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Dynamics of Parameters of Transmitral Blood Flow and Markers of Myocardial Fibrosis in Patients With Myocardial Infarction

Aim	To study possible correlations between echocardiography (EchoCG) indexes and markers of myocardial fibrosis, procollagen I C-terminal propeptide (PICP) and procollagen III N-terminal propeptide (PIIINP) during one year following ST-segment elevation myocardial infarction (STEMI).
Material and methods	120 patients with STEMI were evaluated. EchoCG was used to assess dimensions and volumes of heart chambers, left ventricular (LV) systolic function, mean pulmonary arterial pressure (mPAP), and indexes of LV diastolic function (Em, early diastolic lateral mitral annular velocity; e', peak early diastolic septal mitral annular velocity; E/e', ratio of peak early diastolic transmitral inflow velocity and mitral annular velocity – E/A, ratio of peak early and late transmitral inflow velocities; DT, deceleration time of LV early diastolic filling). EchoCG indexes and serum concentrations of PICP and PIIINP were determined at 1 (point 1) and 12 (point 2) days of disease and one year after STEMI (point 3). The sample was divided into two groups: group 1 (n=86; 71.7%) included patients with a LV ejection fraction (EF) ≥50% and group 2 (n=34; 28.3%) consisted of patients with LV EF ≤49%.
Results	At one year, the number of patients with signs of diastolic dysfunction increased by 10% in group 1 whereas myocardial systolic dysfunction worsened in both groups. LV EF decreased in 15 (17.4%) patients of group 1 and in 4 (11.8%) patients of group 2. Concentrations of PIIINP were correlated with Em, E/e', mPAP, PICP, e', and LV EF.
Conclusion	Direct correlations between PIIINP concentrations and Em, E/e', and mPAP were found in the group with LV EF ≥50%. In the group with LV EF <50%, correlations were observed between PICP concentrations, LV EF, and e'. Also, in this group, the increase in PIIINP was statistically more significant. These results indicate continuing formation of myocardial fibrosis in a year following MI, which may underlie progression of chronic heart failure.

Keywords	Myocardial infarction; myocardial fibrosis markers; myocardial remodeling; diastolic dysfunction; chronic heart failure
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Coronary artery disease (CAD) has been the leading cause of high mortality and disability in the working-age population in recent decades [1]. Myocardial infarction (MI) is still one of the most prognostically unfavorable forms of CAD. Studies on chronic heart failure (CHF) after MI, including with preserved left ventricular (LV) contractility, are ongoing.

Diastolic heart failure makes up more than 50% of all CHF cases in the Russian Federation [2]. Fibrosis one of the key mechanisms of the development and progression of LV myocardial dysfunction. Researchers are currently focused on serum biomarkers of myocardial fibrosis, including collagen precursors. For example, markers characterizing the activity of collagen synthesis and collagen degradation are under discussion [3]. More emphasis should be put on procollagen type I carboxyterminal propeptide (PICP), which is a precursor of collagen type I and procollagen III amino-terminal propeptide (PIIINP), a precursor of collagen type III [3]. There are ambiguous data on the correlation between serum biomarkers of myocardial fibrosis and the echocardiographic structural characteristics of the heart, particularly after MI, which provides an incentive for further scientific research.

Our objective was to study the changes in myocardial diastolic dysfunction (DD) in patients with preserved

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and reduced LV ejection fraction (EF) within 1 year after ST-segment elevation MI (STEMI) and assess the correlation between the echocardiographic measurements and levels of biomarkers of myocardial fibrosis (PICP and PIIINP).

Material and methods

The study included 120 patients with STEMI who were admitted on an emergency basis to the Kemerovo Regional Clinical Cardiology Center n.a. Academician L. S. Barbarash. Patients were included according to a continuous sampling method.

Inclusion criteria:

1) STEMI diagnosed according to the European Society of Cardiology (ESC) Guidelines of 2015.
2) Signed informed consent to be included in the study.
3) Killip I–III acute heart failure.
4) Age >18 years.

Exclusion criteria:

1) Age >80 years.
2) Clinically significant comorbidity (exacerbated chronic diseases and/or the presence of mental illnesses).
3) Acute coronary syndrome caused by percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery.
4) Killip IV acute heart failure.
5) Aortic and/or mitral valve pathology.
6) Lethal outcome within the first 24 hours of hospitalization.

The mean age of patients in the analysis sample was 57.8 years. The study included 75.8% (n=91) male and 24.2% (n=29) female patients. All female patients were postmenopausal. All patients underwent standard laboratory and clinical examinations to verify MI during hospital admission. Moreover, at admission, all patients underwent coronary angiography using an INNOVA 3100 system (General Electric, USA), followed by PCI with stent implantation to the infarct-related artery.

Echocardiography was performed on a Sonos 2500 system on Day 1 (point I) and Day 12 (point II) of the disease and 12 months after STEMI (point III) [4]. The following parameters were determined according to the standard method in two- and one-dimensional modes: LV end-diastolic volume (EDV), LV end-systolic volume, LV end-diastolic dimension (EDD), LV end-systolic dimension (ESD), dimensions of the left atrium (LA) and right atrium, LV systolic function, mean pulmonary artery pressure (mPAP), condition of the valvular apparatus, LV wall thickness, the presence and amount of dyskinesia of the area of myocardial necrosis and scarring, the presence of an aneurysm, damage of papillary muscles, and areas of myocardial rupture. LV diastolic function was assessed based on the analysis of transmitral flow in pulse-wave Doppler mode and mitral annular displacement in tissue Doppler mode (Em, early mitral inflow velocity, e', mitral early diastolic velocity, E/e', the ratio between early mitral inflow velocity and mitral early diastolic velocity, E/A, the mitral ratio of peak early and late filling velocities, DT, deceleration time of early diastolic filling of LV). DD was confirmed if the following criteria were positive: Em <10 cm/s; e'<8 cm/s; LA volume index >34 mL/m^2.

LVEF was assessed by the Simpson's biplane method. The mean values of LVEF 40–49% were determined in 3 (2.5%) patients, LVEF <40% in 31 (26%) patients, and LVEF ≥ 50% in 86 (71.7%) patients.

The levels of PICP and PIIINP in the venous blood serum were studied at the hospital by enzyme immunoassay using BCM diagnostics laboratory kits in all patients on Day 1 (point I) and Day 12 of the disease (point II) and in 12 months after STEMI (point III). All hospitalized patients received standard therapy according to the ESC 2015 guidelines.

The control group of 20 healthy volunteers comparable to the study sample by age (mean age 57.9 years) and sex was formed to compare the values of serum biomarkers of interest: 15 (75%) male and 5 (25%) female patients. In the control group, PICP was 179.2 [163.5; 194.9] ng/mL, PIIINP 7.2 [6.8; 7.5] ng/mL. Patients were divided into two groups for further study because of the small number of patients with midrange LVEF and the fact that patients with preserved systolic function were of interest in this study. Group 1 comprised patients with LVEF ≥ 50% (n=86; 71.7%), and Group 2 included patients with LVEF<50% (n=34; 28.3%). Table 1 provides clinical data and medical history of the study sample.

The high prevalence of cardiovascular risk factors is obvious. Because 50% of patients were active smokers at the time of the disease, and almost 70% had a long history of hypertension. Moreover, hypercholesterolemia (23.3%) and carbohydrate metabolism disorders (14.2%) were highly reported.

It should be noted that a comparable number of patients in the comparison groups underwent routine revascularization within 12 months of follow-up. In Group 1, PCI with stent implantation was performed in five (5.8%) cases and CABG in one case. In Group 2, a stent was implanted to one patient (2.9%), and no CABG was performed.

Statistical analysis of the findings was carried out using Statistica 7.0. Nonparametric methods of statistical processing were used in the case of the non-normal

Table 1. Clinical data and medical history of patients with STEMI

Parameter	Abs.	%
Male	91	75.8
Female	29	24.2
Obesity (BMI ≥ 30 kg/m^2)	30	25.0
Carbohydrate disorder	17	14.2
Smoking at the time of hospitalization	61	50.8
Hypertension	83	69.2
Hypercholesterolemia	28	23.3
Family history of coronary artery disease	3	2.5
Postinfarction cardiosclerosis	7	5.8
History of angina	27	22.5
History of chronic heart failure	10	8.3
Atrial fibrillation	6	5.0
Cerebrovascular accident (within 12 months before the study)	4	3.3
Peripheral artery disease	1	0.8
Chronic kidney disease	2	1.7
Percutaneous coronary intervention (within 12 months before the study)	5	4.2

STEMI, ST-segment elevation myocardial infarction; BMI, body mass index.

distribution of data. Data are presented as the median and the interquartile range (Me [25th percentile; 75th percentile]). Two independent groups were compared quantitatively using the Mann – Whitney U-test. Three independent groups were compared using the Kruskal – Wallis rank analysis of variance and pairwise comparison using the Mann – Whitney test with Bonferroni correction. The Wilcoxon test was used to estimate the changes in parameters in the dependent groups. The correlation between variables was estimated by Spearman's rank correlation test. The differences between the comparison groups were statistically significant at $p<0.05$.

Results

Echocardiographic findings were compared in two ways (Table 2). At baseline, the comparison was carried out separately in each group between points I, II, and III. The parameters were then compared between the groups for each point as well. LVEF significantly decreased during the 12-month follow-up period in Group 1 versus the values obtained on Day 1 of the disease ($p=0.018$). A statistically significant decrease in LVEF on Day 12 after MI ($p=0.0001$) returned to the baseline level ($p=0.043$) in Group 2.

The negative trend of e' from Day 1 of the disease and after 12 months of follow-up with significant differences between all the points of determination was observed in Group 1. There were no statistically significant differences in the values obtained during the entire follow-up period in Group 2. When the obtained e' values were compared between two groups at each point, it was shown that there were statistically significant differences only on Day 12 of hospitalization.

E/e' ratio increased throughout the study in Group 1, which indicates the progression of DD in this group. This is also proven by statistically significant differences between all points in Group 1 and when compared to Group 2. Pathologically elevated values of e' were detected throughout the follow-up period in Group 2, with no significant differences between the three points.

In Group 1, Em decreased during the entire follow-up period from a normal value (7.2 [6.3; 7.8] cm/s) to a pathologically low value in 12 months. The obtained values differed statistically significantly between all three points. Differences were also found between the two groups at point I. Initially, reduced values of this parameter did not differ from each other in Group 2.

mPAP did not show statistically significant changes in either group during the entire follow-up period. However, there was a significant difference between the values obtained in Group 1 and Group 2 at each cut-off point. LA volume increased statistically significantly during hospitalization and the 12-month follow-up period in both groups. Moreover, the values of this parameter in the group of patients with preserved LVEF were statistically significantly higher than those in the group of patients with reduced LVEF (Table 2) at each cut-off point.

On Day 1 of MI, 29.1% (n=25) of patients in Group 1 had signs of DD. The number of patients with signs of DD in Group 1 increased by 10% (n=9) in 12 months, which made a total of 34 patients with signs of DD and demonstrated an aggravation of systolic myocardial dysfunction in both groups. LVEF decreased in 15 (17.6%) patients in Group 1 and 4 (11.7%) patients in Group 2.

Similarly, the levels of the analyzed biomarkers were compared within and between groups. Changes in the PICP levels showed a similar trend for 12 months in both groups (Figure 1).

Elevated baseline values of this parameter – 605 [560; 670] ng/mL in Group 1 and 588 [538; 634] ng/mL in Group 2 – decreased and in 12 months were 441 [315; 530] ng/mL in Group 1 and 468 [354; 524] ng/mL in Group 2. There were no intergroup differences at any cut-off point. However, statistically significant differences were found between points II and III and points I and III in each group.

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Table 2. Changes in the echocardiographic findings in the comparison groups during hospitalization and 12 months after STEMI

Parameter	Group	Cut-off points			p (intra-group differences)	p (intergroup differences)
		I	II	III		
LVEF, %	Group 1	59 [54; 63]	62.0 [56.0; 65.0]*, ***	53 [47; 56]*, **	0.000	^{I}0.000, ^{II}0.000, ^{III}0.000
	Group 2	45 [44; 48]	43 [37; 46]*, ***	45 [37; 48]*, **	0.000	
Em, cm/s	Group 1	7.2 [6.3; 7.8]	6.4 [4.2; 7.9]***	6.5 [4.0; 7.3]*, **	0.048	^{I}0.050, ^{II}0.048, ^{III}0.229
	Group 2	6.29 [5.4; 7.0]	6.1 [5.5; 8.3]	6.4 [5.4; 7.6]	0.687	
E/e'	Group 1	9.9 [9.4; 10.2]	11.1 [9.3; 13.2]*, ***	13.9 [12.1; 14.5]*, **	0.027	^{I}0.000, ^{II}0.027, ^{III}0.042
	Group 2	14.7 [14.1; 15.3]	14.8 [13.8; 14.9]	15.6 [14.9; 15.8]	0.658	
mPAP, mmHg	Group 1	25.0 [21.0; 26.0]	25.0 [23.0; 27.0]	24.0 [21.0; 28.0]	0.157	^{I}0.000, ^{II}0.002, ^{III}0.030
	Group 2	28.0 [25.0; 33.0]	26.5 [25.0; 31.0]	27.0 [24.0; 29.0]	0.137	
e', cm/s	Group 1	9.0 [8.6; 11.4]	8.8 [7.5; 10.4]	8.6 [7.2; 9.4]**	0.047	^{I}0.049, ^{II}0.467, ^{III}0.055
	Group 2	9.1 [7.2; 10.2]	8.6 [7.6; 10.2]	8.6 [6.06; 9.3]	0.663	
LA volume	Group 1	80 [73; 90]	84 [77; 92]*	84.5 [79; 95]*	0.004	^{I}0.000, ^{II}0.006, ^{III}0.005
	Group 2	69.5 [64; 79]	76.5 [71; 82]*	78 [73; 86]*	0.003	
E/A	Group 1	0.80 [0.71; 1.22]	0.79 [0.68; 1.21]	0.77 [0.66; 1.13]	0.896	^{I}0.453, ^{II}0.659, ^{III}0.828
	Group 2	0.74 [0.68; 1.08]	0.80 [0.68; 1.32]	0.79 [0.63; 1.21]	0.150	

The differences versus * point I, ** point II, *** point III are statistically significant ($p<0.05$).
STEM, ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; Em, early mitral inflow velocity; E/e', the ratio between early mitral inflow velocity and mitral early diastolic velocity; mPAP, mean pulmonary artery pressure; e', peak mitral early diastolic velocity; LA, left atrium; E/A, the mitral ratio of peak early and late filling velocities.

The PIIINP levels changed differently between the groups (Figure 2). Elevated baseline I levels of this marker in both groups (311.2 [220.1; 376.3] ng/mL in Group 1 and 309.0 [200.6; 423.0] ng/mL in Group 2) decreased by Day 12 of disease (223.3 [195.3; 312.1] ng/mL in Group 1 and 223.3 [200.2; 281.2] ng/mL in Group 2), almost reached the baseline values after 12 months of follow-up in Group 1 (312.6 [228.0; 383.8] ng/mL), which were higher than the baseline values in Group 2 (354.0 [222.0; 574.0] ng/mL). No differences were found between the groups at any of the cut-off points. The PIIINP levels statistically significantly decreased during hospitalization (p=0.000) and increased in 12 months versus Day 12 after MI (p=0.002) in Group 1. In Group 2, differences were found only between points II and III (p=0.004). A correlation analysis was performed to identify a possible relationship between echocardiographic measurements after 12 months of follow-up and markers of myocardial fibrosis, which were determined on Day 1 of the disease (Table 3).

Figure 1. Changes in the levels of procollagen type I carboxyterminal propeptide in the study groups within 12 months after ST-segment elevation myocardial infarction

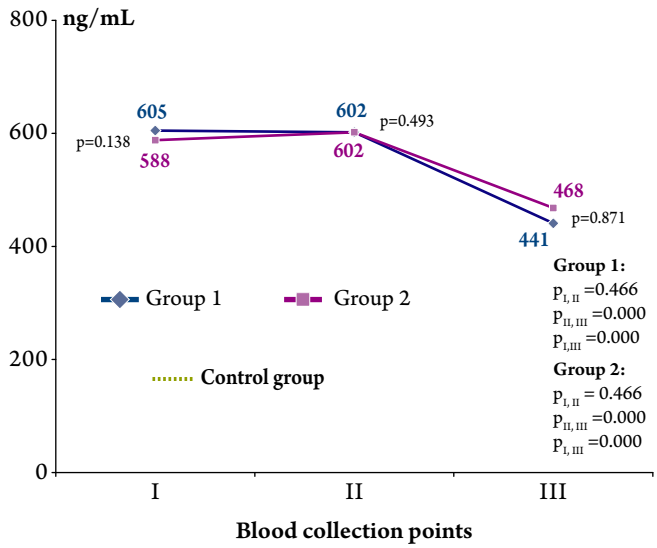
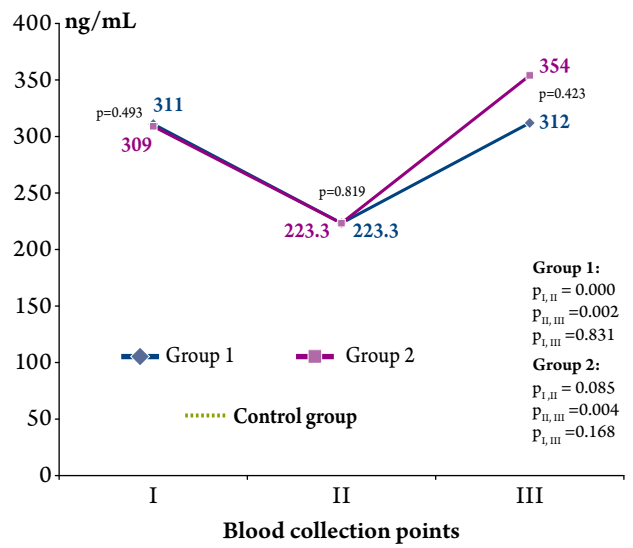


Figure 2. Changes in the levels of N-terminal propeptide of procollagen type III in the study groups within 12 months after ST-segment elevation myocardial infarction



PICP and PIIINP levels are clearly correlated with the parameters of diastolic function. It should be noted that the correlation between a decrease in LVEF and PICP levels was found only in patients with reduced baseline contractility (in both groups). Moreover, PICP levels were more significantly correlated with the parameters of diastolic function in patients with reduced LVEF, and PIIINP levels with those in patients with preserved systolic function.

Table 3. Results of the correlation analysis in the comparison groups

Parameter	r	p
Group 1		
PIIINP/Em	0.41	0.028
PIIINP/E/e'	0.47	0.029
PICP/DT	0.27	0.044
Group 2		
PICP/e'	-0.41	0.049
PIIINP/mPAP	0.41	0.042
PICP/LVEF	0.37	0.049

PIIINP, N-terminal propeptide of procollagen type III; Em, early mitral inflow velocity; E/e', the ratio between early mitral inflow velocity and mitral early diastolic velocity; PICP, procollagen type I carboxyterminal propeptide; DT, deceleration time of early diastolic filling; e', peak mitral early diastolic velocity; mPAP, mean pulmonary artery pressure; LVEF, left ventricular ejection fraction.

Discussion

We compared changes in echocardiographic parameters in patients with different systolic function and the levels of markers of myocardial fibrosis. Both groups showed a statistically significant decrease in LVEF and progression of LV DD in the 12 months after MI. Em and e' significantly decreased in the group with preserved LVEF.

The study of myocardial dysfunction, which causes CHF, is ongoing. At the same time, the role of DD (both isolated and combined with systolic dysfunction) in the unfavorable course of CHF is clear, though it presents objective difficulties for an adequate assessment and effective prediction of outcomes. The mechanism of DD development with subsequent formation of CHF with preserved LV contractility has been increasingly discussed in recent years. The mechanisms of transition from asymptomatic DD to diastolic CHF are still unclear. Perhaps an imbalance of collagen in the myocardium has a key role in this case. The predominance of collagen type I and type III synthesis versus degradation is thought to cause the accumulation of excess fibers and the formation of myocardial fibrosis followed by diastolic dysfunction [5].

Due to the high prevalence in patients with an unfavorable course of CAD, LV DD caused by recurrent myocardial ischemia and cardiosclerosis is currently of increased scientific interest. Data on the formation of DD, its early diagnosis, and treatment are ambiguous [6]. DD is known to develop independently from systolic disfunction, be associated with a decrease in exercise tolerance and quality of life; systolic dysfunction develops together with diastolic dysfunction and is not independent [7]. The long-term prognosis in such cases is unfavorable and depends on a combination of clinical factors and echocardiographic parameters of LV myocardial function. It is suggested that diastolic dysfunction precedes the onset of electrocardiographic signs of ischemia and impaired contractility and is an early marker of myocardial ischemia in patients with angina [8]. The severity of DD was established as dependent on the number and localization of post-infarction scars [9]. The correlation between the development of LV DD and the duration of CAD, LV mass, wall thickness, LV EDV, and EDD has been studied [10, 11]. Increased myocardial stiffness due to fibrosis is one of the main causes of DD. It was shown that patients with diastolic heart failure experience an intensive increase in levels of collagen type III in the interstitial space with age [12].

The comparison of changes in the PICP levels over the entire follow-up period in both groups revealed that there was a significantly high decrease in the levels of this marker during the 12 months from the onset of disease. A different trend was found for the PIIINP levels. The decrease in its levels in both groups during hospitalization was replaced by the increase during the 12-month follow-up period. Interestingly, the PIIINP levels in Group 2 were higher than those in the group with preserved systolic function.

Myocardial compliance was shown to decrease when the collagen levels increase twofold, and contractile function was damaged with a fourfold increase [13]. CHF is known to be associated with the changes in cardiomyocytes and the extracellular matrix. Collagen type I (more than 50%) and collagen type III (45%) are the main extracellular matrix proteins. Collagen types I and III are synthesized from procollagen precursors containing PICP and PIIINP [14]. The integrity of cardiomyocytes and the orientation of myofibrils depend on the presence of collagen types I and III. An imbalance in the synthesis and degradation of collagen, the predominance of collagen type III over

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ТОРГОВОЕ НАИМЕНОВАНИЕ: Сувардио® **МЕЖДУНАРОДНОЕ НЕПАТЕНТОВАННОЕ НАЗВАНИЕ:** розувастатин. **Регистрационный номер: ЛП-003023. ПОКАЗАНИЯ К ПРИМЕНЕНИЮ:** первичная гиперхолестеринемия по классификации Фредриксона (тип IIa, включая семейную гетерозиготную гиперхолестеринемию) или смешанная гиперхолестеринемия (тип IIb) в качестве дополнения к диете, когда диета и другие немедикаментозные методы лечения оказываются недостаточными; семейная гомозиготная гиперхолестеринемия в качестве дополнения к диете и другой липоснижающей терапии (например, ЛПНП-аферез) или в случаях, когда подобная терапия недостаточно эффективна; гипертриглицеридемия (IV тип по классификации Фредриксона) в качестве дополнения к диете; для замедления прогрессирования атеросклероза в качестве дополнения к диете у пациентов, которым показана терапия для снижения концентрации общего ХС и ХС-ЛПНП; первичная профилактика основных сердечно-сосудистых осложнений (инсульта, инфаркта, нестабильной стенокардии, артериальной реваскуляризации) у взрослых пациентов без клинических признаков ишемической болезни сердца (ИБС), но с повышенным риском ее развития (возраст старше 50 лет у мужчин, старше 60 лет у женщин, повышенная концентрация С-реактивного белка (≥ 2 мг/л) при наличии как минимум одного дополнительного фактора риска, таких как артериальная гипертензия, низкая концентрация ХС-ЛПВП, курение, семейный анамнез раннего начала ИБС). **ПРОТИВОПОКАЗАНИЯ.** Для суточной дозы 5 мг, 10 мг и 20 мг: повышенная чувствительность к розувастатину или любому из компонентов препарата; заболевания печени в активной фазе, включая стойкое повышение активности «печеночных» трансаминаз, а также любое повышение активности «печеночных» трансаминаз в сыворотке крови более чем в 3 раза по сравнению с верхней границей нормы (ВГН); тяжелые нарушения функции почек (КК менее 30 мл/мин); миопатия; одновременный прием циклоспорина; беременность, период грудного вскармливания; применение у пациентов, предрасположенных к развитию миотоксических осложнений; дефицит лактазы, непереносимость лактозы, синдром глюкозо-галактозной мальабсорбции (препарат содержит лактозу); возраст до 18 лет (эффективность и безопасность не установлены). Для суточной дозы 40 мг: повышенная чувствительность к розувастатину или любому из компонентов препарата; заболевания печени в активной фазе, включая стойкое повышение активности «печеночных» трансаминаз, а также любое повышение активности «печеночных» трансаминаз в сыворотке крови более чем в 3 раза по сравнению с верхней границей нормы (ВГН); наличие факторов риска развития миопатии/рабдомиолиза: почечная недостаточность умеренной степени тяжести (КК < 60 мл/мин), гипотиреоз, миопатии в анамнезе, включая наследственные; миотоксичность на фоне приема других ингибиторов ГМГ-КоА-редуктазы или фибратов в анамнезе, чрезмерное употребление алкоголя; состояния, которые могут приводить к повышению плазменной концентрации розувастатина, одновременный прием фибратов, применение у пациентов монголоидной расы; одновременный прием циклоспорина; беременность, период грудного вскармливания; применение у пациентов, предрасположенных к развитию миотоксических осложнений; дефицит лактазы, непереносимость лактозы, синдром глюкозо-галактозной мальабсорбции (препарат содержит лактозу); возраст до 18 лет (эффективность и безопасность не установлены). **СПОСОБ ПРИМЕНЕНИЯ И ДОЗЫ.** Внутрь. В любое время суток, независимо от приема пищи. Таблетку не разжевывать, не измельчать, проглатывать целиком, запивая водой. До начала терапии препаратом Сувардио® пациент должен начать соблюдать стандартную гипохолестеринемическую диету и продолжать соблюдать ее в течение всего периода терапии. Дозу препарата Сувардио® подбирают индивидуально с учетом целевых показателей концентрации холестерина и индивидуального терапевтического ответа на проводимую терапию. Рекомендуемая начальная доза препарата Сувардио® составляет 5 мг или 10 мг 1 раз в сутки как для пациентов, ранее не принимавших статины, так и для пациентов, переведенных на прием данного препарата после терапии другими ингибиторами ГМГ-КоА-редуктазы. При выборе начальной дозы следует руководствоваться концентрацией холестерина и возможным риском развития сердечно-сосудистых осложнений у данного пациента, а также следует оценить потенциальный риск развития побочных эффектов. При необходимости через 4 недели можно скорректировать дозу препарата. В связи с возможным развитием побочных эффектов при приеме дозы 40 мг по сравнению с более низкими дозами препарата окончательное титрование до максимальной дозы 40 мг следует проводить только у пациентов с тяжелой формой гиперхолестеринемии и высоким риском возникновения сердечно-сосудистых осложнений (особенно у пациентов с наследственной гиперхолестеринемией), у которых при приеме дозы 20 мг не была достигнута целевая концентрация холестерина и которые будут находиться под врачебным наблюдением. При назначении дозы 40 мг рекомендовано тщательное наблюдение врача. Не рекомендуется назначение дозы 40 мг пациентам, ранее не обращавшимся к врачу. **ПОБОЧНОЕ ДЕЙСТВИЕ.** Со стороны нервной системы — часто: головная боль, головокружение; нарушения со стороны эндокринной системы — часто: сахарный диабет 2-го типа; со стороны пищеварительной системы — часто: запор, тошнота, боль в области живота; лабораторные показатели: повышение активности креатинфосфокиназы (КФК), концентрации глюкозы, гликозилированного гемоглобина, билирубина в плазме крови, активности гамма-глютамилтранспептидазы, щелочной фосфатазы, нарушение функции щитовидной железы; прочие - часто: астенический синдром, гинекомастия, периферические отеки; нарушения со стороны мочевыделительной системы — при приеме розувастатина может наблюдаться протеинурия. Изменения содержания белка в моче (от отсутствия до наличия следовых количеств до уровня ++ и выше) наблюдаются менее чем у 1% пациентов, принимающих розувастатин в дозе 10 мг и 20 мг, и примерно у 3%, принимающих препарат в дозе 40 мг. Нарушения со стороны опорно-двигательного аппарата и соединительной ткани — часто: миалгия. **ОСОБЫЕ УКАЗАНИЯ.** Через 2—4 недели после начала лечения и/или при повышении дозы препарата необходим контроль показателей липидного обмена (при необходимости требуется коррекция дозы). Розувастатин, как и другие ингибиторы ГМГ-КоА-редуктазы, следует с особой осторожностью назначать пациентам с имеющимися факторами риска миопатии/рабдомиолиза. Рекомендуется проинформировать пациентов о необходимости незамедлительно сообщать врачу о случаях неожиданного появления мышечных болей, мышечной слабости или спазмах, особенно в сочетании с недомоганием или лихорадкой! Определение показателей функции печени рекомендуется проводить до и через 3 месяца после начала лечения. Возможны взаимодействия с другими лекарственными препаратами (см. соответствующий раздел инструкции). **ВЛИЯНИЕ НА СПОСОБНОСТЬ УПРАВЛЯТЬ ТРАНСПОРТНЫМИ СРЕДСТВАМИ, МЕХАНИЗМАМИ:** необходимо соблюдать осторожность при управлении автотранспортными средствами, занятиях потенциально опасными видами деятельности, требующими повышенной концентрации внимания и быстроты психомоторных реакций (риск развития головокружения).

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4. Согласно данным базы ООО «АЙКЬЮВИА Солюшнс» «Розничный аудит ГЛС и БАД в РФ» средняя розничная цена на национальном уровне в сентябре 2019 г. для лекарственного препарата Сувардио® таблетки, покрытые пленочной оболочкой 10 мг № 28 ЗАО «Сандоз» составляет 481,24 руб., для лекарственного препарата Сувардио® таблетки, покрытые пленочной оболочкой 10 мг № 90 ЗАО «Сандоз» составляет 970,48 руб., для лекарственного препарата Сувардио® таблетки, покрытые пленочной оболочкой 20 мг № 28 ЗАО «Сандоз» составляет 604,20 руб., для лекарственного препарата Роксера® таблетки, покрытые пленочной оболочкой 10 мг № 30 ООО «КРКА-РУС» составляет 596,32 руб., для лекарственного препарата Роксера® таблетки, покрытые пленочной оболочкой 10 мг № 90 ООО «КРКА-РУС» составляет 1296,60 руб., для лекарственного препарата Роксера® таблетки, покрытые пленочной оболочкой 20 мг № 30 ООО «КРКА-РУС» составляет 884,71 руб.

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Материал предназначен для медицинских (фармацевтических) работников.
GO FOR GOAL cholesterol control for life = ДВИЖЕНИЕ К ЦЕЛИ. Контроль холестерина в течение жизни.
Реклама.

collagen type I, and the breakdown of connections between cardiomyocytes are observed in the process of myocardial remodeling, which causes structure disorders and changes in myocardial function.

Our study demonstrated an increase in PIIINP levels (elevated at baseline) in 12 months of follow-up in both groups. The levels of this marker were the highest in the group with reduced LVEF versus Group 1, although the differences between the two groups were not statistically significant. The increased level of PIIINP may indicate an active synthesis of collagen type III. Moreover, active synthesis is most evident in the group with reduced LVEF. This fact became an additional key to the study of the complex process of fibrosis development and myocardial remodeling. Moreover, positive and negative correlations were found between the fibrosis markers and the parameters of LV diastolic function.

Interestingly, there is a correlation between PIIINP levels and the transmittal peak E in the group with preserved LVEF. This parameter identifies the moment when the ventricle expands to pull in blood from the atrium. The correlation between PICP levels and the transmitral peak A was shown in the group with reduced LVEF. This parameter is characterized by the process of returning residual blood from the atrium to the ventricle after equalization of pressure in the atrium and the ventricle due to active atrial systole.

Our findings are partially consistent with available data and confirm the assumption that procollagens I and III are actively involved in the development of myocardial fibrosis and subsequent LV diastolic dysfunction.

The correlation between PIIINP levels and echocardiographic parameters in patients with CHF has been studied by several groups. For example, Drapkina et al. [14] revealed the correlation between PIIINP levels and the E/A ratio, which led to the conclusion that PIIINP can be used as an early marker of DD. High PIIINP levels are associated with the most severe clinical course of CHF and an increased risk of death in patients with CHF and metabolic syndrome. Other studies have shown that elevated PIIINP levels are associated with a high risk of death in patients with CHF [14].

Conclusions

A statistically significant decrease in the left ventricular ejection fraction was detected within 12 months after myocardial infarction regardless of its value in the acute period of the disease. The number of patients with left ventricular diastolic dysfunction increased in the group with preserved myocardial contractility. Correlations were established between the levels of PIIINP, Em, and E/e' ratio, between the levels of PICP and DT – that is, the fibrosis markers are associated with the parameters of left ventricular diastolic function. More correlations between the levels of procollagen I, left ventricular ejection fraction, e' index, and the mean pulmonary artery pressure were found in the group with impaired left ventricular contractility.

These markers of myocardial fibrosis may contribute to varying extents in the development of diastolic dysfunction, depending on the initial left ventricular myocardial function. Increased PIIINP levels were detected, which were more pronounced in patients with reduced left ventricular ejection fraction. The obtained data indicate the continuous formation of myocardial fibrosis in 1 year after myocardial infarction, which may cause the progression of chronic heart failure.

No conflict of interest is reported.

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