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Original research article

Impact of patient-related and treatment-related factors on in-hospital mortality of patients with ST-elevation myocardial infarction: Data of Russian Acute Coronary Syndrome Registry

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ABSTRACT

Objective: We examined relationships between inpatient medical treatment, reperfusion therapy and in-hospital mortality among patients with ST-elevation myocardial infarction (STEMI) in Russia.

Methods: Clinical information about 25,682 patients with STEMI enrolled in the 2010–2011 registry was included retrospectively in the study. Performance of the key guideline-recommended treatment interventions was assessed. Timeliness of reperfusion therapy was evaluated with the help of the following ACC/AHA clinical measures (2008): Time to fibrinolytic therapy, Time to primary percutaneous coronary intervention (PCI) and Reperfusion therapy. Multivariate logistic and Cox's regression models were used to assess the relationship between different in-hospital treatment interventions and the risk of in-hospital death among patients with STEMI under the control of patient characteristics and comorbidities.

Results: The average age of patients was 63 (55–74) years. 34% of patients were female. Survived patients differed significantly from deceased ones in the majority of demographic, anamnesis, clinical presentation and treatment parameters. Hospital treatment with ACE-Is or ARBs, β-blockers and statins was significantly associated ($\chi^2 = 482.1$, $P < 0.0001$) with lower inpatient mortality. Prognostic value of reperfusion therapy and measures of its timeliness were not statistically significant ($P \geq 0.05$ for Wald test for each factor).

Conclusion: STEMI treatment with ACE-Is or ARBs, β-blockers and statins during hospital stay (not necessarily at arrival) influences upon the rate of death in hospital as strong as the patient clinical status at admission. Reperfusion and its performance are additional factors that influence indirectly on the risk of in-hospital mortality in patients with STEMI.

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Introduction

The study of risk factors among patients with acute coronary syndrome (ACS) is an important problem of contemporary cardiology. Many studies are devoted to this problem [1–4, etc.]. Different algorithms have been proposed for estimating the risk of death after ACS (GRACE, TIMI) [5,6]. In the most known algorithms, all factors determining the probability of death in patients with ACS are patient-related, e.g. age, sex, history of cardiovascular diseases (CVD), family history of coronary artery disease (CAD) and premature death, and clinical status at admission. To optimize treatment it is important to study the impact of treatment-related factors (hospital drug treatment and timeliness of reperfusion) on the patient risk.

Recently, much attention is paid to the study of risk factors in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) [7,8, etc.]. It is well known that the quality of reperfusion therapy is a risk factor of a short-term mortality in patients with STEMI patients [9,10]. The American College of Cardiology and the American Heart Association have published in 2008 the task force on performance measures for STEMI and non-STEMI [11]. Clinical measures (Time to fibrinolytic therapy, Time to PCI and Reperfusion therapy) have been designed to assess the quality of primary reperfusion therapy in patients with STEMI.

In the present retrospective study we examined relationships between different patient-related factors (patient's clinical characteristics), treatment-related factors (hospital drug treatment and reperfusion therapy and its performance) and in-hospital mortality among Russian patients with STEMI.

Materials and methods

Data source

The Registry of Acute Coronary Syndrome of the Ministry of Health of Russian Federation (hereafter referred as Russian ACS Registry) was used as a source of data about ACS patients [12]. It is a retrospective, continuous, nation-wide, Web-based registry operating on-line. Participation in the Russian ACS Registry is voluntary. The access to the registry is given only to registered members.

The Registry database was developed using ACCF/AHA 2011 Key Data Elements and Definitions of a Base Cardiovascular Vocabulary for Electronic Health Records [13]. Data on clinical characteristics, prior, hospital drug treatment and reperfusion therapy was collected. Data on post-hospital treatment of ACS patients was not included in the Russian ACS Registry database. The source of patient's data was a hospital chart.

Centers participating in the Russian ACS Registry are asked to include continuously all patients following inclusion/exclusion criteria who were treated from ACS during the year prior to the year of participation.

Russian ACS Registry inclusion criteria [14] are the following:

(i) age ≥18 years;
(ii) any type of ACS as a presumptive diagnosis;
(iii) patient's hospital chart is finished;
(iv) absence of any exclusion criteria.

Russian ACS Registry exclusion criteria [14] are the following:

(i) symptoms considered as consistent with acute cardiac ischemia are absent within the last 24 h prior to admission;
(ii) patient was transferred into a registry hospital in more than 24 h after admission to the initial hospital;
(iii) patient was transferred out of a registry hospital in less than 24 h after admission;
(iv) ACS symptoms occurred after hospitalization at other reasons;
(v) ACS is accompanied by a significant co-morbidity such as a motor vehicle accident, trauma, severe gastrointestinal bleeding, operation or procedure directly before admission.

Patient selection

Retrospective data on clinical characteristics, prior and hospital drug treatment, reperfusion therapy and in-hospital mortality contained in the 2010–2011 Russian ACS Registry from 25,682 patients with STEMI were examined. The average age of patients was 63 (55–74) years. 34% of patients were female. These patients were treated in 155 cardiological units located in 46 regions of Russia. Death was defined as endpoint of study. Duration of hospital treatment was from 9 to 21 days for survived patients. Mortality rate was 8.1%. Most definitions of clinical data in the Russian ACS Registry are consistent with W.S. Weintraub et al. [13].

We used the following criteria to select patients for the study:

(i) diagnosis of STEMI (data from the Russian ACS Registry)
(ii) age between 18 and 80 years.

The patients were excluded from the study if they had missing data on the time of reperfusion (time of fibrinolytic agent injection and/or time of balloon inflation during PCI), hospital presentation and treatment.

The patients over 80 years were not included in the present study because of proven disparities in treatment of ACS in the elderly and younger subjects [15–17]. It was previously reported that high age itself is a predominant clinical factor influencing on implementation of recommended (especially invasive) treatment among aged patients in Russia in spite of their higher risk of in-hospital death [18,19]. This limitation of the present study is indicated in the Limitation section.

Patient-related and treatment-related factors in patients with STEMI

All clinical factors, which could not be changed by medical care of present event, were named as patient-related factors. Other factors, which could be modified by treatment, were named as treatment-related factors.

Patient-related factors included age, sex, body mass index (BMI), smoking, prior myocardial infarction (MI), history of

stable angina pectoris, prior PCI, family history of premature heart disease (PHD), history of chronic heart failure (CHF), prior stroke, history of peripheral vascular disease (PVD), history of chronic renal insufficiency (CRI), history of chronic lung disease (CLD), history of arterial hypertension (AH), diabetes, acute heart failure (AHF) Killip 1–4 at admission, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), pathologic Q wave on electrocardiogram (ECG), right ventricle (RV) dilatation, acute left ventricle (LV) aneurism, thrombus into LV, prior treatment with aspirin, clopidogrel, nitrates, angiotensine converting enzyme inhibitors (ACE-Is) or angiotensin receptors blockers (ARBs), beta-blockers, dihydropyridine calcium antagonists (DCA), non-dihydropyridine calcium antagonists (NDCA) and statins.

Treatment-related factors included hospital treatment with aspirin, clopidogrel, nitrates, heparin, fondaparinux, ACE-Is or ARBs, beta-blockers, DCA, NDCA, statins, the fact of any reperfusion and timeliness of reperfusion.

One of the factors considered in the analysis was LV ejection fraction (LVEF). LVEF was regarded as combined patient- and treatment-related factor. In Russian STEMI patients LVEF is measured later during the hospital stay. Thus, contractile dysfunction due to infracted myocardium (patient-related component) is compensated by myocardium salvage and recovery of function due to timely treatment (treatment-related component).

Definitions for all clinical factors are shown in Table 1.

Performance measures for reperfusion

Reperfusion therapy was estimated basing on the following performance measures powered by American College of Cardiology and American Heart Association (ACC/AHA) in 2008 year [11]:

(i) No. 7 – Time to fibrinolytic therapy, which determines the part of patients with STEMI whose time from hospital admission to fibrinolytic therapy is 30 min or less,
(ii) No. 8 – Time to PCI, which determines the part of patients with STEMI whose time from hospital admission to primary PCI is 90 min or less,
(iii) No. 9 – Reperfusion therapy, which determines the part of patients with STEMI who receive any reperfusion treatment within 12 h of symptom onset.

ACC/AHA performance measures were estimated in those STEMI patients who met the measure inclusion and exclusion criteria [11].

Statistical analysis

We applied the Shapiro–Wilk test to check whether the data were approximately normally distributed. Since some data occurred to be non-normal, their further analysis was carried out using non-parametric statistical methods. We applied the Chi-square (χ^2) test to compare the binary variables and to compute the significance level for the difference between two proportions. Mann–Whitney test was used to compare the continuous variables. Categorical data are presented as frequencies and percentages. Continuous variables are reported as mean, medians (Me) with standard deviations (SD) and inter-quartile ranges (Q1, Q3).

Cox's proportional hazard models were used for multivariate analysis of dependence between fatal cardiovascular event (death) and various factors (patient-related and treatment-related) during inpatient admission (in hours). We selected the factors for multivariate analysis basing on the results of univariate comparison between deceased patients and survived patients ($P < 0.05$ in Table 2).

In our study the risk index Exp(B) estimates the hazard ratio of in-hospital mortality. The risk index Exp(B) is the ratio of hazards between two individuals whose values of x_1 differ by one unit while all other covariates are held constant. In Cox regression the hazard function is modeled as $h(t) = h_0(t)\exp(\beta' x)$, where $h_0(t)$ is the baseline hazard, which cannot be estimated. In spite of this, one can estimate β. If $\beta = 0$, then the hazard ratio for this covariate is equal to $\mathrm{Exp}^0 = 1$, i.e., this covariate does not affect survival.

The obtained estimations were considered statistically significant if $P < 0.05$. For the statistical analysis, the software package Statistica 6.1 (Statsoft Inc., USA) was used.

Results

Characteristics of the registry population with STEMI

Clinical characteristics of enrolled patients with STEMI are presented in Table 2. Total rate of death in hospital was 8.1%. Survival plot is shown in Fig. 1. Clinical characteristics of deceased patients and survive patients are shown separately.

The average age of enrolled patients was 63 (55–74) years. 34% of patients were female. 29.9% of patients admitted to hospital with acute heart failure and 36.6% of patients admitted with pathological Q-wave on electrocardiogram. More than half of all patients with STEMI had the left ventricle systolic dysfunction (ejection fraction is less than 49%). Survived patients differed significantly from deceased patients in the majority of demographics, anamnesis, clinical presentation and treatment parameters (Table 2).

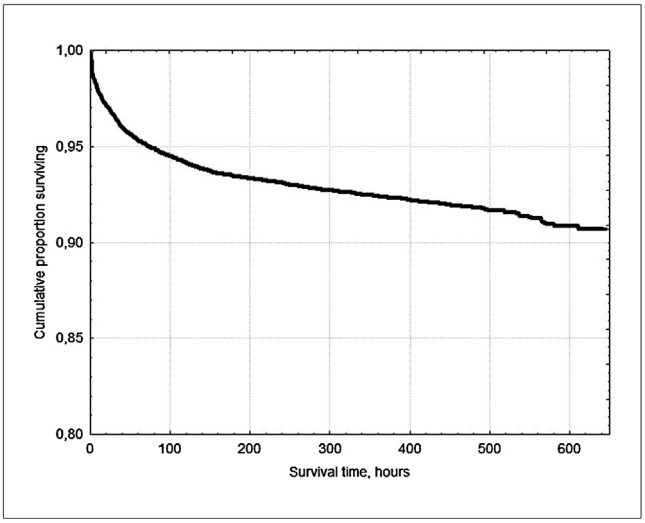

Fig. 1 – Survival plot for patients with STEMI.

Table 1 – Definitions of clinical factors used in the present study.

Factor name	Definition	Value domain
Sex	–	Male Female
Age	Age at admission. Age can be from 18 to 80, according to the following criteria.	Numeric, years
BMI	BMI = height/(weight)^2 Weight is a measured actual weight in kilograms. Height is a measured actual height in meters.	Numeric, kg/m^2
Prior MI	Documented history of MI	Yes No
History of stable angina pectoris	Documented history of stable angina pectoris	Yes No
Family history of PHD	Indicate if the patient has/had any direct blood relatives (i.e., parents, siblings, children) who have had any of the following diagnosis at age <55 years for male relatives or <65 years for female relatives: coronary artery disease (i.e., angina, previous CABG or PCI), MI, sudden cardiac death without obvious cause. If the patient is adopted or the family history is unavailable, code "No".	Yes No
Prior PCI	Documented prior PCI	Yes No
History of CHF	Documented history of CHF	Yes No
Prior stroke	Documented history of stroke, including temporary stroke	Yes No
History of PVD	Current or previous history of PVD (lower extremity from iliac to tibials and upper extremity from subclavian to brachials. Renal, coronary, cerebral, and mesenteric vessels and aneurysms are excluded).	Yes No
History of CRI	Documented history of CRI	Yes No
History of CLD	Documented history of CLD (e.g., CODL, chronic bronchitis) or currently receiving long-term treatment with inhaled or oral pharmacological therapy (e.g., beta-adrenergic agonist, anti-inflammatory agent, leukotriene receptor antagonist, or steroid) for the indication of lung disease.	Yes No
History of AH	Current or previous diagnosis of hypertension	Yes No
Smoking	Current or previous use of any tobacco product, including cigarettes, cigars, pipes, and chewing tobacco, captured as smoking status.	Yes No
History of diabetes	History of diabetes diagnosed and/or treated by a physician.	Yes No
Prior drug treatment - Aspirin - Clopidogrel - Nitrates - ACE-Is or ARBs - β-blockers - DCA - NDCA - Varfarin - Statins	Treatment with selected drugs prior to the current STEMI	Yes No (for each drugs)
Clinical status of patients at admission to hospital		
HR	Number of heartbeats over 1 min HR > 100 bpm	Numeric, bpm Yes No
SBP	SBP in millimeters mercury SBP > 140 mmHg	Numeric, mmHg Yes No
DBP	DBP in millimeters mercury DBP > 90 mmHg	Numeric, mmHg Yes No

Table 1 (*Continued*)

Factor name	Definition	Value domain
AHF	AHF at admission	Killip 1 Killip 2 Killip 3 Killip 4
Pathological Q-wave on ECG	New pathological Q-wave on ECG	Yes No
LVEF	The calculated resting LVEF as either a percentage value or the midpoint value when a range is reported.	Numeric, %
	LVEF < 50%	Yes No
	LVEF < 35%	Yes No
RV dilatation	RV dilatation diagnosed by echocardiography	Yes No
Acute LV aneurism	New LV aneurism diagnosed by echocardiography. If prior data of echocardiography is unavailable, code ''No''.	Yes No
Thrombus into LV	Thrombus into LV diagnosed by echocardiography.	Yes No
Total cholesterol	Blood total cholesterol	Numeric, mmol/L
Triglycerides	Blood triglycerides	Numeric, mmol/L
Creatinine	Blood creatinine	Numeric, micromoles/L
Blood glucose	Fasting blood glucose	Numeric, mmol/L
Hospital treatment		
PCI	Performed PCI	Yes No
CABG	Performed CABG	Yes No
Fibrinolytic therapy	Performed fibrinolytic therapy	Yes No
Drug treatment, %: - Aspirin - Clopidogrel - Nitrates - Anticoagulants - ACE inhibitors or ARBs - β-blockers - DCA - NDCA - Varfarin - Statins	Hospital drug treatment	Yes No (for each drugs)

CODL, chronic obstructive disease of lungs; CABG, coronary artery bypass grafting.

20.8% of all patients with STEMI followed PCI (18.5% during the first day and 2.3% later than 24 h after admission). 29.3% of all STEMI patients received fibrinolisys and 0.4% of patients received coronary artery bypass graft (CABG) during the first 24 h after admission.

Selection of patients for carrying out ACC/AHA measures showed the following results. ACC/AHA measure ''Time to fibrinolisys'' could be estimated for 5119 STEMI patients (19.9% of general group of 25,682 patients). ACC/AHA measure ''Time to PCI'' could be estimated for 3993 STEMI patients (15.5% of general group of 25,682 patients). ACC/AHA measure ''Reperfusion therapy'' could be estimated for 12,043 patients with STEMI (46.9% of general group of 25,682 patients).

Assessment of the quality of reperfusion with the help of ACC/AHA measures (see the section Performance measures for reperfusion) showed the following results. In 65.3% of applicable STEMI patients (3343 from 5119 patients) the time from hospital arrival to fibrinolytic therapy was 30 min or less (ACC/AHA measure No.7 ''Time to fibrinolisys''). In 70.0% of applicable STEMI patients (2795 from 3993 patients) the time from hospital arrival to primary PCI was 90 min or less (ACC/AHA measure No. 8 ''Time to PCI''). 81.4% of applicable STEMI patients (9803 from 12,043 patients) received fibrinolytic therapy or primary PCI (ACC/AHA measure No. 9 ''Reperfusion therapy''). It is important that obtained results of ACC/AHA measures were derived from the data of applicable STEMI

Table 2 – Baseline characteristics of 25,682 patients with STEMI.

Parameter	All patients (*n* = 25682)	Deceased patients (*n* = 2080)	Survived patients (*n* = 23602)	*P*-level
Male sex, %	66.0	47.4	67.6	<0.001
Age, years, Me (Q1, Q3)	63 (55, 74)	74 (64, 80)	62 (54, 72)	<0.001
Height, m, Me (Q1, Q3)	1.67 (1.55, 1.74)	1.60 (1.55, 1.69)	1.67 (1.56, 1.74)	<0.001
Weight, kg, Me (Q1, Q3)	75 (58, 85)	68 (59, 80)	75 (60, 85)	<0.001
BMI, kg/m^2, Me (Q1, Q3)	27.2 (24.7, 30.4)	27.3 (24.6, 30.8)	27.2 (24.8, 30.4)	0.774
Prior MI, %	21.6	25.0	21.3	<0.001
History of Stable angina pectoris, %	46.1	50.0	45.6	0.001
Family history of PHD, %	32.0	24.0	33.6	<0.001
Prior PCI, %	2.2	0.9	2.3	<0.001
Prior CABG, %	0.03	0	0.03	0.430
History of CHF, %	36.4	43.2	35.8	<0.001
Prior stroke (including temporary stroke), %	8.1	13.1	7.7	<0.001
History of PVD, %	5.2	6.1	5.1	0.049
History of CRI, %	2.7	5.3	2.5	<0.001
History of CLD, %	8.8	9.7	8.7	0.122
History of AH, %	84.0	88.4	83.6	<0.001
Smoking, %	33.0	16.0	34.5	<0.001
History of Diabetes 1 type, %	0.7	1.4	0.6	<0.001
History of Diabetes 2 type, %	14.5	19.4	14.1	<0.001
Prior drug treatment, %				
- Aspirin	26.8	25.9	28.1	0.679
- Clopidogrel	3.4	2.2	3.5	0.002
- Nitrates	24.3	28.4	23.9	<0.001
- ACE-Is or ARBs	38.0	39.7	37.8	0.087
- β-blockers	25.4	23.1	25.6	0.012
- DCA	5.3	4.8	5.3	0.327
- NDCA	1.5	1.6	1.5	0.720
- Varfarin	0.8	0.9	0.8	0.625
- Statins	9.5	6.6	9.8	<0.001
Clinical status of patients at admission to hospital				
HR, bpm, median (Q1, Q3)	78 (68, 88)	84 (70, 100)	78 (68, 88)	<0.001
SBP, mmHg, median (Q1, Q3)	135 (120, 150)	120 (90, 140)	140 (120, 150)	<0.001
DBP, mmHg, median (Q1, Q3)	80 (70, 90)	70 (60, 90)	80 (75, 90)	<0.001
AHF, %				
- Killip 1	70.1	42.2	70.8	
- Killip 2	22.3	36.3	21.9	
- Killip 3	4.7	9.6	4.6	
- Killip 4	2.9	11.9	2.7	
Pathological Q-wave on ECG, %	36.6	41.9	36.1	<0.001
LVEF, %, median (Q1, Q3)	49 (38, 57)	21 (12, 32)	50 (41, 58)	<0.001
RV dilatation, %	7.3	21.3	6.1	<0.001
Acute LV aneurism, %	8.5	19.7	7.5	<0.001
Thrombus into LV, %	4.2	7.1	3.9	<0.001
Total cholesterol, mmol/L, median (Q1, Q3)	4.8 (3.5, 5.8)	4.6 (3.1, 5.0)	4.9 (3.8, 5.9)	<0.001
Triglycerides, mmol/L, median (Q1, Q3)	0.9 (0.2, 1.6)	0.76 (0.3, 0.98)	1.0 (0.2, 1.7)	<0.001
Creatinine, micromoles/L, median (Q1, Q3)	87 (60, 107)	91 (62, 132)	87 (65, 106)	0.065
Blood glucose, mmol/L, median (Q1, Q3)	5.5 (4.4, 7.2)	6.5 (2.7, 9.8)	5.5 (4.5, 7.1)	<0.001
Hospital treatment				
PCI at the 1st day, %	18.5	7.9	19.6	<0.001
PCI after the 1st day, %	2.3	0.9	2.3	<0.001
CABG at the 1st day, %	0.02	0	0.02	0.519
CABG after the 1st day, %	0.4	0.5	0.4	0.829
Fibrinolytic therapy, %	29.3	24.5	29.7	<0.001
Drug treatment, %				
- Aspirin	96.9	90.2	97.5	<0.001
- Clopidogrel	81.3	66.6	82.6	<0.001
- Nitrates	86.1	72.9	87.3	<0.001
- Anticoagulants	96.0	96.6	95.9	0.120
- ACE inhibitors or ARBs	82.4	44.6	85.7	<0.001
- β-blockers	89.4	56.0	92.3	<0.001
- DCA	9.7	2.1	10.4	<0.001
- NDCA	1.9	1.0	2.0	0.001
- Varfarin	2.7	1.0	2.8	<0.001
- Statins	78.2	46.4	81.0	<0.001
Hospital stay length, hours, median (Q1, Q3)	377 (293, 457)	34 (5, 117)	385 (315, 465)	<0.001

patients. The proportions of STEMI patients who met ACC/AHA measures differed significantly on conversion to the general group of patients. ACC/AHA measure No. 7 ''Time to fibrinolisys'' was fulfilled in 13.0% of all STEMI patients enrolled in the study (3343 from 25,682 patients). 10.9% (2795 from 25,682 patients) and 38.2% (9803 from 25,682 patients) of all studied STEMI patients met ACC/AHA measure No. 8 ''Time to PCI'' and ACC/AHA measure No. 9 ''Reperfusion therapy'', respectively.

Effect of treatment- and patient-related factors on survival in patients with STEMI

We evaluated a relationship between all patient- and treatment-related factors and the risk of in-hospital mortality from any cardiovascular event in the general group of patients with STEMI using multivariable Cox's regression model. This model gives $\chi^2 = 482.1$ ($P < 0.0001$). The values of the main clinical characteristics in the model are summarized in Table 3. Statistically significant parameters have *P-level* less than 0.05 (these 15 factors are marked with bold type in Table 3).

The regression coefficient β for these factors indicates that the risk of in-hospital mortality in patients with STEMI increases with the increase of age, heart rate, acute heart failure Killip, blood glucose and right ventricular dilatation and with the presence of pathological Q-wave on ECG and acute left ventricular aneurism. The risk increases with the decrease of left ventricular ejection fraction, diastolic blood pressure and triglycerides and with the lack of hospital treatment by angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin-receptor blockers (ARBs), β-blockers and statins.

Prognostic value of other clinical factors, including any reperfusion therapy and measures of its timeliness, exploited the assessment of risk of in-hospital mortality using Cox's regression models was not statistically significant ($P \geq 0.05$ for Wald test for each factor), Table 3.

Since short duration of stay in hospital may hamper performance of recommended treatment interventions and consequently distort the extent of their influence on in-hospital mortality, we compared clinical characteristics and treatment of STEMI patients who have died during the first 24 h after admission ($n = 125$; 6.0% of all deceased pts.) and later on ($n = 1955$; 94.0% of all deceased pts.). Statistically significant difference between the selected subgroups was observed just in administration of ACE-Is/ARBs (30.4% vs 45.5%, respectively, $P = 0.024$). The subgroups were comparable with respect to other clinical and treatment parameters. In patients who have died during the first 24 h after admission, ACE-Is or ARBs were administered rarely in comparison with the patients who have deceased later. But it was not associated with the severity of their clinical status. Thus, the degree of ACE-Is and ARBs influence on the first-day mortality needs further research. As for in-hospital mortality in general, the Cox's regression model used for the analysis took into account the time (in hours) from hospital admission

Table 3 – Clinical characteristics in the Cox's regression model for evaluation of the risk of in-hospital mortality in patients with STEMI.

Parameter	Regression coefficient β	Standard error	Risk index Exp(B)	Wald test	Statistical significance level P
LVEF	**−0.035**	**0.005**	**0.965**	**52.26**	**<0.001**
ACE-Is or ARBs (H.tr.)	**−0.854**	**0.154**	**0.426**	**30.93**	**<0.001**
Age	**0.026**	**0.006**	**1.026**	**18.00**	**<0.001**
HR	**0.009**	**0.002**	**1.009**	**13.09**	**<0.001**
DBP	**−0.012**	**0.007**	**0.977**	**13.01**	**<0.001**
AHF Killip 1–4	**0.240**	**0.066**	**1.271**	**12.97**	**<0.001**
β-blockers (H.tr.)	**−0.608**	**0.175**	**0.544**	**12.12**	**<0.001**
Statins (H.tr.)	**−0.531**	**0.153**	**0.588**	**12.09**	**<0.001**
Path. Q-wave on ECG	**0.448**	**0.135**	**1.565**	**11.07**	**<0.001**
Blood glucose	**0.007**	**0.003**	**1.007**	**7.78**	**0.005**
RV dilatation	**0.456**	**0.171**	**1.578**	**7.13**	**0.008**
Male sex	**−0.344**	**0.146**	**0.709**	**5.51**	**0.019**
Acute LV aneurism	**0.407**	**0.180**	**1.503**	**5.11**	**0.024**
Triglycerides	**−0.161**	**0.079**	**0.851**	**4.08**	**0.043**
Aspirin (H.tr.)	−0.564	0.302	0.569	3.48	0.062
Prior stroke (including temporary stroke)	0.257	0.204	1.293	1.59	0.207
Total cholesterol	−0.038	0.030	0.963	1.55	0.212
Clopidogrel (H.tr.)	0.206	0.175	1.228	1.37	0.240
SBP	−0.005	0.004	0.995	1.22	0.269
Family history of PHD	−0.133	0.157	0.875	0.71	0.397
Thrombus into LV	−0.250	0.309	0.779	0.65	0.419
β-blockers (Pr.tr.)	−0.133	0.193	0.875	0.47	0.489
Prior MI	−0.117	0.177	0.889	0.43	0.508
Nitrates (H.tr.)	0.118	0.196	1.125	0.36	0.548
Prior PCI	−0.384	0.724	0.681	0.28	0.596
etc.					

Path., pathological; Pr.tr., prior treatment; H.tr., hospital treatment; meas., measure.

to death in order to assess the influence of treatment-related factors on patient.

Discussion

In our study we examined the impact of guideline-recommended inpatient interventions on in-hospital mortality of patients with STEMI using the data of Russian Acute Coronary Syndrome Registry. It is shown that

(1) the lack of in-hospital treatment with ACE-Is, ARBs, β-blockers and statins is the major treatment-related factor related significantly with the increased risk of death in hospital;
(2) the performance of reperfusion therapy is not the leading factor influencing on in-hospital mortality;
(3) the present-day completeness of data obtained retrospectively from patients' medical records is deficient for estimating ACC/AHA measures of reperfusion quality (ACC/AHA measures ''Time to fibrinolisys'', ''Time to PCI'' and ''Reperfusion therapy'' were estimated for 19.9%, 15.5% and 46.9% of patients, respectively, from general group).

The obtained results allowed us to reveal the most important treatment interventions. The showed the care gaps and gave the opportunities to upgrade the national STEMI performance measurement set.

We have found only one similar study in literature, which investigate relationship between hospital process performance and outcomes in patients with non-ST elevation acute coronary syndrome [20,21]. This study has shown that guidelines adherence and in-hospital mortality correlate significantly.

In the present study we tried to analyze the factors influencing on the risk of death in hospital after STEMI with respect to its modifiability by treatment. It is important to know the impact of treatment-related factors to the risk of death in order to concentrate medical care efforts on such factors.

It is already known that the majority of factors contributing to in-hospital mortality from MI and STEMI are associated in particular with patient clinical status at admission and cannot be modified by hospital treatment. These factors are age [5,6,22–27], ST-segment deviation [5,6], AH [6,28], smoking [6,28], family history of PHD [6], prior stroke, untreated dyslipidaemia [6,23], diabetes [6,23], low SBP (up to hypotension, which is associated with the increasing Killip class of AHF) [5,6], Killip class (up to cardiogenic shock) [5,22,25,29], cardiac arrest at presentation [5], LVEF (up to congestive heart failure) [27], elevated cardiac markers [5,6], HR [5,24,25], prior treatment with aspirin, known CAD (stenosis ≥50%) and severe angina (≥2 episodes within 24 h) [6].

In our study we confirmed the importance of the majority of above-mentioned patient-related factors. Some of these factors were qualified as the main ones and the other as additional. We have identified the following main patient-related factors of in-hospital mortality: male sex (some studies obtained the opposite result [30,31]), acute LV aneurism, pathological Q-wave on ECG, blood glucose level, triglyceride level and RV dilatation. In-hospital mortality of STEMI patients was not associated with the history of AH. We also showed that DBP had more impact on in-hospital mortality risk in patients with STEMI than SBP. As for TIMI study [6], only the age was fully consistent with our results on major patient-related risk factors.

Comprehensive information on impact of treatment-related factors on in-hospital mortality in patients with STEMI was absent in literature. We have shown that hospital treatment with ACE-Is, ARBs, β-blockers and statins are the main treatment-related factors of in-hospital mortality. Among the set of all significant predictors of in-hospital mortality these medications were the most modifiable factors influencing the risk of death. The first additional treatment-related predictor of in-hospital mortality in our study was hospital treatment with aspirin. It is of interest that C.P. Gale et al. considered aspirin and out-of-hospital thrombolysis as the strongest predictors of in-hospital survival in patients with STEMI [24].

The key point in treatment of STEMI is reperfusion [32,33]. Prompt reperfusion for all eligible patients with STEMI is a present-day challenge for healthcare. In context of present research, the performance of reperfusion evaluated in terms of ACC/AHA measures was one of treatment-related factors influencing on the risk of death in hospital after STEMI. Gharacholou et al. [34] have previously shown that the absence of timely performed reperfusion is associated with greater in-hospital mortality in patients with STEMI without contra-indications. The results of our study in Russian patients with STEMI suggest that reperfusion may reduce short-term mortality risk, if it is performed additionally to basic treatment with main drugs such as ACE-Is, ARBs, β-blockers and statins, which are the main predictors of in-hospital mortality. In [35] it was shown that the mortality benefits from primary PCI and the hazard of primary PCI-related delay depend on baseline risk due to patients-related factors.

Previously, it was found out that the absolute reduction of the risk of mortality from fibrinolytic therapy or primary PCI depend on the patient baseline risk [36]. Our results confirmed this conclusion.

For patients with STEMI treated with primary PCI, it is known that renal insufficiency is an independent predictor of in-hospital mortality [37,38]. The results of the present study did not confirm it.

Shao et al. [39] has shown that differences in therapeutic approach influenced on thirty-day mortality from any reason in STEMI patients. The authors have also revealed gender-related differences in therapeutic approaches. Reperfusion therapy was more often applied to male patients than female ones. As the result, female patients had worse prognosis than male patients. According to [39], the frequency of β-blockers, ACE-Is, statins and other drugs administration in Chinese patients with STEMI was significantly higher in men than in women. Similar gender differences in mortality due to differences in treatment in patients with STEMI were reported by some other authors [40–43]. According to their results, reperfusion therapy gave the main impact on mortality.

In STEMI population with small in-hospital mortality rate (1.9%) [44], evidence-based medications (aspirin, statins,

β-blockers, etc.) were prescribed to the majority of enrolled patients during hospitalization. It was shown in [45] that evidence-based treatments with both reperfusion (fibrinolytic reperfusion or primary PCI) and drug (aspirin, β-blockers, statins, ACE-Is, etc.) decrease in-hospital mortality in patients with STEMI from 12.5% to 7.2%. Similar value of evidence-based drug administration was shown in [46,47]. The results of our study revealed greater influence of some drugs prescription on in-hospital mortality than early reperfusion. But it is unquestionable that the performance of reperfusion is the major factor influencing on long-term survival of patients with STEMI [32,33].

It is obvious that all above mentioned risk predictors are important for short-term prognosis of patients with STEMI and should be taken into account during patients' hospital stay, especially treatment-related factors. In our study we examined the peculiarities of in-hospital mortality predictors in Russian patients with STEMI.

Study limitations

The results have been derived from selected population of Russian ACS patients included in the Russian ACS Registry. Thus, the results extrapolation to the ACS patients from other countries is limited.

Various external factors (non-clinical factors, cancer, anemia, dementia, prior non-cardiac surgery, etc.) that were not taken into account may impact on the results of our study. We cannot account for all such factors, especially unmeasured characteristics.

Since the patients with STEMI who have died were older and often had a history of prior MI, diabetes, congestive heart failure, prior stroke and higher prevalence of AHF Killip class >1 (Table 2), the higher mortality in patients not receiving these drugs could partially be the result of severity of illness.

The results of the study were derived from the data on ACS patients included in the Russian ACS Registry with voluntary participation. Since participation in the Russian ACS Registry was voluntary, the centers, which participated in it could be highly equipped and highly motivated willing to expose their practice to criticism. It is probable that these centers more often adhere to guidelines. Thus, extrapolation of results to ACS patients of the whole country, as well as from other countries is limited.

We did not include subjects older than 80 years in this study. The reasons to exclude them are indicated in the Methods section. Exclusion of all patients over 80 years limits the extrapolation of the results.

In the present study, the date and/or the time of several findings and interventions were not considered (see the Data source section). It was caused by the absence of corresponding information in the Russian ACS Registry database. Missing such data may influence the results of the study.

We revealed the statistically significant differences in administration of ACE-Is/ARBs in STEMI patients who have died during the first 24 h after admission and later. These differences were not determined by the patient clinical status. The extent of their influence on the total in-hospital mortality needs further investigation.

Conclusion

The majority of leading predictors of in-hospital death in Russian STEMI patients was associated with the patient clinical status at hospital presentation and can not be modified by treatment. The treatment with ACE-Is or ARBs, β-blockers and statins during the hospital stay (not necessarily at arrival) influenced the risk of death in hospital as strong as the clinical status of patient at admission. The results of our study assume that these inpatient interventions should be carefully controlled and improved to reduce in-hospital mortality from STEMI. It is also shown that reperfusion and its quality are additional factors, which influence indirectly on the risk of death in hospital in Russian patients with STEMI.

Conflict of interest

The Russian Ministry of Health was not involved in the collection, analysis, and interpretation of data; in the writing of this manuscript; or in the decision to submit the paper for publication.

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Ethical statement

This study was approved by the local Ethics Committee of Saratov Research Institute of Cardiology (Saratov, Russia).

Informed consent

Each patient fulfilled informed consent form prior to his/her data was included in Russian Acute Coronary Syndrome Registry.

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