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Long-term mortality risk in hospitalized patients with heart failure after myocardial infarction

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Aim. Comparative assessment of laboratory and instrumental parameters of patients with heart failure (HF) after myocardial infarction at admission and discharge from the hospital to determine the long-term mortality risk.

Material and methods. The clinical outcomes of 117 patients with stage II-III (Strazhesko-Vasilenko Classification) heart failure (64 men and 53 women) were studied. All patients admitted to the hospital underwent laboratory and instrumental examination. The average follow-up for patients after discharge from the hospital was 3 years (12 to 44 months). The long-term mortality risks of HF patients were compared according to the examination data upon admission and discharge from the hospital.

Results. The long-term mortality risk factors of HF patients at admission are the levels of pro-brain natriuretic peptide (proBNP) (risk 1,08, p=0,001), D-dimer (risk 1,062, p=0,018), urea (risk 1,048, p=0,016), creatinine (risk 1,006, p=0,016), alanine transaminase (risk 1,002, p=0,009). The long-term mortality risk factors of HF patients at discharge are urea (risk 1,141, p=0,001), N-terminal proBNP (risk 1,101, p=0,002), and the number of neutrophils (risk 1,064, p=0,002).

Conclusion. There is a difference in risk factors for long-term mortality risk of HF patients at admission and discharge from the hospital.

Key words: heart failure, long-term risk.

Relationships and Activities: not.

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Over the previous three decades, significant progress has been achieved in the treatment of heart failure (HF) using angiotensin-converting enzyme inhibitors, beta-blockers, mineralocorticoid receptor antagonists. Nevertheless, patients with HF usually have an unfavorable prognosis [1]. There are numerous studies to assess the risk of adverse events in HF patients; a number of prognostic scales have been proposed [2-4]. However, these scales are not always convenient in clinical practice.

The aim of our study was a comparative assessment of laboratory and instrumental parameters of patients with decompensated HF at admission and discharge from the hospital to determine the long-term mortality risk.

Material and methods

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The local medical ethics committee approved this study. All participants gave written informed consent. The inclusion criterion was HF confirmed by clinical and laboratory tests in patients 1 year or more after myocardial infarction. There were following exclusion criteria: cancer, blood disorders, obstructive pulmonary diseases, patient unwillingness to participate in the study.

The clinical outcomes of 117 patients (64 men and 53 women) with stage II-III HF (Strazhesko-Vasilenko Classification) were studied. The average follow-up after discharge from the hospital was 3 years (12 to 44 months). The inclusion criterion was HF in patients with a myocardial infarction history. There were following exclusion criteria: atrial fibrillation, severe liver disease, blood disorders, cancer, patient unwillingness to participate in the study.

All patients received medications in accordance with the Russian Heart Failure Society guidelines [5].

All patients admitted to the hospital underwent following examinations: complete blood count, determination of N-terminal pro-brain natriuretic peptide (N-proBNP) level, liver tests (aspartate transaminase (AST), alanine transaminase (ALT), bilirubin, alkaline phosphatase), total protein, albumin, renal function (blood urea and creatinine concentrations, glomerular filtration rate estimation using MDRD equation), carbohydrate metabolism (blood glucose, glycated hemoglobin), coagulation (prothrombin time, fibrinogen and D-dimer tests), highly sensitive C-reactive protein, parameters of myocardial injury (myoglobin, troponin I), serum electrolytes (potassium, sodium, calcium, magnesium), electrocardiography, the Simpson's method of echocardiography with determination of cavity dimensions and left ventricle ejection fraction (LVEF). For each patient, 71 parameters were analyzed during their hospital stay.

Statistical processing was carried out using the parametric and non-parametric methods for data analysis. The accumulation, adjustment, systematization of the baseline data and visualization of the results were conducted using Microsoft Office Excel 2016. Statistical analysis was performed using the IBM SPSS Statistics v.23 software package. The dependence of patient survival on the studied factors was analyzed using the Cox regression model. The data obtained at hospital admission, after discharge and survival on outpatient stage after 44 months of the mean follow-up were assessed and compared.

Table 1

Comparison of significant risk factors for long-term mortality with baseline hazard in HF patients at admission to hospital

Risk factor	Hazard changes in the presence of a factor		p
	$h_i(t)/h_0(t)$	95% CI	
Alanine transaminase, ME/L	1,002	1,001-1,004	0,009
Urea, mmol/L	1,048	1,009-1,088	0,016
Creatinine, μmol/L	1,006	1,001-1,011	0,016
Hematocrit, %	0,928	0,866-0,994	0,034
Hemoglobin	0,98	0,961-0,999	0,044
Color index	0,011	0,0-0,971	0,049
D-dimer, ng/ml	1,062	1,01-1,117	0,018
NT-proBNP, ng/ml	1,08	1,039-1,123	<0,001
Left ventricular ejection fraction by Simpson's method, %	0,965	0,936-0,995	0,022

Abbreviations: $h_i(t)$ — predicted hazard for long-term mortality in patient i at time t (%), $h_0(t)$ — shared baseline hazard for long-term mortality at time t (%), CI — confidence interval, BNP — brain natriuretic peptide.

Table 2

Comparison of significant risk factors for long-term mortality with baseline hazard in HF patients at discharge from the hospital

Risk factor	Hazard changes in the presence of a factor		p
	$h_i(t)/h_0(t)$	95% CI	
Duration of treatment, days	1,086	1,002-1,177	0,048
Urea, mmol/L	1,141	1,08-1,206	<0,001
Glomerular filtration rate, ml/min	0,968	0,943-0,994	0,015
Hemoglobin	0,975	0,961-0,99	0,001
Color index	0,007	0,0-0,542	0,025
Neutrophils, %	1,064	1,024-1,105	0,002
Lymphocytes, ng^{-1}	0,427	0,221-0,826	0,012
Lymphocytes, %	0,93	0,89-0,971	0,001
Prothrombin time	1,056	1,001-1,113	0,045
Quick's prothrombin time	0,981	0,963-0,999	0,038
NT-proBNP, ng/ml	1,101	1,036-1,171	0,002
Serum sodium	0,913	0,847-0,985	0,019
Left ventricular ejection fraction by Simpson's method, %	0,965	0,936-0,995	0,022

Abbreviations: $h_i(t)$ — predicted hazard for long-term mortality in patient i at time t (%), $h_0(t)$ — shared baseline hazard for long-term mortality at time t (%), CI — confidence interval, BNP — brain natriuretic peptide.

Results

The all-cause out-hospital mortality of patients with HF after myocardial infarction during the follow-up period was 22,2% (26/117).

Among the analyzed laboratory and echocardiographic parameters upon hospital admission of patients with HF, the following factors were significant: values of ALT, urea, creatinine, hematocrit, hemoglobin, color index, D-dimer, NT-proBNP and LVEF by Simpson's method. These parameters in HF patients observed at admission to the hospital are presented in Table 1.

Among the analyzed laboratory and echocardiographic parameters during discharge from the hospital, the following factors were significant: duration of treatment, values of urea, glomerular filtration rate, hemoglobin, color index, neutrophil count, lymphocyte count, prothrombin time, Quick's prothrombin time test, NT-proBNP, serum sodium and LVEF by Simpson's method. These parameters in HF patients observed at discharge from the hospital are presented in Table 2.

Discussion

At least 50 biomarkers for assessment of HF severity were studied in clinical trials [6]. There is an opinion of authors [7] that the routine clinical data obtained upon admission of HF patients do not sufficiently predict repeated hospitalizations, but they are more useful as predictors of mortality. At the same time, the authors emphasize that neither the determination of NT-proBNP, nor cardiac troponin levels upon admission improve prediction.

Over the years, researchers have developed various scales for assessing the risk of adverse outcome for HF patients. A meta-analysis of 64 predictive models [8] and a meta-regression of 117 predictive models [9] showed only moderate accuracy in mortality prediction. One of the prognostic scales [2] is devoted to assessing simple parameters of congestive HF (dyspnea, edema, jugular vein distention). The study included 2061 patients with decompensated HF with LVEF <40% and two or more signs of fluid retention. The follow-up period lasted 9 months. Daily, shortness of breath, orthopnea, lower limb swelling, the degree of jugular vein distention, and lung wheezing were evaluated using a 4-point score (0-3). Based on the sum of the scores of three parameters (orthopnea, jugular vein distention and lower limb swelling), a combined congestion scale was developed. The composite endpoints were hospitalizations for HF, all-cause mortality, and their sum. Using the multivariate Cox regression model, the outcomes were estimated at the hospital discharge. Comparisons of the parameters at hospital admission and discharge showed its decrease from 4,07±1,84 to 1,11±1,42. The levels of BNP and NT-proBNP decreased from 734 pg/ml and 4857 pg/ml at admission to 477 pg/ml and 2834 pg/ml at discharge, respectively. The number of points at hospital discharge was associated with an increased risk of end-

points by the 30th day of follow-up and at the end of the study.

In one relatively new analysis, several prognostic risk scores were compared: CHARM, GISSI-HF, MAGGIC, and SHFM [3]. The MAGGIC showed the best overall accuracy, similar to the GISSI-HF but better than the CHARM and particularly better than the SHFM. Researchers have come to the conclusion that performance of prognostic risk scores is still limited and physicians are reluctant to use them in daily practice.

In the previous decade, researchers have developed various prognostic risk scores for mortality and/or hospitalization for HF progression [10] but they have not received wide clinical application. A multiparametric prognostic score has been proposed for patients with reduced LVEF [11], which, from the authors' point of view, is more informative than the SHFM.

In addition, researchers [12] propose using the five strongest predictors of mortality in HF patients: old age, high blood urea nitrogen and NT-proBNP, low hemoglobin levels and non-use of beta-blockers.

The analysis of the initial clinical, laboratory, biochemical, and echocardiography data allowed us to answer very important clinical question — what factors can affect the prognosis of outpatients with HF. To this end, we analyzed the clinical, laboratory, biochemical and instrumental parameters of HF patients at admission to the hospital.

The highest long-term mortality risk upon admission to the hospital for HF patients was due to the levels of the NT-proBNP (risk 1,08, p=0,001), D-dimer (risk 1,062, p=0,018), urea (risk 1,048, p=0,016), creatinine (risk 1,006, p=0,016), ALT (risk 1,002, p=0,009).

The highest long-term mortality risk upon discharge from the hospital for HF patients was due to urea (risk 1,141, p=0,001), NT-proBNP (risk 1,101, p=0,002), neutrophil count (risk 1,064, p=0,002).

The findings may indicate several important management features for HF patients.

According to our data, the prognosis of outpatients with HF depends on the following parameters: HF severity confirmed by the NT-proBNP values; coagulation status (D-dimer); functional state of the kidneys (serum urea and creatinine); functional state of the liver (ALT).

The last two factors may reflect the congested liver and kidneys.

This should lead the doctor to the idea that a patient with HF should take drugs to reduce the severity of HF and diuretics, taking into account the increased risk of thrombosis in this category of patients.

According to our data, the prognosis of HF patients at the hospital stage with adequate therapy is corrected, mainly due to the reduction of kidneys and liver congestion. This is due to the fact that when a patient is discharged from the hospital, the long-term significance of factors such as creatinine and ALT decrease, and the role of D-dimer disappears (possibly due to anticoagulant therapy). However, there remains a risk factor such as serum NT-proBNP, indicating that patients should continue conventional therapy (angiotensin-converting enzyme inhibitors, beta-blockers, mineralocorticoid receptor antagonists).

The contribution of neutrophil count to long-term unfavorable prognosis was unexpected for us. It is known that neutrophils are key mediators in cardiac remodeling, causing an inflammatory response to remove necrotic tissue [13]. The experiment demonstrated the involvement of neutrophils in the mechanisms of cardiac dysfunction, expressed in an increase in type I collagen, which contributed to the remodeling progression and the formation of HF [14]. Our data suggest that peripheral blood neutrophils to some extent contribute to the prognosis of HF patients. This fact must be taken into account when evaluating patients upon discharge from the hospital and upon further outpatient observation.

A comparison of the factors involved in the long-term unfavorable prognosis of HF patients upon hospital admission and discharge leads us to another important conclusion — with an adequate therapy, the long-term prognosis of patients can be significantly changed by reducing both the number of factors and their role.

Study limitations: small sample size.

Conclusion

The long-term mortality risk factors of HF patients at admission are the levels of proBNP (risk 1,08, p=0,001), D-dimer (risk 1,062, p=0,018), urea (risk 1,048, p=0,016), creatinine (risk 1,006, p=0,016), ALT (risk 1,002, p=0,009). The long-term mortality risk factors of HF patients at discharge are urea (risk 1,141, p=0,001NT-proBNP (risk 1,101, p=0,002), and the neutrophil count (risk 1,064, p=0,002).

Relationships and activities: not.

References

1. Ponikowski P, Voors A, Anker S, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18:891-975. doi:10.1093/eurheartj/ehs104.
2. Ambrosy A, Fonarow G, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol. 2014;63:1123-33. doi:10.1016/j.jacc.2013.11.053.
3. Canepa M, Fonseca C, Chioncel O, et al. Performance of Prognostic Risk Scores in Chronic Heart Failure Patients Enrolled in the European Society of Cardiology Heart Failure Long-Term Registry. J Am Coll Cardiol HF. 2018;6:452-62. doi:10.1016/j.jchf.2018.02.001.
4. O'Connor C, Fiuzat M, Mulder H, et al. Clinical factors related to morbidity and mortality in high-risk heart failure patients: the GUIDE-IT predictive model and risk score. Eur J Heart Fail. 2019;6:770-8. doi:10.1002/ejhf.1450.
5. Mareev V, Fomin I, Ageev F, et al. Russian Heart Failure Society, Russian Society of Cardiology. Russian Scientific Medical Society of Internal Medicine Guidelines for Heart failure: chronic (CHF) and acute decompensated (ADHF). Diagnosis, prevention and treatment. Kardiologiia. 2018;58(6S):8-158. (In Russ.) doi:10.18087/cardio.2475.
6. De Buyzere M. Multi-biomarker risk stratification in heart failure: a story of diminished marginal returns after Herculean efforts? European Journal of Heart Failure. 2018;20:278-80. doi:10.1002/ejhf.1035.
7. Cleland J, Teerlink J, Davison B, et al. Measurement of troponin and natriuretic peptides shortly after admission in patients with heart failure — does it add useful prognostic information? An analysis of the Value of Endothelin Receptor Inhibition with Tezosentan in Acute heart failure Studies (VERITAS). European Journal of Heart Failure. 2017;19:739-47. doi:10.1002/ejhf.786.
8. Rahimi K, Bennett N, Conrad N, et al. Risk prediction in patients with heart failure. JACC Heart Fail. 2014;2:440-6. doi:10.1016/j.jchf.2014.04.008.
9. Ouwerkerk W, Voors A, Zwinderman A. Factors influencing the predictive power of models for predicting mortality and/or heart-failure hospitalization in patients with heart failure. JACC Heart Fail. 2014;2:429-36. doi:10.1016/j.jchf.2014.04.006.
10. Pocock S, Ariti C, McMurray J, et al. Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. Eur Heart J. 2013;34:1404-13. doi:10.1093/eurheartj/ehs337.
11. Agostoni P, Paolillo S, Mapelli M, et al. Multiparametric prognostic scores in chronic heart failure with reduced ejection fraction: a long-term comparison. European Journal of Heart Failure. 2018;20:700-10. doi:10.1002/ejhf.989.
12. Voors A, Ouwerkerk W, Zannad F, et al. Development and validation of multivariable models to predict mortality and hospitalization in patients with heart failure. European Journal of Heart Failure. 2017;19:627-34. doi:10.1002/ejhf.785.
13. Bonaventura A, Montecucco F, Dallegri F. Novel findings in neutrophil biology and their impact on cardiovascular disease. Cardiovascular Research. 2019;115:1266-85. doi:10.1093/cvr/cvz084.
14. Horckmans M, Ring L, Duchene J, et al. Neutrophils orchestrate post-myocardial infarction healing by polarizing macrophages towards a reparative phenotype. Eur Heart J. 2017;38:187-97. doi:10.1093/eurheartj/ehw002.