, LDL demonstrates high specificity for dyspnea in CHF (accuracy in determining the absence of dyspnea).

Discussion

An analysis of the parameter dynamics in patients with CHF revealed that the recommended DMT contributes to the improvement of their functional status and metabolic parameters. Optimization of DMT results in a statistically significant increase in the 6MWT distance, indicating improved exercise tolerance and treatment effectiveness. These results are consistent with those of P.L. Myhre et al. (2024) who demonstrated that an increase in the 6MWT distance was a predictor of better survival in patients with CHF [27].

Lipid profile parameters play an important role in the prognosis of patients with CHF. Many studies demonstrated that low levels of LDL are paradoxically associated with adverse outcomes in CHF. A. Nakagomi et al. (2014) showed that LDL concentration below 120 mg/dL was independently associated with an increased risk of cardiovascular events (hazard ratio [HR] 9.41; p=0.048) and demonstrated an inverse correlation with the production of proinflammatory cytokines (TNF-α and IL-6), thereby indicating the role of inflammatory mechanisms in the formation of the lipid paradox in patients with CHF [28]. Similar results were obtained by G. Charach et al. (2014, 2018) who showed that LDL levels above 115 mg/dL were associated with higher survival in elderly patients with CHF. The authors also noted that low LDL values (<110 mg/dL) were associated with more aggravated adverse outcomes, especially in patients under the age of 70 years and receiving statins, which further confirmed the presence of the so-called lipid paradox in CHF [29-30]. Based on the above-mentioned publications, low LDL levels are assumed an unfavorable prognostic factor for CHF. At the same time, absence of dyspnea is generally considered an indirect sign of CHF compensation. In this regard, the revealed association of low LDL levels with the absence of dyspnea (assessed based on 6MWT results) seems very interesting. Unfortunately, the peculiarities of our study design, described in the *Limitations of the study* section, do not allow interpreting the significance of the identified phenomenon for assessing the current status and prognosis in patients with CHF. Hence, further research on the topic is needed.

Conclusion

The results of our study reveal that low LDL levels are associated with the absence of dyspnea in patients with CHF against the background of DMT. The importance of this finding for assessing the current status and prognosis of patients with CHF requires further investigation.

Limitations of the study

This study did not perform echocardiography for the confirmation of patients' CHF status, thereby making it impossible to distinguish between various types of CHF or objectively assess the dynamics of CHF compensation or decompensation against the background of DMT.

Therefore, CHF compensation and decompensation in our study were assessed solely by indirect methods in the course of clinical examination. Confirmation of the CHF diagnosis was based exclusively on anamnestic data.

Also, the study did not analyze the dynamics of natriuretic peptide levels against the background of DMT, which diminishes the validity of an objective assessment of the treatment effectiveness.

Our data analysis did not evaluate the impact of comorbidities on the study results or assess lipid-lowering drug therapy.

We plan to further investigate the patients with different types of CHF, taking into account all polyfactorial therapies (including lipid-lowering drug therapy) with subsequent quantitative assessment of natriuretic peptide, CRP, and lipid profile in this cohort of patients.

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