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Prognostic value of short-term trajectories of left ventricular ejection fraction in patients with first myocardial infarction and percutaneous coronary intervention

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ABSTRACT

Aim. To assess periprocedural dynamics of left ventricular ejection fraction (LVEF) in patients with first acute myocardial infarction (AMI) and percutaneous coronary intervention (PCI) without heart failure (HF) in the medical history, as well as its prognostic value in the development of cardiovascular complications in the postinfarction period.

Materials and methods. A prospective, single-center observational study included 131 patients with first AMI without HF in the past medical history and successful PCI. LVEF was assessed before PCI at admission and before discharge. In patients with reduced baseline LVEF of less than 50%, the criteria for its periprocedural improvement were chosen: 1) LVEF ≥ 50%; 2) ΔLVEF of more than 5%, but EF < 50%. The endpoints were hospitalization for the development of HF and death from cardiovascular disease in combination with the development of HF. The average follow-up period was 2.5 years.

Results. At admission, LVEF was < 50% in 74 (56.5%) patients. At discharge, according to the criteria for LVEF improvement, the proportion of patients in this group was 40.5 and 14.9%, respectively. In 44.6% of cases, no increase in LVEF was noted.

The predictors of the absence of periprocedural dynamics in LFEF included impaired regional contractility index > 1.94, left ventricular end-systolic volume > 57 ml, left ventricular end-diastolic diameter > 5.1 cm, pulmonary artery systolic pressure >27 mm Hg, NT-proBNP > 530 pg / ml, and E / A ratio > 1.06. During the follow-up period, 28 (21.4%) patients were hospitalized for the development of HF, 33 (25.2%) patients had a combined endpoint.

The absence of periprocedural improvement in left ventricular contractility was independently associated with higher odds of hospitalization for HF (relative risk (RR) 3.5; 95% confidence interval (CI) 1.63–7.55; $p = 0.001$) and the combined endpoint (RR 2.6; 95% CI 1.28–5.48; $p = 0.009$) in the postinfarction period.

Conclusion. In patients with first AMI and left ventricular systolic dysfunction, periprocedural evaluation of LVEF is reasonable to stratify the risk of adverse cardiovascular outcomes.

Keywords: acute myocardial infarction, periprocedural dynamics, ejection fraction, heart failure

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

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Conformity with the principles of ethics. All individuals signed an informed consent to participate in the study. The study was approved by the Ethics Committee at RUDN University.

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Прогностическое значение перипроцедурной динамики фракции выброса левого желудочка у пациентов с первым инфарктом миокарда и чрескожным коронарным вмешательством

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РЕЗЮМЕ

Цель исследования. Оценка перипроцедурной динамики фракции выброса левого желудочка (ФВ ЛЖ) у пациентов с первым острым инфарктом миокарда (ОИМ) и чрескожным коронарным вмешательством (ЧКВ) без анамнеза сердечной недостаточности (СН) и ее прогностическое значение в развитии сердечно-сосудистых осложнений в постинфарктный период.

Материалы и методы. В проспективное одноцентровое наблюдательное исследование включен 131 пациент с первым ОИМ без анамнеза СН и успешным ЧКВ. ФВ ЛЖ оценивалась до ЧКВ при поступлении и перед выпиской. У пациентов с исходно сниженной ФВ ЛЖ менее 50% были выбраны критерии перипроцедурного ее улучшения: 1) ФВ ЛЖ ≥ 50%; 2) ΔФВ ЛЖ более 5%, но ФВ < 50%. Конечными точками являлись госпитализация по поводу развития СН и смерть от сердечно-сосудистых заболеваний в комбинации с развитием СН. Средний период наблюдения составил 2,5 года.

Результаты. При поступлении у 74 (56,5%) пациентов отмечена ФВ ЛЖ менее 50%. При выписке в этой группе по критериям улучшения ФВ ЛЖ доля пациентов составила 40,5 и 14,9% соответственно. В 44,6% случаев прирост ФВ ЛЖ отсутствовал.

Предикторами перипроцедурного отсутствия динамики ФВ ЛЖ явились индекс нарушения локальной сократимости >1,94, конечно-систолический объем ЛЖ >57 мл, конечно-диастолический размер ЛЖ >5,1 см, систолическое давление легочной артерии >27 мм рт. ст, уровень NT-proBNP > 530 пг/мл, соотношение скоростей трансмитрального кровотока в фазу раннего наполнения к кровотоку в систолу предсердий >1,06. За период наблюдения 28 (21,4%) пациентов были госпитализированы по поводу развития СН, у 33 (25,2%) зарегистрирована комбинированная конечная точка.

Отсутствие перипроцедурного улучшения сократительной способности ЛЖ независимо ассоциировано с более высокой вероятностью госпитализации по поводу СН (относительный риск (ОР) 3,5; 95%-й доверительный интервал (ДИ) 1,63–7,55; p = 0,001) и наступления комбинированной конечной точки (ОР 2,6; 95%-й ДИ 1,28–5,48; p = 0,009) в постинфарктном периоде.

Заключение. У пациентов с первым ИМ и систолической дисфункцией ЛЖ целесообразна перипроцедурная оценка ФВ ЛЖ для стратификации риска развития неблагоприятных сердечно-сосудистых исходов.

Ключевые слова: острый инфаркт миокарда, перипроцедурная динамика, фракция выброса, сердечная недостаточность

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследование одобрено комитетом по этике Медицинского института РУДН.

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INTRODUCTION

Left ventricular (LV) systolic dysfunction is one of the key negative prognostic factors in patients with acute myocardial infarction (AMI) [1]; therefore, an assessment of left ventricular ejection fraction (LVEF) is recommended for all patients in this group [2, 3]. At the same time, LVEF is the only echocardiography parameter which is currently used as a predictor of the outcome in patients with ST-elevation myocardial infarction (STEMI) [4]. Depending on the value of LVEF after the first myocardial infarction (MI) at discharge, the authors recommend to identify groups with a high risk of mortality with follow-up periods of 1 year [5, 6] and 3 years [7]. However, several studies showed that a significant proportion of MI patients with reduced baseline LVEF may improve over time [8, 9], which results in a reduced risk of cardiovascular events in the postinfarction period. Conversely, patients who do not show an improvement in LVEF values after MI have an increased risk of adverse LV remodeling [10], life-threatening arrhythmias, cardiac arrest, cardiovascular disease, and all-cause mortality, regardless of revascularization, drug therapy, peak troponin level, and baseline LVEF [11, 12]. Studies on the dynamics of left ventricular contractility revealed the association of an improvement in LVEF with baseline levels of natriuretic peptide and MB-creatine kinase and the affected artery [13, 14]. Patients, whose LVEF improved from 2 weeks to several months after MI, had a better disease prognosis [11, 12, 15]. The rate of improvement in LVEF within a shorter period after percutaneous coronary intervention (PCI) and its relationship with distant outcomes are not well understood in patients with the first MI and without heart failure (HF) in the past medical history.

Despite recent advances in diagnosis and treatment, the incidence of complications after MI remains high [16–18]. Moreover, a lack of compliance and a possibility of long-term follow-up in such patients indicates relevance of assessing the role of short-term trajectories of LVEF after PCI at discharge and their impact on the development of HF and cardiovascular mortality. Since much attention is paid to the development of HF in the distant postinfarction period, the aim of this study was to assess the periprocedural dynamics of LVEF in patients with first MI and PCI without HF in the medical history, as well as its prognostic value in the development of cardiovascular complications in the postinfarction period.

MATERIALS AND METHODS

Our prospective, single-center observational study included 131 patients hospitalized in the Intensive Care Unit (ICU) of Vinogradov City Clinical Hospital. The average age was 61.85 ± 11.3 years; 68% of patients were men. STEMI was diagnosed in 74% of patients; the average LVEF at admission was 46 (44; 50)%. In 57 (43.6%) patients, LVEF was more than 50%, in 56 (42.7%) patients, it was 40–49%, in 18 (13. 7%) patients, it was less than 40%.

Inclusion criteria were the following: the first AMI diagnosed according to the Fourth Universal Definition of MI [19]; successful primary PCI in patients with STEMI, early (within 24 hours) PCI in patients with non-ST elevation myocardial infarction (NSTEMI), i.e. achieving TIMI grade III blood flow in the affected vessel; the sum of B-lines of less than 5 during lung ultrasound; no history of HF and dyspnea at admission, Killip 1.

Exclusion criteria were the following: intake of diuretics and vasopressors, the presence of primary pathology of the lungs (pneumonia), lung cancer, development of AMI complications (ventricular septal rupture, papillary muscle rupture with detachment), severe arrhythmia at the time of inclusion, including atrial fibrillation and(or) flutter.

The study was performed in compliance with the ethical principles of the Declaration of Helsinki developed by the World Medical Association "Ethical Principles for Medical Research Involving Human Subjects" and Rules of Clinical Practice in the Russian Federation.

All patients underwent a routine physical examination, electrocardiography, chest X-ray, echocardiography (EchoCG), lung ultrasound, coronary angiography, and coronary angioplasty with stenting. Laboratory studies were performed in accordance with Russian standards of medical care. Complete blood count and blood biochemistry were performed, including measurement of the troponin level twice (at admission and 6–12 hours after hospitalization) and additional measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP).

EchoCG was performed at admission to the ICU before PCI and at discharge, followed by post-processing using the EchoPAC station (General Electric Healthcare, USA) with an automatic assessment of LVEF [20–22]. LV diastolic function was assessed by the following parameters: E, E / A, e'lat, E / e'lat, left atrial volume index, peak tricuspid regurgitation velocity [23].

Patients with the baseline LVEF of less than 50% were additionally stratified based on the periprocedural dynamics of LV contractility. In patients with baseline LVEF of less than 50%, criteria for short-term improvement of LVEF were selected: 1) ≥ 50%; 2) ΔLVEF of more than 5%, but EF < 50% [15].

To assess pulmonary edema, eight-point lung ultrasound at admission was performed along the anterior surface of the chest. The sum of B-lines of less than 5 corresponded to the absence of pulmonary edema [4, 22]. During the hospital stay and within a year after the discharge, all patients received standard dual antiplatelet therapy before and after the intervention.

Endpoints. The main endpoints were hospitalization for HF and death from cardiovascular disease. These data were collected in a unified medical information and analytical system, as well as via telephone interviews with patients during a follow-up period of 2.5 years.

Statistical analysis. A data analysis was performed using SPSS software (version 23.0) and MedCalc Version 19. Quantitative variables were presented as the arithmetic mean and the standard deviation $M \pm SD$ (for normal distribution) and as the median and the interquartile range Me (Q_1; Q_3) (for non-normal distribution). Qualitative variables were described by absolute and relative values *n* (%). The distributions were checked using the Kolmogorov – Smirnov test. The Spearman's rank correlation coefficient was used to measure rank correlation. To assess the differences in quantitative variables between two independent samples, the Mann – Whitney *U* test was used. The Pearson's chi-square test ($\chi 2$) was used to compare the frequencies of qualitative variables. Results were considered statistically significant at two-tailed $p < 0.05$. The impact of a lack of improvement in LVEF on the risk of developing endpoints was assessed by the univariate and multivariate Cox regression model. Using logistic regression, predictors of changes in LVEF were studied, the odds ratio (OR) and 95% confidence interval (CI) were determined. Threshold values for quantitative predictors were set based on the ratio of marginal probabilities with the selected cut-off score. The cut-off score was chosen for the optimal trade-off between sensitivity and specificity. The primary criterion for evaluating survival was cumulative survival – the interval between the date of discharge and the date of the endpoint. The survival probability was estimated by constructing Kaplan-Meier survival curves; comparison was made using the log-rank test.

RESULTS

Comparative characteristics of patients with LVEF of more and less than 50% at admission are summarized in Table 1. Patients were matched by sex and age. In the group of patients with LVEF of less than 50%, atrial fibrillation in the past medical history was significantly more frequent; laboratory tests revealed significantly higher levels of troponin and NT-proBNP at admission and 6–12 hours after hospitalization. In addition, they had a higher risk of mortality according to the GRACE score.

Table 1

Characteristics of patients with AMI, *n* = 131

Parameter	LVEF 50%, *n* = 57 (43.5%)	LVEF < 50%, *n* = 74 (56.5%)	*p*
Age, years, $M \pm SD$	57 ± 10.97	62.5 ± 11.8	0.172
Men / women, *n* (%)	39(68)/18(32)	50(68)/24(32)	0.917
Body mass index, kg / m^2, $M \pm SD$	28.03 ± 4.26	28.71 ± 4.56	0.375
Atrial fibrillation in the past medical history, *n* (%)	2 (3.5)	10 (14)	0.049
NT-proBNP, pg / ml, Me (Q_1; Q_3)	330.70 (199; 988)	785 (314; 1768)	0.011
Troponin 1, ng / ml, Me (Q_1; Q_3)	0.11 (0.03; 0.73)	0.39 (0.07; 2.93)	0.005
Troponin 2, ng / ml, Me (Q_1; Q_3)	3.64 (0.68; 19.73)	23.68 (3.45; 61.24)	<0.000
STEMI / NSTEMI, *n* (%)	38(67)/19(33)	59(80)/15(20)	0.090

Note: Troponin 1 – at admission in the ICU; Troponin 2 – 6–12 hours after the hospitalization.

In a repeated EchoCG study before discharge of patients with baseline LVEF of less than 50%, an improvement in LV systolic function was observed in 55.4% of cases, which was assessed as 1) improvement in LVEF ≥ 50% (in 30 patients); 2) Δ LVEF of more than 5%, but not reaching 50% (in 11 patients). There was a slight decrease in LVEF in 4.6% of cases, and these patients were assigned to the group without changes in LVEF, which consisted of 33 patients.

Comparative characteristics of patients with improved LVEF and patients with no changes in this parameter are presented in Table. 2.

Predictors of the absence of short-term recovery of LVEF are listed in Table 3.

The relative risk of developing HF and the combined endpoint, obtained by univariate and multivariate analysis, was statistically significant in the group of patients with no short-term recovery of LVEF (Table 4).

Table 2

Comparative characteristics of patients with recovered LVEF and patients without changes in LVEF, *n* = 74

Patients	Patients with improved LVEF, *n* = 41	Patients without changes in LVEF, *n* = 33	*p*
IRCI, *M* ± *SD*	1.87 ± 0.15	1.96 ± 0.15	0.025
LVESV, ml	41 (35; 56)	58 (42; 71)	0.0055
SV, ml	47 (41;59)	41 (37; 47)	0.040
LVRWT	0.47 ± 0.1	0.53 ± 0.1	0.041
Patterns of LV geometry, *n* (%) Normal CR CH EH	 6 (14.6) 9 (22) 24 (58.5) 2 (4.9)	 2 (6) 7 (21.2) 15 (45.5) 9 (27.3)	 0.244 0.937 0.293 0.006
E, cm / s E / A LAVI, ml / m^2 PTRV, m / s	0.44 (0.40;0.60) 0.70 (0.60;0.82) 28.4 (24; 33) 1.9 (1.40; 2.20)	0.56 (0.42;0.66) 0.77 (0.57;1.36) 30 (23.5; 40) 2.5 (2.2; 2.8)	0.197 0.002 0.333 < 0.000
Systolic pressure in the pulmonary artery, mm Hg	20 (14;27)	30 (25;37)	< 0.000

Note: A – rate of transmitral blood flow in the atrial systole; E – rate of transmitral blood flow in the early filling phase; PTRV – peak tricuspid regurgitation velocity; IVLC – impaired regional contractility index; LAVI – left atrial volume index ; CH – concentric hypertrophy; CR – concentric remodeling; ESV – end-systolic volume; LVRWT – left ventricular relative wall thickness; SV – stroke volume; EH – eccentric hypertrophy.

Table 3

Predictors of the absence of short-term recovery of LVEF

Parameter	OR	95% CI	*p*
IRCI > 1.94	7.86	2.57–24.06	0.0001
LVESV > 57 ml	6.94	2.82–17.05	< 0.0001
LVEDD > 5.1 cm	8.45	2.99–23.87	< 0.0001
Systolic pressure in the pulmonary artery >27 mm Hg	5.39	2.31–12.56	0.0001
NTproBNP > 530 pg / ml	3.22	1.42–7.29	0.0044
E / A > 1.06	6.32	1.81–22.0	0.004
PTRV > 2.1 m / s	10.87	3.57–33.04	0.000

Note: IRCI – impaired regional contractility index; LVESV – left ventricular end-systolic volume; LVEDD – left ventricular end-diastolic diameter; E / A – ratio of transmitral blood flow rates in the early filling phase to blood flow in atrial systole; PTRV – peak tricuspid regurgitation velocity.

Table 4

Risk ratio for development of heart failure and a combined endpoint in patients, depending on the periprocedural dynamics of LVEF

Parameter	Development of HF					Combined endpoint				
	Frequency of the events,%	Univariate analysis, 95% CI	*p*	Multivariate analysis, 95% CI	*p*	Frequency of the events,%	Univariate analysis, 95% CI	*p*	Multivariate analysis, 95% CI	*p*
LVEF ≥ 50%, *n* = 30	14	0.50 (0.27–1.89)	0.71	0.75 (0.28–2.05)	0.58	19	0.73 (0.30–1.77)	0.48	0.69 (0.27–1.74)	0.44
Increase in LVEF ≥ 5%, *n* = 11	17	0.75 (0.18–3.18)	0.70	0.53 (0.12–2.35)	0.40	22	0.62 (0.14–2.61)	0.51	0.41 (0.09–1.81)	0.24

Table 4 (continued)

Parameter	Development of HF					Combined endpoint				
	Frequency of the events,%	Univariate analysis, 95% CI	*p*	Multivariate analysis, 95% CI	*p*	Frequency of the events,%	Univariate analysis, 95% CI	*p*	Multivariate analysis, 95% CI	*p*
No dynamics of LVEF, *n* = 33	39	3.1 (1.46–6.47)	0.003	3.5 (1.63–7.55)	0.001	42	2.3 (1.17–4.86)	0.017	2.6 (1.28–5.48)	0.009

Note: the multivariate analysis included sex, age, atrial fibrillation, diabetes mellitus, multivessel damage.

Patients without changes in LVEF at discharge after AMI were significantly more likely to develop endpoints (hospitalization for HF and CVD) than patients with normal baseline and improved LVEF (Fig. 1).

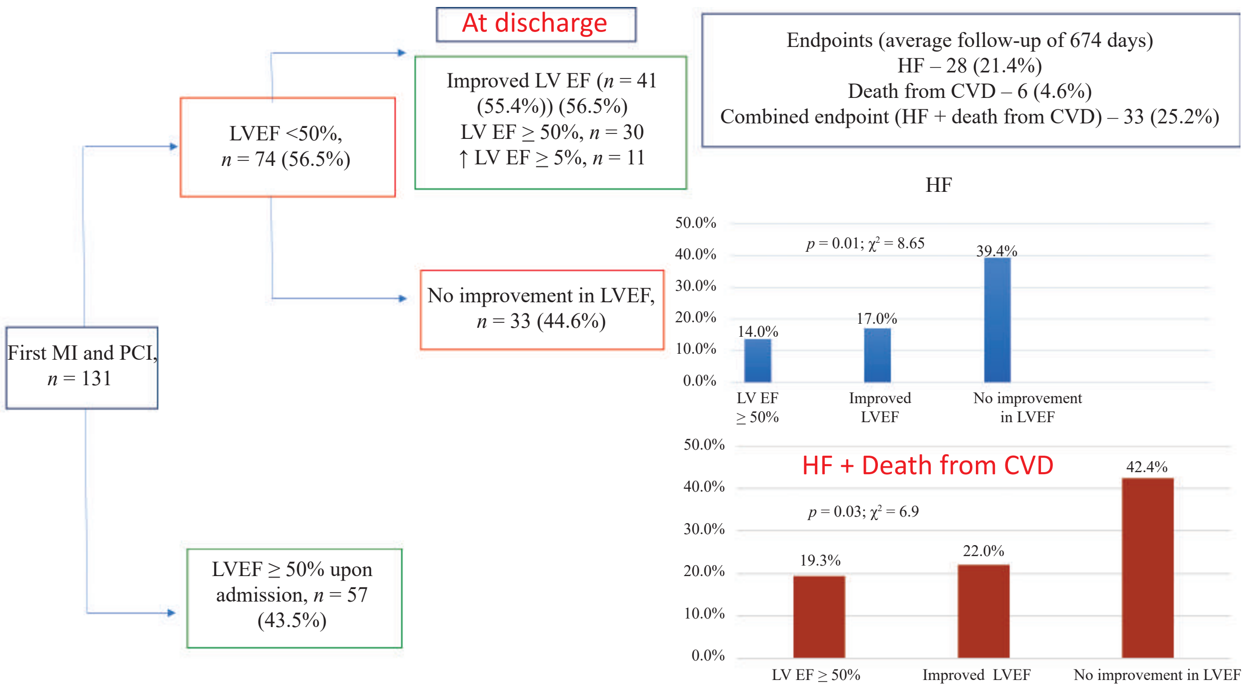

Fig. 1. Distribution of patients with AMI and PCI by LVEF at admission and discharge. Kaplan – Meier curves for cumulative survival probability depending on the improvement in LVEF at discharge are presented on fig. 2,3

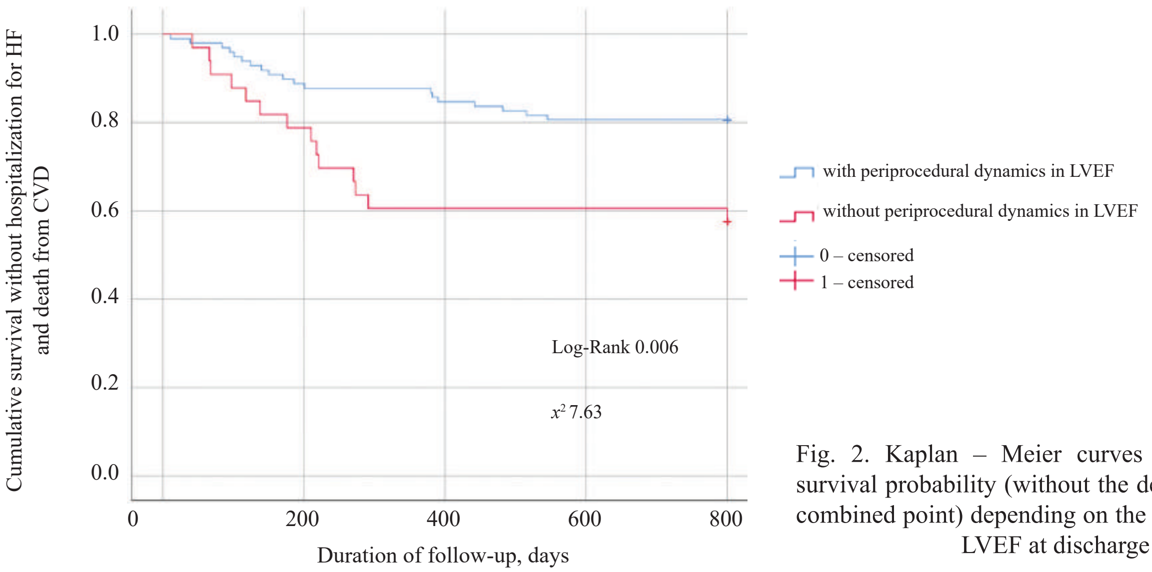

Fig. 2. Kaplan – Meier curves for cumulative survival probability (without the development of a combined point) depending on the improvement in LVEF at discharge

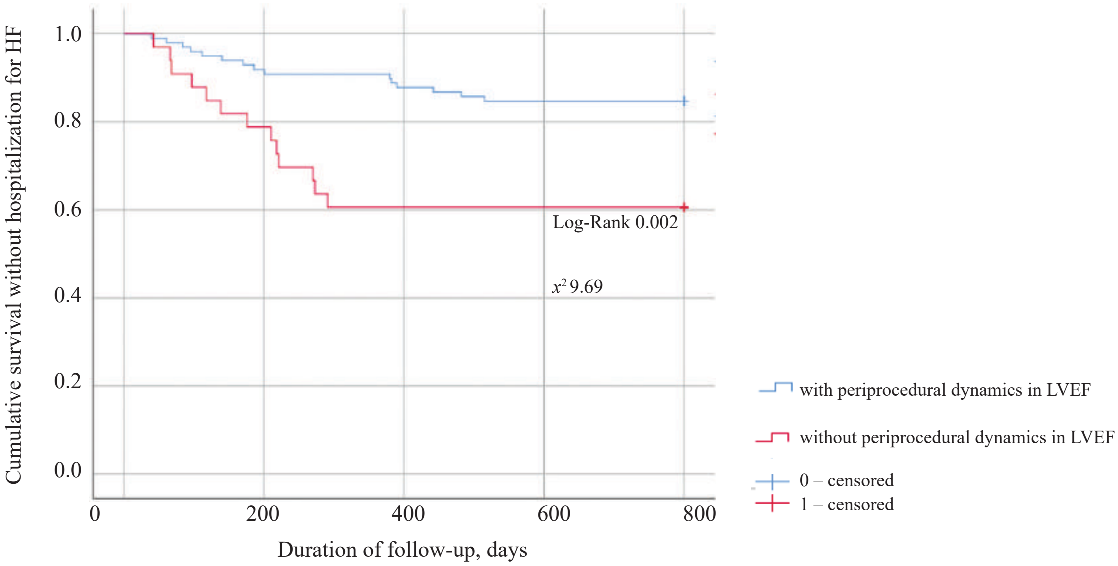

Fig. 3. Kaplan – Meier curves for cumulative survival probability (without hospitalization for HF) versus improvement in LVEF at discharge

DISCUSSION

Our study is the first attempt to assess the prognostic value of short-term improvement in LVEF in patients after the first MI and PCI. We demonstrated the association between the absence of improvement in LVEF at discharge according to the selected criteria and a significantly increased risk of developing HF and a combined endpoint. At the time of admission, more than half of the patients had LV systolic dysfunction and 44.6% of them did not recover at discharge.

Patients with and without positive dynamics in LVEF were comparable in terms of sex, age, risk factors for cardiovascular diseases, and the extent of coronary lesion. However, patients without LVEF dynamics had significantly higher LVESV, LVRWT, higher systolic pressure in the pulmonary artery, and eccentric LV hypertrophy, which emphasizes more significant structural and functional damage to the heart [23, 24].

Our data are consistent with the study by M.F Minicucci et al. [14], who revealed the recovery of LV function in the period from 2 weeks to 6 months in 25% of patients after MI. Y.Wu Wanda et al. [15, 25] demonstrated 8-fold reduction of all-cause mortality and a 10-fold decrease in the CVD risk in young AMI patients with improved LVEF. D.S.Chew et al. [11, 12] also found that elderly patients with MI and an improvement in LVEF of > 40% within 2 weeks had a 4-fold lower risk of future adverse events, all-cause mortality, and CVD compared with patients without changes in LVEF.

It was noted in the earlier studies that low LVEF at discharge in elderly patients after MI was correlated with an increased risk of mortality and rehospitalization [26]. In our study a decrease in baseline LVEF below 50% was not significantly associated with higher rates of hospitalization for HF and CVD per se ($p = 0.070$). However, we found an association of the absence of short-term dynamics in LV contractility with high frequency of hospitalizations for HF during the follow-up, as well as with the development of a combined endpoint. In addition, we identified predictors of the absence of LVEF dynamics in patients with the first MI, such as IRCI > 1.94, LVESV > 57 ml, LVEDD > 5.1 cm, systolic pressure in the pulmonary artery > 27 mm Hg, concentration of NT-proBNP > 530 pg / ml, and the E / A ratio > 1.06.

We did not find studies on periprocedural dynamics of LVEF in patients with the first MI and successful PCI and its effect on the prognosis of CVD. A detailed study of the contractility dynamics before and after PCI during hospitalization may be of great importance, since there is no decrease in the incidence of MI, and patients' compliance with follow-up, as well as its possibility, is not always optimal.

Assessment of LV EF is recommended in all patients presenting with AMI (grade 1 recommendation); however, recommendations are less clear in terms of the dynamic assessment of LVEF [2, 3]. It has been shown that many traditional EchoCG parameters, such as LV volumes, LVEF, and IRCI, can be used as prognostic markers [27]. Our work demonstrates that in patients with the first AMI, assessment of LV linear dimensions, LV diastolic function, and dynamic assessment of LVEF before and after PCI can provide valuable information on long-term prognosis, outcomes, and potential ongoing need for drug therapy.

Limitations and prospects of the study. Our study was limited by a small sample size and a relatively short follow-up period. There were also inherent limitations to the evaluation of LVEF using echoCG. However, echoCG has shown its accuracy in the assessment of LVEF compared with other imaging modalities and is widely used in clinical trials. In our work, all echoCG studies were performed by one doctor using one device, followed by post-processing on the EchoPAC station (General Electric Healthcare, USA) with an automatic assessment of LVEF, which allowed to minimize errors [20, 21]. There is an obvious need for a multicenter clinical study that would research the significance of short-term dynamics of LVEF in patients with the first AMI in relation to long-term prognosis.

CONCLUSION

In patients with the first MI, the frequency of LV systolic dysfunction at admission was 58.8%. 44.6% of patients had no improvement in LV contractility after successful PCI. The absence of improvement in LVEF is associated with a significantly increased risk of hospitalization for HF and a combined point. Therefore, in patients with the first AMI and LV systolic dysfunction, a short-term assessment of LVEF is reasonable to stratify the risk of developing adverse cardiovascular outcomes.

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