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## Prospective 5-year follow-up of patients with acute coronary syndrome and percutaneous coronary intervention

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### Abstract

**Background.** The study of predictors that negatively affect the long-term prognosis of patients with an increased risk of coronary syndrome can improve the effectiveness of measures for the secondary prevention of cardiovascular events.

**Aim.** To determine the factors that have a negative impact on 5-year survival in patients with acute coronary syndrome and percutaneous coronary intervention.

**Material and methods.** 135 patients with acute coronary syndrome enrolled in the “Register of percutaneous coronary interventions” in 2012–2013 at the Tyumen Cardiology Center, a branch of the Tomsk Research Institute of Cardiology of the Russian Academy of Sciences, were included in the study. After 12 and 60 months, the clinical status of patients and ongoing drug therapy were evaluated, and an examination including echocardiography with an ultrasound scanner, daily monitoring of the electrocardiogram and standard blood pressure measuring was performed. Laboratory studies included general and biochemical blood tests. To calculate the factors associated with poor prognosis, a Cox proportional hazards regression model with stepwise inclusion was used. Survival was assessed by the Kaplan–Meier method using the Log-rank test (logarithmic test).

**Results.** After 1 year, only three-quarters of patients continued the recommended drug therapy, a similar trend continued after 5 years of follow-up. The number of patients without any antiplatelet therapy increased from 19.9% after 12 months to 29.7% after 60 months. Overall survival after 1 year was 97.1%, after 5 years — 86.7%. The risk of death increased in the presence of chronic kidney disease (risk ratio 15.1; 95% confidence interval 4.30–52.93;  $p=0.001$ ); type 2 diabetes mellitus (risk ratio 3.67; 95% confidence interval 1.18–11.43;  $p=0.025$ ), history of stroke (risk ratio 9.07; 95% confidence interval 1.85–44.60;  $p=0.007$ ), in patients with a heart rate  $>80$  beats per minute [risk ratio 4.3; (95% confidence interval 1.51–12.26;  $p=0.006$ ) and at pulse pressure  $\geq 60$  mm Hg (risk ratio 4.68; 95% confidence interval 1.60–13.72;  $p=0.005$ ).

**Conclusion.** The predictors that influenced the 5-year survival of patients after acute coronary syndrome and percutaneous coronary intervention were chronic kidney disease, diabetes mellitus, a history of stroke, high pulse pressure, and increased heart rate of more than 80 beats per minute.

**Keywords:** acute coronary syndrome register, percutaneous coronary intervention, predictors of 5-year survival.

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### Background

Reducing mortality from acute coronary syndrome (ACS) is an important medical and social goal. Recently, there has been an improvement in long-term survival of patients after ACS due to the availability of percutaneous coronary interventions (PCI) and the optimization of therapeutic and preventive measures aimed at preventing cardiovascular events [1, 2]. An important role has been assigned

to maintaining patient adherence to treatment. Determination of survival predictors helps to increase the efficiency of secondary prevention and medical care for patients with ACS.

In Russia, ACS registry-based studies are very limited in number and mainly investigate the hospital stage treatment aspects. Few registries evaluated the five-year survival rate and investigated the factors determining long-term prognosis in

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**Table 1.** Clinical and anamnestic characteristics of patients included in the register.

Parameter	n = 135	
	Upon inclusion in the register, n (%)	Survivors/deceased, n
Men	88 (64.7)	78/10
Smoking	83 (61.0)	73/10
Obesity	61 (44.9)	53/8
History of ischemic heart disease	47 (34.6)	42/5
History of myocardial infarction	21 (15.4)	19/2
History of stroke	5 (3.7)	3/2
Arterial hypertension	121 (89)	105/16
Type 2 diabetes mellitus	28 (20.6)	23/5
Chronic kidney disease stage 3–5	10 (7.4)	6/4
Patients with heart rate >80 per minute	47 (34.8)	36/11
Patients with pulse pressure >60 mmHg	52 (38.5)	41/11

Note: n—number of patients; %—of the total number of patients included in the register.

this category of patients [3, 4]. The results of studies evaluating the factors influencing the prognosis of patients with a history of ACS often differ. This may be due to the difference in regional characteristics of risk factors and comorbidity, and the difference in the methods of treatment and revascularization of the affected artery.

### Aim

This study aimed to determine the factors negatively affecting the five-year survival of patients with a history of ACS and PCI.

### Materials and methods

The analysis involved 135 patients with ACS included in the “Registry of Percutaneous Coronary Interventions” in the period from October 2012 to November 2013 (Table 1) at the Tyumen Cardiology Center, a branch of Tomsk Research Institute of Cardiology of the Russian Academy of Sciences. The study protocol was approved by the ethical committee of the institution, protocol No. 63 dated 05/21/2012.

The findings revealed that 74 (54.8%) patients had ACS with *ST*-elevation, and 61 (45.2%) patients had ACS without *ST*-segment elevation. All patients underwent coronary arteries angioplasty with stenting.

The time from the onset of pain to PCI in patients with *ST*-elevation ACS was 245.0 [165.0; 371.0] min; in 11 (18.0%) ACS patients without *ST*-segment elevation and indications for urgent invasive treatment, it was 331.5 [260.0; 460.0] min. In 3 (4.9%) patients with ACS without *ST*-segment elevation, PCI was performed within the first 24 h, and in 47 (77.1%) patients, it was performed within 24–72 h.

After one year and five years, the clinical status of patients and those ongoing drug therapy were assessed. When included in the register, the average age of patients was  $60.1 \pm 9.54$  years, blood pressure was  $137.93 \pm 26.11/82.91 \pm 15.60$  mm Hg, pulse arterial pressure (PAP) was  $54.85 \pm 15.82$  mm Hg, and heart rate (HR) was  $77.18 \pm 19.6$  per min.

The distribution of continuous data was tested using the Kolmogorov–Smirnov test. Continuous variables were presented as the arithmetic mean and mean square deviation ( $M \pm SD$ ), and variables with a non-normal distribution were presented as the median, lower, and upper quartiles (Me [25%; 75%]). The probability of survival for 5 years among patients with a history of ACS and PCI was assessed by the Kaplan–Meier method using the Log-rank test. To determine the factors associated with survival and the development of adverse cardiovascular events in the long-term period, we used a Cox proportional hazards regression model with stepwise inclusion and assessment of the risk of development of events as the risk ratio (RR), 95% confidence interval (CI).

### Results

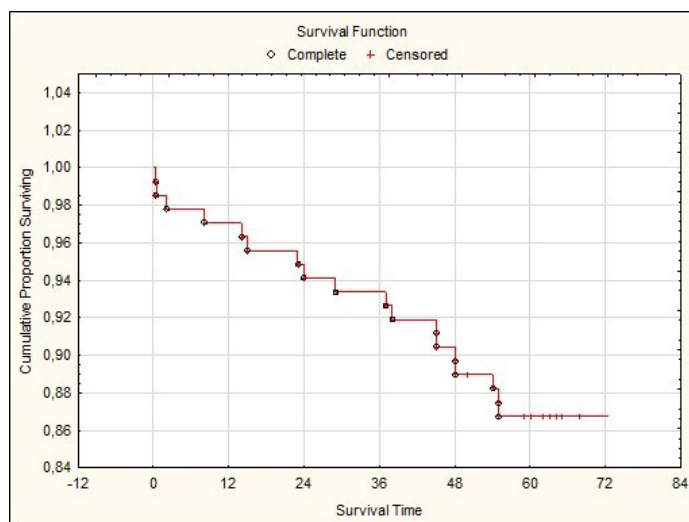
At discharge from the hospital, optimal drug therapy was recommended to all patients (Table 2). It is noteworthy that after 12 months, only three-quarters of patients continued taking  $\beta$ -blockers, statins, and renin-angiotensin system blockers. This tendency continued after 5 years of follow-up; the number of patients not taking antiplatelet drugs increased from 19.9% after 12 months to 29.7% after 60 months.

The overall survival rate after 12 months and 60 months was 97.1%, and 86.7%, respectively (Fig. 1). The proportion of deaths from cardiovascular diseases

**Table 2.** Therapy of patients during the follow-up period.

Group of drugs	Before admission to the hospital, %	Discharge from the hospital, %	12 months, %	60 months, %
Acetylsalicylic acid	24.2	98.2	83.2	70.3
P2Y12 blockers (clopidogrel/ticagrelor)	6.7 (6.7/0)	98.5 (87.5/11.0)	88.5 (78.6/9.9)	11.0 (9.3/1.7)
Statins	11.9	99.1	79.4	74.6
$\beta$ -blockers	23.0	97.3	73.6	71.9
RAS inhibitors	36.7 (27.1/9.6)	99.1 (84.4/14.7)	73.6 (54.7/18.9)	77.1 (48.8/28.3)

Note: %—of the total number of patients included in the register; RAS—renin-angiotensin system.

**Fig. 1.** Survival rate of patients with a history of acute coronary syndrome and percutaneous coronary intervention during 60 months of follow-up.

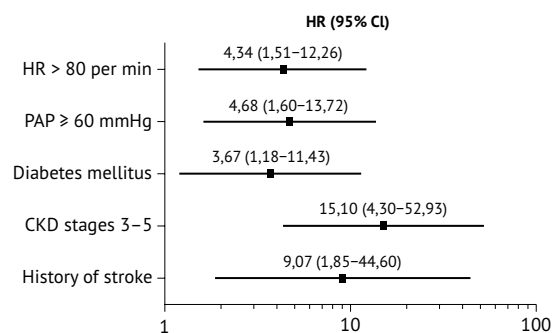
es was 66.7%. Patients in the groups with chronic kidney disease (CKD), type 2 diabetes mellitus, history of stroke, and impaired hemodynamic parameters in the form of HR >80 per min and PAP >60 mmHg registered a significant decrease in survival rate.

In the analysis of the five-year survival rate in these groups by the Kaplan–Meier method, the survival rate was 42.7% in CKD patients vs. 89.1% in patients without CKD ( $p < 0.001$ ). The same dynamics was registered in patients with diabetes mellitus compared with those without diabetes (73.7% vs. 88.9%;  $p = 0.045$ ). Survival was influenced by previous strokes (33.4% vs. 83.9%;  $p = 0.007$ ), HR > 80 per min (76.6% vs. 92.0% in patients with HR < 80 per min  $p = 0.013$ ), and PAP > 60 mmHg (78.8% vs. 91.5%,  $p = 0.027$ ).

According to the Cox regression analysis in the study group, the risk of death increased with an increase in HR > 80 per min and PAP > 60 mmHg. The relative risk of a poor prognosis was higher in patients with diabetes mellitus, stage 3–5 CKD, and a history of stroke (Fig. 2).

## Discussion

In our registry, a high adherence rate of the patients to medications was noted, especially at the

**Fig. 2.** Risk of fatal events in patients after acute coronary syndrome and percutaneous coronary intervention within 60 months of follow-up; RR—risk ratio; CI—confidence interval; HR—heart rate; PAP—pulse arterial pressure; CKD—chronic kidney disease.

end of the first year of follow-up. However, we did not evaluate the effect of adherence to therapy on the five-year survival.

The incidence of comorbid pathology among patients included in the study was comparable to that in other studies [1, 3]. The exception was patients with CKD (7.4%), as glomerular filtration rate <30 ml/min/1.73 m<sup>2</sup> occurred in 30%–40% of ACS patients and was associated with a worse prognosis and a high risk of hospital complications

in other registries [5]. A history of stroke is a predictor of mortality in patients with myocardial infarction after three years of follow-up [6].

The results obtained are consistent with the study by D.A. Shvets et al., in which the greatest contribution to the risk of lethal outcome was made by a history of stroke and stage 3 CKD, along with aging, previous myocardial infarction, and the absence of PCI [7]. Our results confirmed the literature data that diabetes mellitus is a factor that increases mortality from cardiovascular diseases, despite timely revascularization and optimal therapy [8].

Arterial hypertension was recorded in 89% of cases, corresponding to the average indicators in other registries [1, 5]. The value of excess PAP and the prevalence of isolated systolic arterial hypertension increase with age and are associated with increased stiffness of the vascular wall [9]. Nowadays, PAP of 60 mmHg or higher is considered as a marker of vascular damage in patients with arterial hypertension in the older age group ( $\geq 60$  years), and isolated systolic arterial hypertension is independently associated with the risk of cardiovascular mortality [10, 11]. Changes in hemodynamics in isolated systolic arterial hypertension (increase in PAP) can provoke episodes of ischemia at the level of peripheral organs and lead to an increase in afterload on the left ventricle.

Many studies have revealed an association between increased HR and cardiovascular diseases and all-cause mortality [12, 13]. In patients with ischemic heart disease, HR at rest was an indicator of increased activity of the sympathetic nervous system, and serves as an independent predictor of their survival. Thus, in patients with *ST*-segment elevation myocardial infarction who received primary PCI and optimal drug therapy, HR at discharge was an important predictor of mortality during follow-up for up to four years [14]. Our study confirmed the negative impact of increased HR on 5-year survival in patients after ACS and PCI.

Based on the analysis of data from the Tyumen registry, we studied the regional characteristics of risk factors and comorbidity in patients after ACS and PCI, which confirmed existing data on the interdependence of pathological processes in the cardiovascular system and kidneys, the significant contribution to reducing the survival rate of carbohydrate metabolism disorders, and the impact on the prognosis of hemodynamic parameters, such as HR and PAP.

### Conclusion

According to a registry study, the predictors that influenced the 5-year survival of patients after

ACS and percutaneous coronary intervention were CKD, type 2 diabetes mellitus, a history of stroke, high pulsed blood pressure, and an increase in HR  $> 80$  per min.

**Author contributions.** N.A.M created the concept and design of the study, analyzed the data obtained, and wrote the manuscript; A.I.T. collected and processed the materials and performed diagnostic studies; T.I.P. created the study concept and design and reviewed the literature; E.A.G. collected and processed the materials and analyzed the data obtained; I.S.B. analyzed the data obtained and performed surgical treatment; and L.I.G. created the concept and design of the study and reviewed the literature.

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**Conflict of interest.** The authors declare no conflict of interest.

**Study limitation.** The study included a small number of patients with a history of stroke. Further analysis of all ACS patients included in the register (262 patients in total) will enable to substantiate more fully the results obtained.

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