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Assessment of the effectiveness of treatment in patients after acute coronary syndrome

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Aim. To assess the effectiveness of secondary drug prevention and surgical myocardial revascularization in patients with coronary artery disease (CAD) during long-term follow-up after acute coronary syndrome (ACS).

Material and methods. The study involved 400 patients with ACS discharged from the hospital in 2012-2016. The diagnosis was verified according to the European Society of Cardiology (ESC) guidelines. There were no exclusion criteria. We analyzed the data of medical records (complaints, medical history, physical examination, laboratory and instrumental data). Repeated data collection was carried out by distance survey and during a face-to-face examination during 2018. According to the clinical course of CAD, all patients were divided into 2 groups. Group 1 consisted of 151 patients with complicated course of CAD, group 2 — 249 patients with stable CAD. We analyzed drug therapy recommended at hospital discharge and taken at the time of the repeated examination. The drug names and daily dosage used for the secondary prevention of CAD were recorded. Assessment of survival without cardiovascular complications was carried out according to the Kaplan-Mayer analysis.

Results. Seven-year mortality was 22,5%. The total number of cardiovascular events was 37,7%. The main reason for the frequent complications was the insufficient secondary prevention of CAD after ACS. We found that the drugs and their dosage did not have a significant effect on survival. Statin use is associated with a paradoxical increase in the number of complications. The increased frequency of use and dosage of statins are a consequence of unfavorable course of CAD and do not have the proper preventive effect. For some groups of drugs, we observed irregular intake over the observation period. The low effectiveness of therapy is not only due to insufficient doses, but also in the frequent use of generic drugs. The significant effect of coronary angiography on the probability of cardiovascular complications compared with stenting is due to high proportion of coronary angiography use without revascularization.

Conclusion. The combination of following factors of drug therapy can explain the low effectiveness of secondary CAD prevention: low dose (26,1±2,8 mg for atorvastatin), irregular intake and common use of generic drugs (97,6% for statins). The contribution of surgical treatment to reducing cardiovascular complications is lower, the more significant residual coronary artery stenosis.

Key words: acute coronary syndrome, prevention, prediction of complications.

Relationships and Activities: not.

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The epidemic of coronary artery disease (CAD) reached the maximum in the 1960s. Over the past decades, cardiovascular mortality in all industrialized countries has been steadily declining. Primary and secondary prevention of atherosclerosis played an undeniable positive role [1-5]. Introduction of interventional treatment significantly contributed to improving the prognosis in patients with acute coronary syndrome (ACS). Nevertheless, it is believed that preventive potential has not yet been fully realized. In many patients with indications, myocardial revascularization is not performed effectively [6]. In recent decades, the researchers have created the concept of evidence-based medicine. The science-based approach allowed to reasonably introduce into clinical practice numerous therapeutic strategies and drugs that improve the prognosis of patients with CAD [4, 5]. According to studies, any prevention measures lose traction in patients with low socioeconomic status due to insufficient adherence to treatment. It is not without reason that in studies, along with conventional risk factors, authors assess the income level [7, 8]. The CAD-related standardized mortality rate in patients >50 years of age was 2153,1 for men and 1288,2 for women per 100 thousand patients with CAD. The same parameters in Russia are 2-3 times higher than in countries such as the USA, Great Britain, France, and Germany [2, 3].

The aim of secondary prevention is to reduce the incidence of cardiovascular events (CVE) by achieving the target values of lipids, blood pressure (BP) and heart rate (HR). An important component of prevention is a monitoring of patients. Especially valuable information is provided by registers with long-term follow-up [1]. In the Russian Federation, there are few registers with small number of patients and a short-term follow-up. As a result, cardiologists are forced to use the scores developed using patient registers in North America and Europe. This makes relevant the conduction of studies in Russia with long-term follow-up, assessment of the effectiveness of secondary prevention and interventional treatment of CAD.

The aim of the study was to assess the effectiveness of secondary drug prevention and surgical myocardial revascularization in patients with coronary artery disease (CAD) during long-term follow-up after acute coronary syndrome (ACS).

Material and methods

The study included 6,2% (n=400) of randomly selected patients with ACS discharged from the emergency cardiology department of the Oryol Regional Clinical Hospital in 2012-2016. All participants gave written informed consent. There were no exclusion criteria. We analyzed the data of medical records (complaints, medical history, physical examination, laboratory and instrumental data). Repeated data collection was carried out by distance survey (by telephone or mail), by request to Civil Registry Department of the Oryol Region (death cases), and by face-to-face examination (rehospitalization or outpatient visit). A telephone survey of patients and relatives was carried out during 2018 and included patients rehospitilized until 2018. Thus, 211 patients (52,7%) were re-examined in face-to-face manner, 152 patients — by distance survey (by telephone or mail), and 37 deaths were registered by request to Civil Registry Department.

Upon re-examination of patients, the levels of blood pressure (BP), heart rate (HR), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were determined. The delta% of all parameters was calculated using the formula — ((end value-initial value)/initial value)*100%. Hyperlipidemia was established at TC >5 mmol/L and LDL-C >2,5 mmol/L.

All patients were divided into 2 groups depending on the clinical course of CAD. The criterion for separation into groups was the registration of one of the following major adverse cardiac events (MACE): cardiovascular death, recurrent ACS (unstable angina, myocardial infarction (MI)), stroke, repeat myocardial revascularization, ischemic cardiomyopathy (ICMP) with progressive heart failure (HF) [5, 9]. Group 1 consisted of 151 patients with a complicated course of CAD, group 2 — 249 patients with a stable course of CAD (Figure 1).

Figure 1 shows that most frequent MACE were cardiovascular death and repeated ACS (95,1%). Death was considered cardiovascular by reliable clinical, instrumental and autopsy data, including cases where other causes were unlikely. The 7-year mortality was 22,5%.

Table 1 presents the clinical characteristics of patients.

We analyzed therapy, recommended at discharge and received at the time of re-examination/questioning. The name and daily dosage of drugs from the main pharmacological classes used for the secondary prevention of CAD were taken into account: statins, beta-1 blockers (BB), angiotensin converting enzyme inhibitors (ACE inhibitors)/angiotensin II receptor blockers (ARB), and antiplatelet agents. We also analyzed the effects of different drug dosages on the probability of MACE. For statins, low and moderate doses were considered 10-20 mg/day, and optimal — 30-40 mg/day (equivalent to atorvastatin). For BB, the lowest dose was 2,5 mg/day, and optimal — 5-10 mg/day (equivalent to bisoprolol). For ACE inhibitors/ARB, the low dose was up to 10 mg/day and 50 mg/day, and optimal — 20 mg/

day and 100 mg/day (equivalent to enalapril and losartan, respectively) [10].

For statistical processing, parametric and nonparametric statistics were used. In normally distributed traits (estimated by the Kolmogorov-Smirnov test), the Student's t-test was used to determine the significance of the differences. In non-normally distributed traits, a comparison was made by the Mann-Whitney U-test. Yates's chi-squared test was used for frequency comparison. The data in the tables are presented as mean (M) and standard deviation (SD) for the parametric tests and as the median [Q1; Q3] for the nonparametric tests. Evaluation of the treatment effects on the survival of patients without MACE was carried out by constructing Kaplan-Meier survival curves Differences in empirical survival functions were evaluated by Gehan-Wilcoxon test. The differences were considered statistically significant at $p<0,05$.

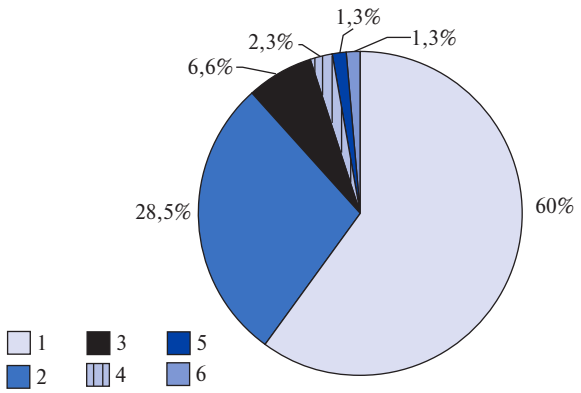

Figure 1. The proportion of major adverse cardiovascular events. **Note:** 1 — deaths (60%); 2 — unstable angina (28,5%); 3 — myocardial infarction (6,6%); 4 — repeated myocardial revascularization (2,3%); 5 — acute cerebrovascular accident (1,3%); 6 — ischemic cardiomyopathy with progressive heart failure (1,3%).

Results

Table 1 shows that patients with a complicated clinical course of CAD are initially older, more likely to have hypertension, have a more severe heart failure (according to NYHA classification) and higher mortality risk estimated by GRACE2

Table 1

Clinical characteristics of patients with coronary artery disease included in the study (M±SD), (n, %)

Parameter			Complicated clinical course (n=151)	Stable clinical course (n=249)	p
Mean age, years			64,2±12,0	59,4±11,3	<0,001
Gender	Men		96 (63,6)	173 (69,5)	>0,05
	Women		55 (36,4)	76 (30,5)	>0,05
Risk factors of coronary artery disease	Hypertension		132 (87,4%)	196 (78,7%)	<0,05
	Smoking		51 (33,8)	115 (46,2)	<0,05
	Dyslipidemia		76 (50,3)	129 (51,8)	>0,05
	Diabetes		30 (19,8)	39 (15,7)	>0,05
	Body mass index, kg/m^2		28,4±5,4	28,6±4,8	>0,05
Disease	MI	Anterior	55 (36,4)	73 (29,3)	>0,05
		Inferior	33 (21,8)	83 (33,3)	<0,01
	Unstable angina		63 (41,8)	93 (37,4)	>0,05
Heart failure (NYHA)		Class 1	20 (13,2)	59 (86,8)	<0,001
		Class 2	67 (44,4)	147 (55,6)	<0,05
		Class 3	64 (42,4)	43 (57,6)	<0,01
Mortality risk (GRACE2 and TIMI)	Low		97 (64,2)	215 (86,3)	<0,001
	Moderate		44 (29,1)	30 (12,0)	<0,001
	High		10 (6,7)	4 (1,7)	<0,01
Number of CA			69 (45,7)	164 (65,9)	<0,001
Number of PCI			46 (30,5)	105 (42,2)	<0,05
Drug therapy before hospitalization	Statins		28 (18,5)	24 (9,6)	<0,05
	BB		41 (27,1)	63 (25,3)	>0,05
	ACE inhibitors/ARB		60 (39,7)	84 (33,7)	>0,05
	Antiplatelet agents		52 (34,4)	63 (25,3)	<0,05

Abbreviations: MI — myocardial infarction, PCI — percutaneous coronary intervention, CA — coronary angiography, BB — beta-1 blockers, ACE inhibitors — angiotensin-converting enzyme inhibitors, ARB — angiotensin II receptor blockers.

and TIMI scores. The proportion of smokers was less, possibly due to the larger number of women in the group with complicated course of CAD. Patients of group 1 received statins and antiplatelet agents more often before entering the study. This possibly due to more severe patients' condition: less cases of inferior MI, and more — anterior MI and unstable angina.

Figure 2 shows that lipid normalization leads to improving the survival without MACE.

There were following TC values: group 1 — 5,4 [4,3; 6,8] mmol/L; group 2 — 4,5 [3,7; 5,3] mmol/L; $p<0,05$.

Figure 3 shows that patients with stable clinical course of CAD had a LDL-C decrease by more than 20%.

Thus, despite a significant decrease, LDL-C values did not reach the target level (<1,8 mmol/L according to ECC guidelines).

At the same time, statin administration did not have a prognostic value in reducing the number of MACE (Figure 4).

Moreover, statin therapy was associated with lower survival. It turns out that statin use and lipid profile changes affect prognosis in different ways. Consequently, lipid profile changes and prognosis improvement are difficult to associate with the statin use.

An analysis of the survival without MACE depending on the statin dosages was made (Figure 5).

An increased dose of statins confirms the above findings about the negative effects of statins on survival.

Figure 6 shows the Kaplan-Mayer curve, which demonstrates the association between BB administration and incidence of MACE.

It can be seen that patients taking BB did not have reduced MACE risk.

Figure 7 shows the dependence of delta% HR on the actual BB intake upon re-examination.

It can be seen that BB administration slightly affects HR, and without BB, it increases by 8%. Statistical analysis showed that delta% HR does not affect the probability of MACE.

There were no differences in MACE incidence depending on BB dosage (Figure 8).

The effects of ACE inhibitors/ARB on the MACE incidence were studied (Figure 9).

There were no statistically significant effects of ACE inhibitors/ARB on the survival of patients without risk of MACE.

Figure 10 shows the dependence of delta% SBP on the clinical course of CAD.

A significant difference of delta% SBP was revealed. In a stable course of CAD, a decrease in SBP was by 3,7% [-15,4; 7,7]. The same differences regarding DBP were not revealed.

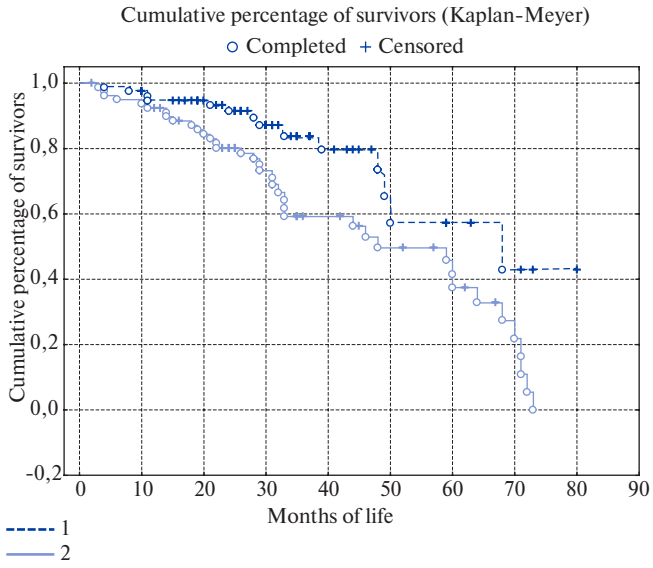

Figure 2. The Kaplan-Mayer curves for the patients without MACE with different changes of the lipid profile.
Note: 1 — lipid profile normalization; 2 — preserved hyperlipidemia; $p<0,05$. At the re-examination time, in the group of complicated clinical course of CAD (n=53), there were 19 patients with hyperlipidemia (64,1%); in the group of stable clinical course of CAD (n=105), there were 35 patients with hyperlipidemia (33,3%). $\chi^2 = 13,6$; p=0,0004.

Figure 11 shows the survival curves in patients without MACE depending on the intake of low or increased doses of ACE inhibitors/ARB. There was no statistically significant difference. However, there was a tendency towards MACE decrease with high doses of ACE inhibitors/ARB.

Figure 12 shows the survival curves depending on the intake of antiplatelet agents. Administration of antiplatelet agents did not significantly decrease the incidence of MACE.

We compared the treatment with four-component therapy (statins, BB, ACE inhibitors/ARB, and antiplatelet agents) and without taking any medication with respect to the risk of MACE. Upon re-examination, no statistically significant differences were found.

To find the reasons for the low effectiveness of drug therapy in the secondary prevention, we analyzed the frequency of use of the branded and generic medicines in patients after ACS (Figure 13).

Most often, patients used branded BB (Concor®, Betaloc® ZOK, Nebilet®). Therefore, this class can be used as an example to consider the effect of branded and generic medicines on survival without MACE (Figure 14).

There was no significant difference in the effect on the prognosis; however, taking the branded medicines at the optimal dose is characterized by a tendency towards better survival of patients without

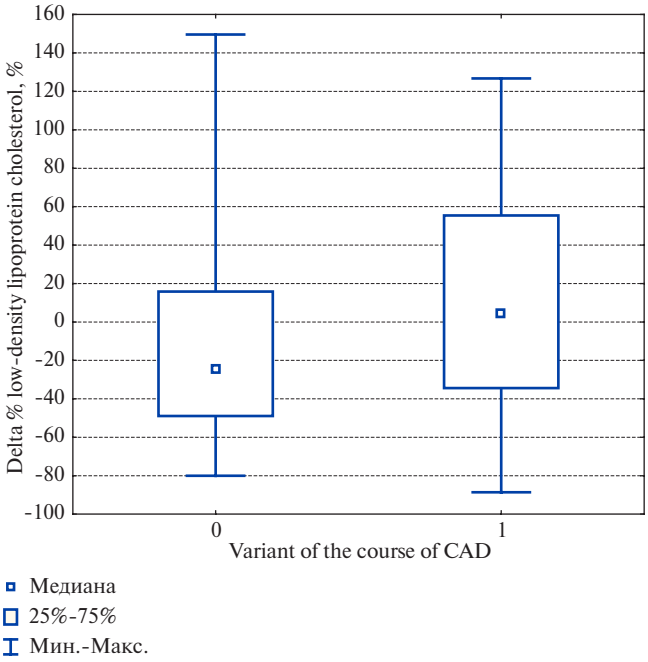

Figure 3. Comparison of delta% of LDL-C depending on the CAD course.
Note: 0 — stable clinical course of CAD; 1 — complicated clinical course of CAD; p<0,05. The median of LDL-C at re-examination time: group of stable clinical course of CAD — 2,78 [2,0; 3,45]; group of complicated clinical course of CAD — 3,6 [2,6; 4,7].

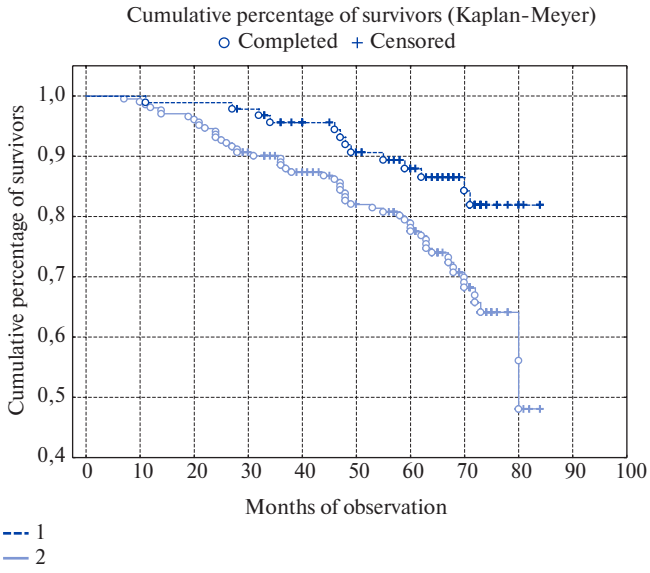

Figure 4. Kaplan-Mayer curves for the patients without MACE and with/without statin therapy.
Note: 1 — without statins; 2 — with statins; p<0,01. In the group of complicated clinical course of CAD (n=72), 59 patients took statins (81,9%). In the group of stable clinical course of CAD (n=225), 146 patients (64,9%) took statins. χ^2=7,4; p=0,01.

MACE [11]. At the same time, we recorded the wave-like nature of the curve divergence: the initial curve divergence after 1 year of treatment was followed by merging until the end of 4 years of follow-up. Such

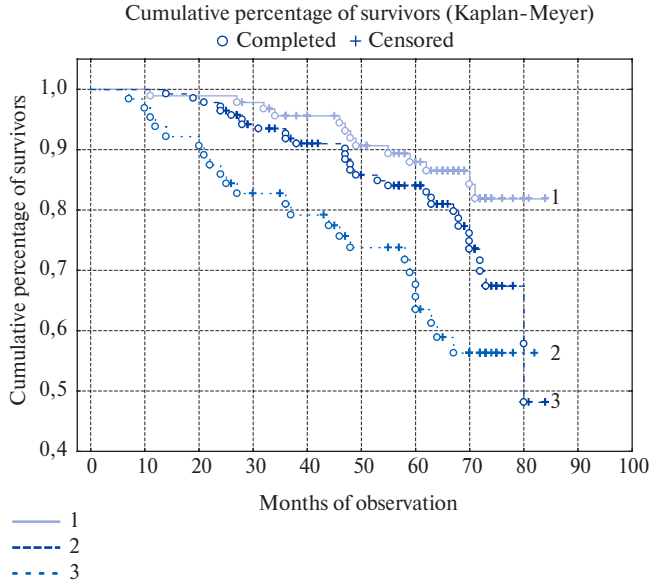

Figure 5. Kaplan-Mayer curves for patients without MACE depending on the statin dose.
Note: 1 — without statins; 2 — low-dose statins; 3 — dose of statins recommended by ECC*; * — p<0,001 (compared with patients not taking statins).
In the group of complicated clinical course of CAD, 13 patients (18,0%) did not take statins, 37 — low-dose statins (51,4%), and 22 — recommended statin dose (30,6%). In the group of stable clinical course of CAD, 79 patients (35,1%) did not take statins, 111 — low dose statins (49,3%), and 35 — recommended statin dose (15,6%). Differences were revealed among patients not taking statins (p=0.009) and patients taking the recommended dose of statins (p=0,006).

changes are possible with irregular treatment, when periods of optimal treatment are followed by low-dose therapy or complete drug withdrawal.

Figure 15 shows the peak number of MACE (except for deaths) during the entire follow-up.

At the beginning of the second year, the effectiveness of secondary prevention is reduced, which leads to an increase in the number of MACE. The peak number of MACE (except for deaths) was observed in the fourth year of follow-up. It is possible that with an increase in the MACE (except for deaths) number, drug therapy intensifies. This, perhaps, contributes to an increase in the effectiveness of prevention with drugs, leading to a divergence of survival curves (Figure 14).

According to the ECC guidelines, mortality risk (GRACE2 and TIMI) was estimated for all patients with ACS, on the basis of which the indications for interventional management were determined. Overall, coronary angiography (CA) were performed in 57,2% (n=229) of all patients with ACS. According to the results, 204 patients with significant coronary stenosis were identified, and 74,0% (n=151) of them underwent percutaneous coronary intervention (PCI). The remaining 26% (n=53) of patients had

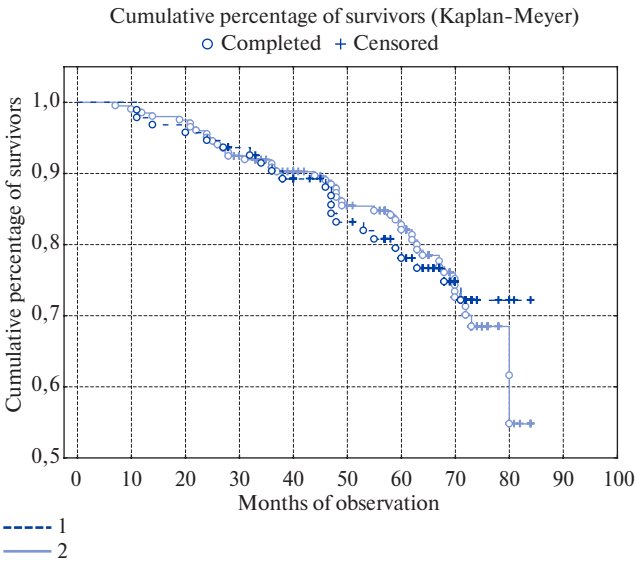

Figure 6. Kaplan-Mayer curves for patients without MACE and with/without BB therapy; p>0,05**.**
Note: 1 — without BB; 2 — with BB.
In the group of complicated clinical course of CAD (n=72), 50 patients took BB (69,4%). In the group of stable clinical course of CAD (n=224), 152 patients (67,8%) took BB. χ^2=0,06; p>0,05.

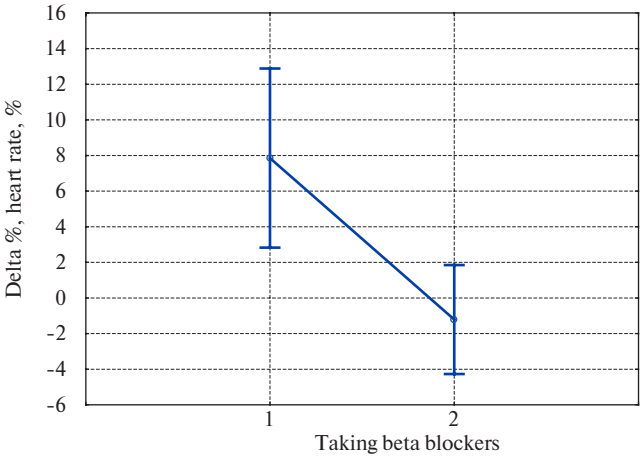

Figure 7. Dependence of delta% of heart rate and BB administration.
Note: 1 — without BB; 2 — with BB; p<0,01.

significant single, double, and triple vessel disease, and due to technical difficulties revascularization was not performed. In such cases, at discharge, we recommended revascularization in the federal center. Twenty five patients had insignificant coronary stenosis or its absence (n=2). In these cases, revascularization was not indicated.

Figure 16 shows the survival curves of patients without MACE depending on the surgical strategies.

It can be seen that there was a tendency towards a decrease in the number of MACE after PCI.

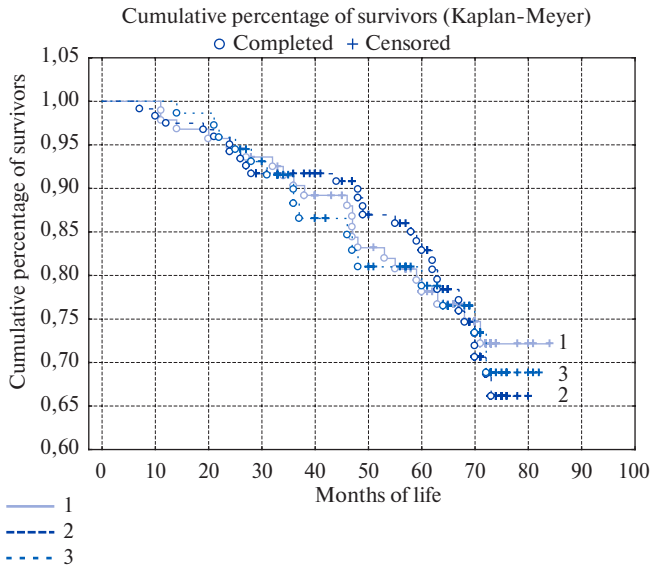

Figure 8. Kaplan-Mayer curves for patients without MACE depending on the BB dose.
Note: 1 — without BB; 2 — low-dose BB; 3 — moderate- and high-dose BB; p>0,05.
In the group of complicated clinical course of CAD, 22 patients did not take BB (30,5%), 33 — low-dose BB (45,8%), and 17 — moderate- and high-dose BB (23,7%). In the group of stable clinical course of CAD, 72 patients (32,1%) did not take BB, 95 — low-dose BB (42,4%), and 57 — moderate- and high-dose BB (25,5%). No differences were found (p>0,05).

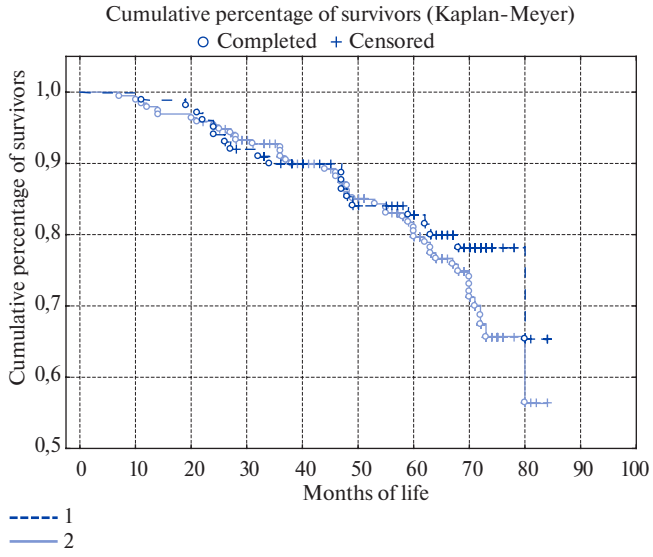

Figure 9. Kaplan-Mayer curves for patients without MACE and with/without ACE inhibitors/ARB therapy.
Note: 1 — without ACE inhibitors/ARB; 2 — with ACE inhibitors/ARB; p>0,05.
In the group of complicated clinical course of CAD (n=71), 51 patients took ACE inhibitors/ARB (71,8%). In the group of stable clinical course of CAD (n=225), 145 patients (64,4%) took ACE inhibitors/ARB. χ^2=1,3; p>0,05.

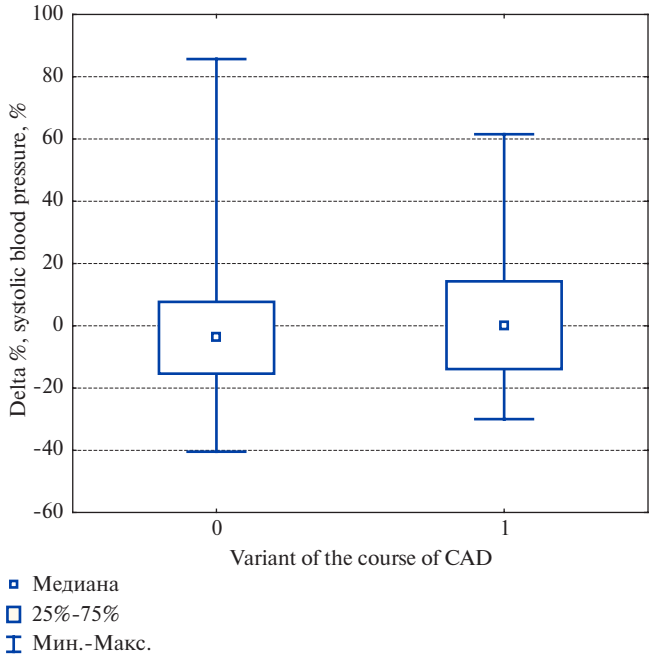

Figure 10. Dependence of delta% of SBP and patients receiving ACE inhibitors/ARB.
Note: 1 — without ACE inhibitors/ARB; 2 — with ACE inhibitors/ARB; p<0,05.

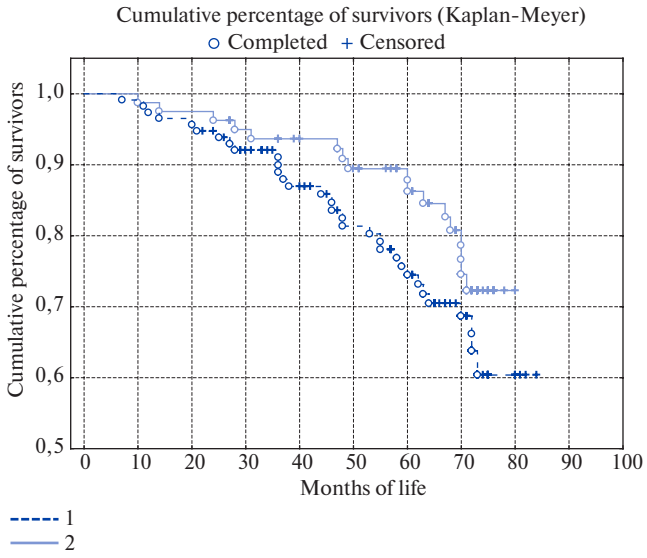

Figure 11. Kaplan-Mayer curves for patients without MACE depending on ACE inhibitors/ARB dose.
Note: 1 — low-dose ACE inhibitors/ARB; 2 — optimal dose of ACE inhibitors/ARB; p>0,05.
In the group of complicated clinical course of CAD, 32 patients (62,7%) took a low-dose ACE inhibitors/ARB, 19 — optimal dose of ACE inhibitors/ARB (37,3%). In the group of stable clinical course of CAD, 78 patients (53,8%) took a low-dose ACE inhibitors/ARB, 67 patients (46,2%) — optimal dose of ACE inhibitors/ARB. No differences were found (p>0,05).

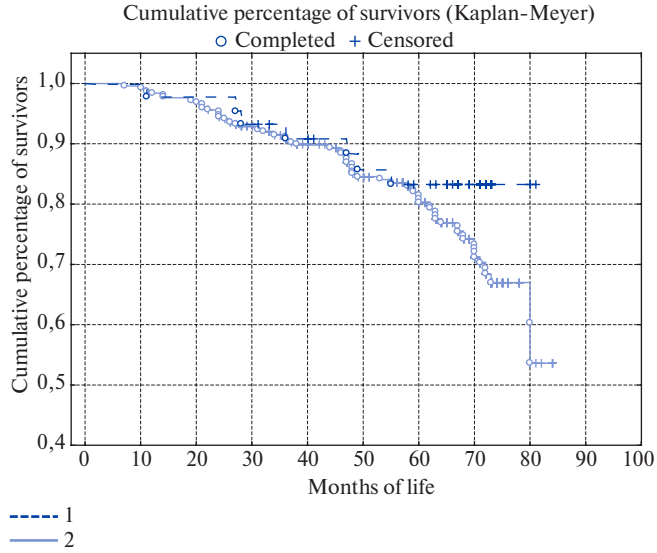

Figure 12. Kaplan-Mayer curves for patients without MACE and with/without taking antiplatelet agents.
Note: 1 — without antiplatelet agents; 2 — with antiplatelet agents; p>0,05.
In the group of complicated clinical course of CAD (n=71), 64 patients took antiplatelet agents (90,1%). In the group of stable clinical course of CAD (n=253), 189 patients (74,7%) took antiplatelet agents. χ^2=1,6; p>0,05.

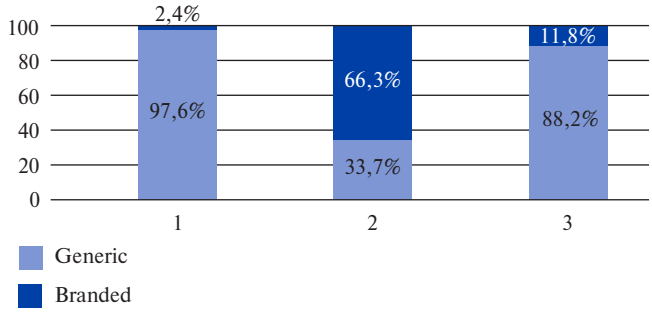

Figure 13. The percentage of the branded and generic medicines of the main drug groups used for secondary prevention in studied patients after ACS.
Note: 1 — statins (n=205); 2 — BB (n=202); 3 — ACE inhibitors/ARB (n=196).

Performing of CA significantly affected the MACE risk (Figure 17).

As can be seen, survival in patients without MACE significantly increased if CA was performed.

Discussion

The study involved 78% of patients with low risk of ACS. Despite this, the mortality rate for 7 years was 22,5%. The total number of cardiovascular events was 37,7%. In comparison, according to the GRACE register, 5-year mortality in patients with initially higher risk of ACS was 20% [1]. The reason for such findings in our study may be associated with improper

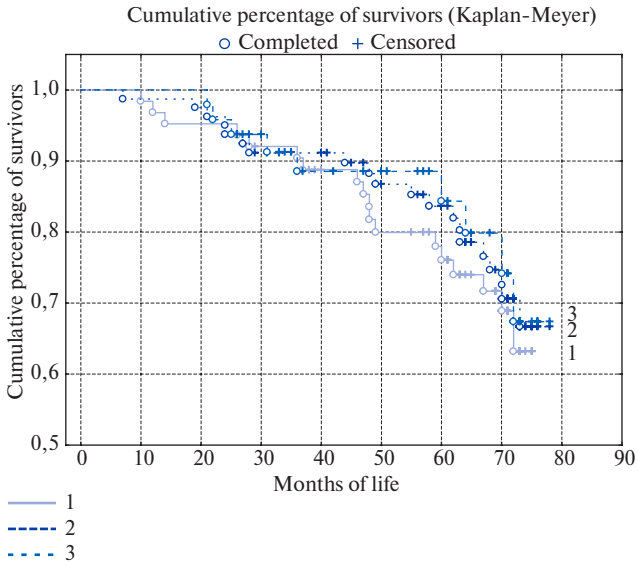

Figure 14. Kaplan-Mayer curves for patients taking various BB and survived for a certain period without MACE**.**
Note: 1 — generic BB; 2 — low-dose branded BB; 3 — branded BB in the optimal dose; p>0,05.
In the group of complicated clinical course of CAD, 19 patients took generic BB (38%), 21 — low-dose branded BB (42%), 10 — branded BB in the optimal dose (20%). In the group of stable clinical course of CAD, 48 patients took generic BB (31,5%), 66 — low-dose branded BB (43,5%), 38 — branded BB in the optimal dose (25%); p>0,05.

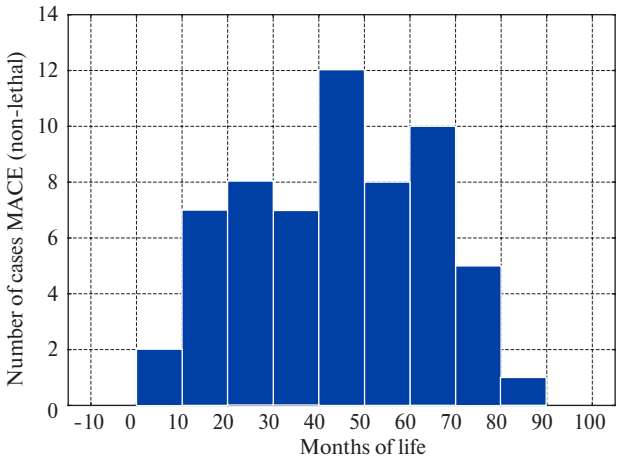

Figure 15. The distribution of MACE (except for deaths) during follow-up in patients with CAD. The median time of MACE is 47 [27,5; 62,5] months.

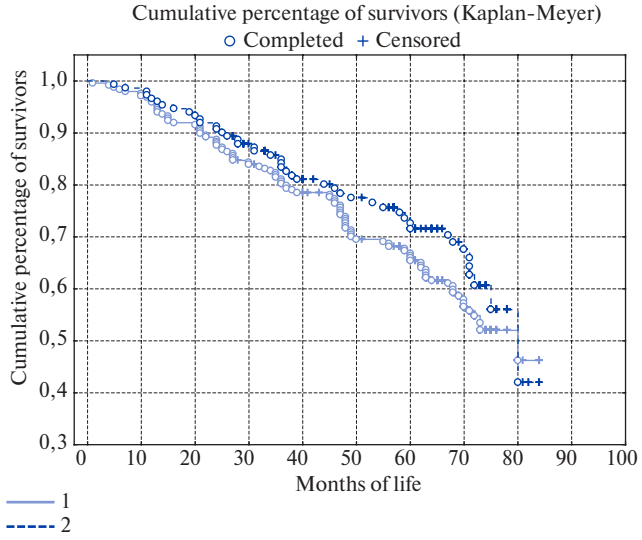

Figure 16. Kaplan-Mayer curves for patients without MACE depending on surgical strategy.
Note: 1 — without PCI; 2 — with PCI; p>0,05. In the group of complicated clinical course of CAD, there were 46 cases of PCI (30,5%). In the group of stable clinical course of CAD, there were 105 cases of PCI (42,2%). χ^2=5,5; p<0,05.

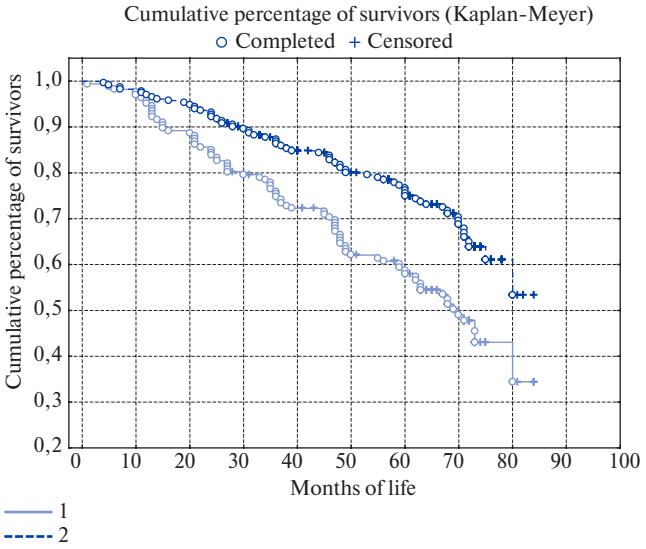

Figure 17. Kaplan-Mayer curves for patients without MACE depending on the CA.
Note: 1 — without CA; 2 — with CA; p<0,001. In the group of complicated clinical course of CAD, there were 69 cases of CA (45,7%). In the group of stable clinical course of CAD, there were 164 cases of CA (65,9%). χ^2=15,7; p<0,0001.

secondary prevention after ACS. On the one hand, we see that the effects of the main drug classes are consistent with generally accepted concepts. Delta% of blood lipids, HR and SBP in the group of patients without MACE show positive changes. On the other hand, long-term follow-up did not revealed significant effect of taking the main classes of drugs and their dosages on the survival of patients without MACE after ACS. Statin use was associated with paradoxical negative effect on the prognosis. This can be explained by the non-optimal use of medications. In addition to the ignorance of the clinical

guidelines, a significant role is played by misinterpretation of the "non nocere" principle, when doctors prescribe the lowest doses of drugs. Instead of therapy, we obtain the illusion of treatment, because prescribing a drug from the recommended group without proper dosage does not guarantee the effectiveness of the treatment.

A paradoxical response to medicines was revealed only with statins. This is due to prevailing opinion about the statin toxicity. During hospitalization and upon discharge, all patients are prescribed full-dose treatment and prevention with statins (atorvastatin 40 mg or rosuvastatin 10-20 mg). Some asymptomatic patients, mostly young, discontinue the treatment for no reason. In majority of patients, primary care physicians reduce statin's dose by half based on TC monitoring. It is noted that the initial atorvastatin dosage of 40 mg after 1-2 years is reduced to <20 mg. At the same time, only the TC levels are controlled. Some patients discontinue statin therapy due to adverse effects: heaviness in the right hypochondriac region, bitter taste in the mouth, muscle weakness and myalgia. Laboratory tests justifying drug withdrawal, as a rule, is not carried out. Thus, 1-2 years after ACS, the number of patients taking statins and its dosage are reduced. By this time period, clopidogrel is discontinued (according to the ECC guidelines). Therefore, by 2-4 years of observation, the number of MACE increases. In patients with recurrent episodes of ACS, statin therapy is resumed at previous doses. At the re-examination, statins were taken by 69% of patients; the average dose (equivalent to atorvastatin) was 26,1±2,8 mg. Consequently, the increased frequency of use and dosage of statins are a consequence of the complicated clinical course of CAD and do not have the proper preventive effect. Arguably, the intensity of therapy is specified by the disease severity.

Evidence of irregular drug intake during the follow-up period may be a divergence of the survival curves in patients without MACE 4 years after the ACS. This period corresponds to the peak number of MACE (except for deaths), which leads to intensification of drug therapy and positive survival changes. This relationship was found for BB and ACE inhibitors/ARB.

The low effectiveness of therapy is not only due to low doses. Comparison between use of recommended doses and low-dose therapy or complete drug withdrawal did not revealed significant differences in survival of patients without MACE. In our opinion, this is due to the low effectiveness of the drugs. Generic medicines may not have the same complete effect as the branded ones. Observed paradoxical effect of statins can be explained not only by low doses, but also by the high prevalence of generic medicines. The problem of cheap and probably low-effective generic medicines lies not only in the pharmacology, but also in the socio-economic aspects, and therefore it cannot be solved only by developing new guidelines. It is necessary to create a register of all generic medicines with description of their coefficient of equivalence to the branded ones.

The low prognostic significance of PCI and the significant effect of CA in reducing the MACE risk are due to high percentage of patients (26%) who had single, double, and triple vessel disease revealed by CA, and PCI was not performed due to technical difficulties. In this case, discharge recommendations included revascularization in the federal center. It is likely that cases of revascularization in the federal center (PCI or CABG), together with optimization of secondary drug prevention, significantly deviate the survival curve after CA (especially by the 4th year of follow-up). Therefore, given all cases of delayed revascularization, it can be said that PCI can significantly affect survival without MACE. It can be expected that the most significant preventive effect is to reduce the mortality risk. CA cases without significant coronary stenosis can also affect the survival of patients without MACE, reducing the number of cases with incorrectly diagnosed unstable angina. Rehospitalization of a patient with provisional diagnosis of ACS, who had a history of CA without significant coronary stenosis, makes a doctor search for other causes of chest pain. Thus, the diagnosis of unstable angina may be confuted. Therefore, previously performed CA reduces the number of incorrect diagnoses of ACS.

Conclusion

The combination of following factors of drug therapy can explain the low effectiveness of secondary CAD prevention: low dose (26,1±2,8 mg for atorvastatin), irregular intake and common use of generic drugs (97,6% for statins). The contribution of surgical treatment to reducing cardiovascular events is lower, the more significant residual coronary artery stenosis.

Relationships and Activities: not.

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