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Research Article

**COURSE OF ACUTE CORONARY SYNDROME
IN PATIENTS WITH FRAILTY**Svetlana G. Gorelik¹, Andrey N. Ilnitsky¹, Olga A. Osipova¹, Alexey V. Khmel'nitsky²,
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(3, Dynamo pr., Saint Petersburg, Russia, 197110).³ "Samara State Medical University", Samara, Russia (89, Chapayevskaya St., Samara,
Russia, 443099).**Abstract:**

Study materials and methods. In recent years, it is relevant to study the relationship of frailty with the outcome of treatment of patients with ischemic heart disease (IHD) and developed acute coronary syndrome (ACS). The goal of this study was to study the course and outcome of acute coronary syndrome with ST-segment elevation and without ST-segment elevation in patients of older age groups with frailty. The research was a retrospective, current and prospective study of the registers of patients with acute coronary syndrome within the framework of the international project "GIRAFFE – Gerontological Research International Against Frailty: Fit Experience". 1635 patients with IHD were examined (1002 patients of middle age, 633 patients of elderly and senile age). Frailty was diagnosed in 368 patients of elderly and senile age, 265 patients had no frailty. One of four treatment strategies was chosen for patients under study: emergency invasive, early invasive, late (delayed) invasive and conservative. **Study results.** The evaluation of unfavorable coronary events carried out according to the criteria of MACE (Major Adverse Coronary Events) showed that in patients with ACS with ST-segment elevation, as well as in patients without ST-segment elevation receiving conservative therapy, the risk of adverse cardiac events is higher than in patients undergoing invasive therapy. When joining frailty syndrome, the development of adverse cardiac events increases significantly. The excess of the average intrahospital lethality was observed only in elderly and senile patients with frailty, what proved the necessity of correction of frailty in order to improve the results of treatment of patients with ACS with ST-segment elevation and without ST-segment elevation by leveling the negative impact of frailty on the outcome of treatment of acute coronary syndrome

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INTRODUCTION:

Coronary heart disease (CHD) is one of the most common diseases in the world. Acute coronary syndrome (ACS) – is a form of CHD, threatening life and requiring active treatment. There are many prognostic scales for prediction of acute coronary syndrome failures, however, there are no prognostic scales for stratification of cardiovascular risk and patients' status evaluation. [1-4]. Mostly it is necessary for older and senile patients with high risk of polymorbidity and frailty development, which is accompanied by expressed life activity suppression and body rehabilitation ability limitation, which is extremely important for patients, who had acute coronary syndrome [5-9].

One of the leading methods for treatment of acute coronary syndrome along with antiplatelet, anticoagulant and anti-ischemic therapy, is in time myocardium reperfusion. Myocardium reperfusion allows to reduce the necrotic zone significantly, hence decreasing mortality and improving prognosis for patients with ACS [5,7,9,10]. It is stated in the latest European Guidelines, that for treatment of patients having ACS with ST elevation in the first 12 hours from the beginning of the disease the chosen reperfusion therapy method is primary angioplasty and stenting [67]. It is considered to be a good indicator if door-to-balloon time does not exceed 120 minutes [10-11].

Treatment strategies for patients with ACS without ST elevation depends on the severity of the patients' condition and risks of complications and is subject to European recommendations for treatment of ACS without ST elevation issued in 2015 [3,11]. Various scales are used to evaluate risks of complications. Choice of approach is specified by the European Guidelines for the managements of ACS without ST elevation [3,4,9]. Thus, patients with cardiogenic shock or those who underwent resuscitation procedures are subject to immediate coronagraphy according to the mentioned guidelines.

It should be noted that all recommendations and scales for diagnostics and treatment of patients with CHD with ACS development are designed on the basis of the patient's condition severity depending on the progress of CHD with development of ACS. There are no scales and guidelines considering severity of physical functions loss, which leads to dependence from help in everyday life and conditions, typical for elderlies, in particular geriatric syndrome and frailty in patients with CHD and ACS. Such age-related geriatric syndromes and conditions as malnutrition syndrome (nutrition scarcity

syndrome), sarcopenia (age-related decrease in muscle strength and muscle mass), a decrease in the metabolic index and physical activity are involved in the development of frailty [10,6,7]. Some authors note unfavorable combination of cardiovascular diseases' risk factors and mutual deterioration of status in patients with frailty and CHD [2,5,11].

Therefore, analysis of frailty impact on outcome in patients with CHD and development of ACS seems to be relevant.

Study objectives. To study the course and outcomes of acute coronary syndrome with ST-segment elevation and without ST-segment elevation in patients of older age groups with frailty.

Study materials and methods. The research was a retrospective, current and prospective study of the registers of patients with acute coronary syndrome within the framework of the international project "GIRAFFE – Gerontological Research International Against Frailty: Fit Experience" for 2011-2115 years [8,11]. The study was approved by the local ethics committees of clinical researches and conducted in accordance with international principles of biomedical ethics. All patients gave informed consent for inclusion in the study.

The subject of the study was represented by a cohort of patients with CHD. During one year 1635 patients were examined. Of these, 1002 patients in middle age, 633 patient of elderly and frailty age. Among patients of elderly and senile age 368 have been diagnosed with frailty, 265 patients were not diagnosed with frailty.

Diagnosis of frailty has been conducted on the basis of the specialized geriatric examination with the help of the original computer program "Comprehensive Geriatric Assessment" (State Registration Certificate No. 2016615973. Registered by the Federal Service for Intellectual Property (ROSPATENT) [Gorelik S. et al. 2016]. This program includes English electronic versions of the scales "Functional mobility assessment in elderly patients", "Mini nutritional assessment" (MNA), "Philadelphia geriatric morale scale", test " Mini-mental state examination" and the Barthel index, which allow to evaluate the main geriatric syndromes and determine the severity of frailty.

All patients were divided into 2 groups:

Group 1 – patients with ACS with ST-segment elevation (n=961),

Group 2 – patients with ACS without ST-

segment elevation (n = 674).

Each group was divided into subgroups:

1.1 - patients of middle age with ACS with ST-segment elevation (n= 598),

1.2 - patients of older age groups with ACS with ST-segment elevation and with frailty (n=129),

1.3 - patients of older age groups with ACS with ST-segment elevation and without frailty (n=234);

2.1 - patients of middle age with ACS without ST-segment elevation (n= 674),

2.2 - patients of older age groups with ACS without ST-segment elevation and with frailty (n=96),

2.3 - patients of older age groups with ACS without ST-segment elevation and without frailty (n=174).

Frailty was diagnosed in 26.5% of elderly patients and 65.6% of senile patients. That is, among elderly patients with ACS with ST-segment elevation frailty was diagnosed in 72 patients, among senile people – in 57 patients. Among elderly patients with ACS without ST-segment elevation frailty was diagnosed in 56 elderly, among senile patients – in 40 patients.

For examined patients with ACS one of four treatment strategies was selected in accordance with European and national guidelines for management of patients with acute coronary syndrome and following patients' management protocols, including organizational capabilities:

1) emergency invasive – within the first two hours of admission to hospital,

2) early invasive– within the first 24 hours from admission,

3) late (deferred) invasive – within 72 hours from admission,

4) conservative strategy.

Among patients in the 1st group (patients with ACS with ST elevation) conservative therapy was conducted in 182 patients, among them 135 patients initially underwent thrombolysis (74.2%).

In subgroup 1.1, conservative therapy was performed in 41 patients (6.9%), of whom 23 (59.1%) initially underwent thrombolysis.

In subgroups 1.2, 1.3, conservative therapy was performed in 141 patients (38.8%), of which 112 (79.4%) underwent thrombolysis. Then, 114 (84.4%) patients who had undergone thrombolysis initially underwent delayed angioplasty. Among them are 16 middle aged patients and 98 patients of older age groups.

We analyzed the effect of frailty on the outcomes of each of the strategies.

Study results. To evaluate the results of unfavorable coronary events, we selected two indicators: the first one – according to the MACE criteria (Major Adverse Coronary Events), the second one – according to the intra-hospital mortality data.

The development of adverse cardiac events was determined by the MACE scale criteria, which includes the development of a lethal outcome, MI, CABG, or repeated unplanned intervention.

The average intrahospital lethality in the hospital where this study was performed in patients with ACS was 17.1% per year for patients with ST-segment elevation and 2.9% for patients without ST-segment elevation. Over 12 months of follow-up, adverse outcomes were assessed after strategies for treatment of patients with ACS. We obtained the following results, given in Table 1.

Table 1: Development of unfavorable outcome in terms of intra-hospital lethality in patients with ACS (%)

Unfavorable outcome evaluation	Strategies			
	Conservative	Invasive		
		Emergency	Early	Late
<i>Development of unfavorable outcome in patients with ACS with ST segment elevation in relation to strategies of chosen therapy (%)</i>				
Intrahospital lethality:				
middle age (n=598)	9.0	1.2*	2.1**	3.9***, ##
older age groups				
without frailty (n=234)	10.1	2.8*	8.6 [#]	9.4 ^{##}
with frailty (n=129)	19.2	9.0*	17.5 [#]	17.1
<i>Development of unfavorable outcome in patients with ACS without ST segment elevation in relation to strategies of chosen therapy (%)</i>				
Intrahospital lethality:				
middle age (n=404)	2.0	1.2	1.1**	1.9
without frailty				
without frailty (n=174)	2.1	1.1	2.6 [#]	2.5 ^{##}
with frailty (n=96)	4.8	2.7*	2.8	3.0

* p<0.05 between groups of patients with conservative and emergency invasive strategies;

** p<0.05 between groups of patients with conservative and early invasive strategies; *** p<0.05 between groups of patients with conservative and late invasive strategies; [#] p<0.05 between groups of patients with emergency invasive and early invasive strategies; ^{##} p<0.05 between groups of patients with emergency invasive and late invasive strategies;

The obtained data show that in patients with ACS with ST-segment elevation receiving conservative therapy, the risk of adverse cardiac events is higher than in patients undergoing invasive therapy. When associated with frailty, the development of adverse cardiac events becomes more frequent. The excess of the average intrahospital lethality was observed only in elderly and frailty patients with frailty development, and to a greater extent in conservative therapy, despite the fact that the majority of such patients underwent thrombolysis followed by delayed angioplasty.

Patients with ACS without an ST-segment elevation had similar risks of developing adverse coronary events. When joining frailty development of adverse coronary events significantly increased. In this group of patients, the excess of the average intrahospital lethality was also observed only in elderly and senile

patients with frailty, and to a greater extent during conservative therapy, which leads to the conclusion that frailty has an adverse effect on the outcomes of ACS in older age groups. Also attracts attention more unfavorable prognoses for ACS with ST-segment elevation compared to patients with ACS without ST-segment elevation in groups with frailty, and without it.

We also analyzed complications based on the MACE scale in patients with ACS with ST elevation and in patients with ACS without ST elevation. Studied the frequency of repeated revascularization, repeated myocardial infarction (MI), acute cerebrovascular accident (ACVA), as well as the number of deaths within 1 year. Data on complications based on the MACE scale for patients with ACS with ST-segment elevation are shown in Table 2.

Table 2: Development of unfavorable outcomes in patients with ACS with ST-segment elevation in relation to age and presence of frailty, (%)

Unfavorable outcome by MACE	Middle age (n=598)	Older age groups	
		without frailty (n=234)	with frailty (n=129)
Repeated revascularizations number (%)	8.2	9.1	15.3
Repeated MI number (%)	9.3	11.1	23.2**,***
ACVA (%)	3.2	25.1*	33.6**,***
Number of deaths within the year (%)	2.3	5.3*	9.6**,***

* p<0.05 between groups of middle-aged patients and a group of older age patients without frailty; ** p<0. 05 between groups of middle-aged patients and a group of older age patients with frailty; *** p<0. 05 between groups of older age patients.

Data on complications based on the MACE scale for patients with ACS without ST segment elevation are shown in Table 3.

Table 3: Development of unfavorable outcomes in patients with ACS with ST-segment elevation in relation to age and presence of frailty (%)

Unfavorable outcome by MACE	Middle age (n=404)	Older age groups	
		without frailty (n=174)	with frailty (n=96)
Repeated revascularizations number (%)	10.1	17.1	29.5**,***
Repeated MI number (%)	14.3	19.1	28.5**,***
ACVA (%)	2.2	24.1*	32.6**
Number of deaths within the year (%)	1.3	2.5*	5.9**,***

* p<0. 05 between groups of middle-aged patients and a group of older age patients without frailty; ** p<0. 05 between groups of middle-aged patients and a group of older age patients with frailty; *** p<0. 05 between groups of older age patients.

Thus, in patients with ACS without ST-segment elevation, MACE index is high due to developed ACVA and equally due to the number of repeated revascularizations and myocardial infarctions. It should be noted that the number of deaths during the year in patients with ACS with ST-segment elevation is higher than in the group with ACS without ST-segment elevation. Patients of older age groups in groups with frailty having ACS with ST-segment elevation and without ST-segment elevation had significantly more frequent complications by the MACE scale, and had significantly more deaths compared to elderly and senile patients without frailty.

CONCLUSION:

Today, invasive methods used in patients with acute coronary syndrome with ST-segment elevation and

without ST-segment elevation are gaining increasing effectiveness and popularity. Elderly and frailty patients make a special group of high risk. In the course of our study, we managed to prove that patients without frailty have better prognosis for the development of intrahospital mortality, according to the evaluation of adverse outcomes by the MACE scale, in particular the number of repeated revascularizations, the number of repeated myocardial infarctions, the number of acute cerebrovascular accidents, the number of deaths in a year, than patients with frailty. The more unfavorable predictions for ACS with ST-segment elevation are noteworthy in comparison with patients with ACS without ST-segment elevation in groups with frailty, and without it. Patients of older age groups in groups without frailty having ACS with ST-segment elevation and without ST-segment elevation had

significantly fewer complications by the MACE scale, and had significantly fewer deaths compared with elderly and senile patients with frailty, in particular 1.8 and 2.4 times less deaths, respectively.

Thus, correction of frailty can improve the results of treatment of patients with ACS with ST-segment elevation and without ST-segment elevation by leveling the negative impact of frailty on the outcome of treatment of acute coronary syndrome.

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