https://russjcardiol.elpub.ru
doi:10.15829/1560-4071-2019-8-132-139

ISSN 1560-4071 (print)
ISSN 2618-7620 (online)

Delayed help-seeking for emergency medical care of patients with acute coronary syndrome/myocardial infarction: review of studies

Kontsevaya A. V., Kononets E. N., Goryachkin E. A.

The review article provides an analysis of domestic and foreign studies evaluating the dynamics of temporary indicators of prehospital medical care for patients with acute coronary syndrome (ACS)/myocardial infarction (MI). It was noted that the delay in applying for medical care of patients with ACS/MI is currently a significant factor determining the effectiveness of the treatment of these diseases. Over the past decades, modern treatment methods and bright-line health system recommendations have appeared. Significant progress has been made in reducing the time from calling an ambulance to receiving treatment, especially in developed countries. However, in spite of the efforts made, the problem of late appealability of patients is still unresolved. In the world and in Russia, experience aimed to educate patients in terms of ACS/MI symptoms and the importance of timely help-seeking has been gained at the population level. There is no doubt that along with organizational measures aimed to treat cardiovascular patients, increasing public awareness of the ACS symptoms and emergency aid should be considered as one of the priority areas.

Key words: acute coronary syndrome, acute myocardial infarction, risk factors, delayed help-seeking.

Conflicts of Interest: nothing to declare.

National Medical Research Center for Preventive Medicine, Moscow, Russia.

Kontsevaya A. V. ORCID: 0000-0003-2062-1536, Kononets E. N.* ORCID: 0000-0002-0874-9337, Goryachkin E. A. ORCID: 0000-0001-6918-0052.

*__Corresponding author:__ kkuncevo@bk.ru

Received: 07.05.2019
Revision Received: 14.06.2019
Accepted: 26.06.2019

For citation: Kontsevaya A. V., Kononets E. N., Goryachkin E. A. Delayed help-seeking for emergency medical care of patients with acute coronary syndrome/myocardial infarction: review of studies. *Russian Journal of Cardiology*. 2019;24(8):132-139. (In Russ.)
doi:10.15829/1560-4071-2019-8-132-139

Cardiovascular diseases (CVD) remain one of the leading causes of high mortality in the Russian Federation (RF) [1]. Since 2003, in Russia there has been a steady downward trend in CVD mortality, amounting to 616,4 deaths per 100 thousand people in 2016 [2].

Nevertheless, the standardized CVD mortality rates in the Russian Federation when compared with most European countries remain still high (647,6 for men and 345,1 for women) [2, 3]. At the same time, coronary artery disease (CAD) makes the largest contribution to the CVD mortality, and mortality rate from myocardial infarction (MI), in 2016 amounted to 42,9 cases per 100 thousand people [2].

CAD is the main component in economic CVD damage (39,6%) in 2016, which amounted to more than 1 trillion rubles. In turn, MI accounted for more than 213,2 billion rubles. [4] But despite all the successes and achievements of recent years associated with the active introduction of modern methods of reperfusion therapy and more frequent use of drugs that prevent CAD progression, the problem of providing medical care (MC) to patients with MI remains global in our country [1, 4]. So, for example, according to the Monitoring of the Ministry of Health of Russia, hospital mortality in acute coronary syndrome (ACS) in 2016 amounted to 13,8% [5], which, unfortunately, is 2 times higher compared to European countries [3].

It is known that mortality from myocardial infarction is determined by a complex of causes depending both on the patient and on the healthcare system. And if today it has been possible to achieve some positive results, mainly due to minimizing time spending at the system level [6, 7], then with regard to the patient-related period, the target time has not yet been established (Fig. 1). It is believed that reducing the time at this stage of primary health care can significantly reduce the mortality rate from acute MI [8, 9].

In this regard, it is of particular interest to analyze the factors that influence a patient with ACS/IM making a decision to seek for MC.

Delays in seeking for MC according to foreign studies

Long-term trends in the interval from the onset of MI symptoms to hospitalization were studied in an American observational study, which included more than 5967 patients with acute MI, from 1986 to 2005 [10]. When analyzing the data, approximately 45% of patients were hospitalized within the first 2 hours of the onset of symptoms of the disease, 34% were hospitalized 2-6 hours after the onset of symptoms, and 21% 6 or more hours after the onset of symptoms. It was shown that the average value and the median of the time of pre-hospital delay were 3,6 and 2 hours in 1986, 3,9 and 2 hours in 1995 and 3,7 and 2 hours in 2005. Thus, over the 20-year period of the study, the time of pre-hospital delay in most patients did not change significantly.

In a randomized multicenter study (893 patients), conducted in Ireland in 2007-2009, the average time from the onset of symptoms of ACS to the hospitalization ranged from 1,5 to 6 hours [11]. A feature of this study was that the delay time in ACS at the pre-hospital stage was largely determined by pain syndrome severity. In particular, patients with a moderate pain syndrome with the development of ACS took an average of 1,5 hours more time to come to the hospital.

According to McKee G, et al. (2013), the average value of the delay time at the pre-hospital stage in patients with ACS was 4,06 h, and in patients with ST elevation MI (STEMI) and non-ST elevation myocardial infarction (non-STEMI) — 2,7 h and 4,51 hours, respectively [12]. A multivariate analysis revealed that in the subgroups of patients with MI, oligosymptomatic or asymptomatic MI course is associated with a longer delay in the pre-hospital phase.

Similar data are provided by Nilsson G, et al. (2016) in study performed in Sweden [13]. According to results, the median of the total time of pre-hospital delay in patients with MI was 5.1 hours. Moreover, the majority of the delay was from the onset of the symptoms to sought treatment, which amounted to 3,1 hours, in turn, the transportation time — 1,2 hours,

The formation of a modern system for MC organizing during ACS/MI in developed countries has made it possible to achieve a significant reduction in the "systemic" time delay at the pre-hospital stage. Thus, according to the Austrian study Vienna STEMI Registry (1053 patients), conducted from 2002 to 2004, it was noted that the average time from the onset of symptoms of STEMI to arrival in the hospital was 180 minutes [14]. But, at the same time, the main time for pre-hospital delay was still in the period from the onset of the symptoms to sought treatment (approximately 120±15 min).

In a large-scale observational study GRACE (44695 patients), conducted in different countries of America and Europe, shorter intervals of pre-hospital delay were reported in groups of patients with STEMI and non-STEMI [15]. The mean pre-hospi-

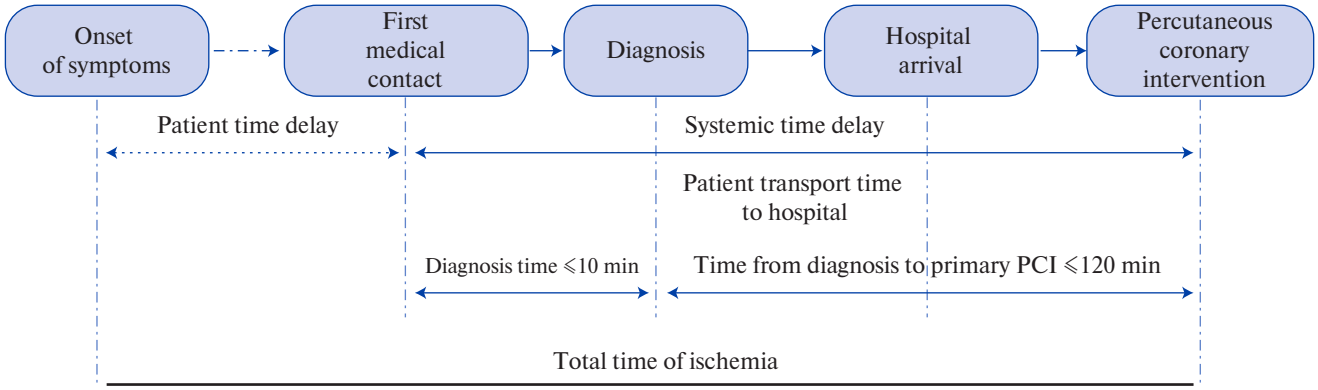

Fig. 1. Components of delayed medical care for MI.

tal delay was the shortest (2,5 hours) in patients with STEMI, while in patients with non-STEMI/unstable angina, there was a longer pre-hospital delay (3,1 hours).

At the same time, in some studies, there was a tendency to a slight decrease in the average time from the onset of the symptoms to the hospital arrival. For example, a comparison of the first and second parts of the EHS-ACS program in terms of time delay showed a decrease in the average time from the onset of ACS symptoms to arrival at the emergency room from 210 min (105-625) in EHS-ACS-I (2000) to 170 min (90-420) in EHS-ACS-II (2004) [16]. This reduction was the result of a decrease in both the time from the onset of disease symptoms to sought treatment, an average of 120 minutes (50-450) in EHS-ACS-I to 105 minutes (40-306) in EHS-ACS-II, and time from the first medical contact (FMC) to arrival at the emergency room, on average from 50 minutes (26-91) in EHS-ACS-I to 42 minutes (15-80) in EHS-ACS-II. At the same time, it was noted that the reduction in time over the indicated period was apparently associated with information campaigns for target population about the need for an immediate response in case of ACS symptoms.

According to European data, the time interval from a call to an emergency MC (EMC) to the FMC should not exceed 20 minutes, and in the Russian EMC this target should also fall within a 20-minute interval [17]. It should be noted that in the organizational plan, further target reduction is no longer possible. In this regard, it is necessary to redirect efforts to optimize the initial time interval from the moment of development of the first ACS symptoms to the sought treatment. According to American standards for EMC for patients with STEMI, the maximum time interval for percutaneous coronary intervention (PCI) should be no more than 120 minutes, while the recommended target time from beginning of symptoms to call to EMC is no more than 5 minutes [18].

So, in the American randomized study IMMEDIATE (871 patients), conducted from 2006 to 2011, the average time from the onset of ACS symptoms to call to EMC was 53 minutes. It is less than in previous studies (NRMI-2, GRACE), but much longer than the target time recommended by the American College of Cardiology [19].

In the prospective observational study ACCESS (11731 patients), conducted in developing countries in Africa, Latin America and the Middle East, the median delay time in the pre-hospital stage was significantly longer and amounted to 4 and 6 hours for patients with STEMI and non-STEMI ($p<0,0001$), respectively [20]. According to the Indian CREATE registry (20937 patients), the median time from symptom onset to hospitalization in patients with STEMI was 5 hours [21].

According to large multicenter observational studies (CREATE, ACCESS, etc.) conducted in developing countries, a greater number of cases of STEMI, longer intervals of pre-hospital delay were recorded. It was largely explained by differences in the level of education, social status and differences in EMC organizing system in developed and developing countries [20, 21].

Delays in seeking for MC according to Russian studies

The results of domestic registers [5, 22–25] which have timeliness analyses of providing MC to patients with ACS/MI at the pre-hospital stage, are generally comparable with the data of foreign studies [15, 16].

Meanwhile, in the study performed in the period from 2004 to 2007 on the basis of several Moscow

clinics, it was found that in most cases, patients with MI seek for MC no earlier than 7 hours after the onset of the first symptoms, moreover, after more than 12 h — 45-53% of patients [23].

In a single-center domestic LIS register with 363 MI patients included from 2010 to 2011, half of the patients took less than 40 minutes to make an decision to call an EMC. However, almost a third of patients applied for MC after an hour or more from onset of the pain syndrome that caused hospitalization with ACS [24].

Quite interesting was the analysis of pre-hospital stage delays according to a series of Russian registers of acute coronary syndrome RECORD. So, the time from the onset of symptoms to hospitalization in a "non-invasive" hospital according to the RECORD-2 register (2009-2011) compared with the results of RECORD-1 (2007-2008) was shorter as in STEACS (3,2 versus 4,1 h, p=0,03), and non-STEACS (4,0 versus 6,5 h, p<0,0001) [25]. According to the "new" RECORD-3 register (2015), which includes much more patients (2370 people), the median time from the onset of symptoms to the first sought treatment was 3,4 hours (1,0-16,8), from FMC to admission to hospital — 1,5 hours (1,0-3,1) for both types of ACS [22].

When comparing data of Monitoring and Register of ACS for 2016, the average time from beginning of symptoms to call to EMC was 115 (60; 177) minutes. According to the data of the ACS Register for the same period, this parameter was 130 (40; 450) minutes. Time medians were comparable and no significant differences between it were found (p>0,05) [5].

As part of the implementation of the national program for the care of patients with acute CVD in the Russian Federation, one of the significant achievements, along with an increase in the quality of specialized care and the number of PCI procedures, is the reduction of all possible time delays from the onset of MI symptoms to reperfusion therapy. But it is mainly due to systemic factors [7]. For example, on the basis of the Kemerovo Regional Vascular Center in 2014 the following time data were achieved: time from beginning of symptoms to call to EMC was 135 minutes, from call to FMC was 27 minutes, and the time period from FMC to PCI was 54 minutes. It is less than the time intervals for 2008 (142, 32 and 40 min, respectively) [26].

Thus, the results of most studies conducted in both developed and developing countries indicate that the majority of the delay in patients with ACS occurs from the moment of first symptoms to patient decides to call to EMC, which is approximately 2/3 of the entire pre-hospital stage [27]. Therefore, one of the priorities in the fight against cardiovascular mortality is a further analysis with a focus on the pre-hospital stage of ACS/MI treatment.

Factors associated with delayed call to EMC

Currently, there are a sufficient number of studies of factors that influence the decision of a MI patient to call to MC. Unfortunately, the results of these studies cannot always clearly determine which of the factors, or their combination, determines the timeliness of a patient's decision to call to MC.

It is known that such socio-demographic characteristics as female gender, old age, and low educational level increase the time until MI patient arrives in the intensive care unit, which was confirmed in review studies [28]. An epidemiological study revealed a negative trend, reflecting an increase in mortality from MI in females [29]. This was largely explained by the peculiarities of clinical manifestations — the predominance of atypical variants of MI in women, which served as an explanation for later treatment among this category. At the same time, according to Efremova O. A. et al. (2015), risk of atypical MI variant remains significantly higher in males aged 56-70 years [30]. In turn, the results of large observational studies also do not confirm the presence of gender differences in the development of atypical MI variants [31].

It should be noted that recently there were publications that cast doubt on the independent contribution of the female sex as a separate factor associated with an increase in the time delay at the pre-hospital stage in patients with MI [31, 32]. So, according to the results of a German study, there was no direct relationship between the female gender and the delay in deciding to call an EMC [31]. According to another study [32], it was also shown that younger women had shorter delay times at the pre-hospital stage compared to men. In the above studies, the authors draw attention to the fact that a combination of two factors (women and the elderly (over 65 years)), is possible to have a synergistic effect, which forms the target group [31, 32]. Similar results were reported in the NRMI register, which included more than 482 thousand patients with STEMI [33]. The study found that in a subgroup of patients with a combination of several factors (old age (70 years and older), female gender, Negroid race or Hispanics, diabetes mellitus), the delay time before arrival to the hospital was significantly longer compared to the reference group (without combination of these characteristics).

Patients with STEMI arrive at the hospital much faster than patients with non-STEMI [12, 20]. Obviously, time difference in admission to the hospital can be explained in terms of the ACS pathogenesis, which determines the development of the corresponding clinical picture of MI. In particular, Perkins-Porras L, et al. (2009) suggest that patients diagnosed with STEMI have symptoms that are likely to be considered more severe, which may increase their motivation for more rapid call to EMC [27].

The development of MI, accompanied by the manifestation of nonspecific symptoms (eg, dyspnea, nausea, weakness), was associated with a long delay of the patient at the pre-hospital stage [34].

In other studies, a clear connection was found between a correct interpretation of the symptoms of MI and a reduction in the time of pre-hospital delay [27]. O'Donnell S, et al. (2014) report that in 65% of patients, the development of ACS was accompanied by a slow onset and moderate pain, while 35% of patients had a classic onset of ACS with the development of an intense pain [11], which makes it difficult to interpret the symptoms of MI as for the patient and for the medical workers.

As for such a characteristic as marital status, ambiguous data are provided in various sources. So, in a prospective study by Fathi M, et al. (2015), it was shown that married patients postpone a visit to a doctor for a longer period, and, on the contrary, patients living alone more quickly apply for MC [35]. The results of the study by Perkins-Porras L, et al. (2009) are consistent with data from Moser D, et al. (2006), which show that marriage and the presence of observer (friend, colleague) were associated with a shorter time for deciding to apply for MC [27, 36]. In contrast, according to studies by Raczynski JM, et al. (1999) and Bolivar J, et al. (2013), family members (especially spouses) increase the delay time before calling the ambulance, trying to propose alternative strategies, while the presence of observer tended to reduce the time of arrival to the intensive care unit [35].

Among the psychoemotional factors associated with the delay of a patient with ACS before hospitalization, a number of authors distinguish anosognosia (denial of their disease) and depressive disorder [37]. So, for example, in a study by Bunde J and Martin R (2006), which included 433 patients, the revealed depressive state, as well as weakness, sleep disturbance and exhaustion, were correlated with a longer patient's decision to apply for MC [38].

According to the Russian LIS register, the rather frequent reasons for late sought treatment of patients with ACS were the fear of hospitalization, the reluctance to disturb the medical workers, and the erroneous assumption that the symptoms may go away on their own or do not pose a serious danger [24].

The level of medical literacy is important in the decision to apply for MC, which was discussed in some works [23, 39]. It was reported that often patients cannot recognize symptoms of ACS in time, attributing them to other diseases [40], due to insufficiency of information on algorithms for providing MC and alertness for the main symptoms of the disease [23].

In a study by Farshidi H, et al. (2013) it was shown that a high level of education and a burdened family history of CVD reliably correlate with a reduction in the time of arrival at the hospital from the onset of MI symptoms [41]. The researchers obtained data that in 73,1% of patients, ignorance of the main CVD risk factors and underestimation of disease severity are causes of untimely sought treatment for MC, and were reliably associated with a low level of education and a lack of CVD history. As noted by Thuresson M, et al. (2007) in their study, 3/4 of the patients were able to correctly interpret the symptoms of MI, as they were previously aware of this disease [39].

The MC time delays in ACS patients at the prehospital stage are also determined by population density, area (urban, rural) [42], geographical features [43], etc.

In the studies of domestic researchers, systemic time delays in rural areas are mainly due to a possible difference in the educational status of urban and rural residents, the low availability of MC in the village, and lack of transport links [42].

Separately, it is also worth dwelling on the geographical features of Russia. It is the main reason for the patient's delay on the way to the PCI center, due to its rather large extent, the significant remoteness of settlements from medical organizations and limited transport links in several regions of the Russian Federation [43].

Interventions aimed at improving the literacy of the population and reducing the time for sought treatment

According to experts, a reduction in cardiovascular morbidity and mortality in the Russian Federation can only be achieved if comprehensive measures are taken to prevent and control CVD complications and to increase the level of public awareness of symptoms and the course of action in ACS/MI [1].

Dracup K, et al. (2009) reported that through educational programs among patients with high cardiovascular risk, an increase in the frequency of aspi-

rin use by patients with ACS at the pre-hospital stage was noted [44]. In an earlier American study by Wright R, et al. (2001) it was shown that the implementation of an educational project to increase public awareness of MI symptoms contributed to a significant increase in the number of calls to EMC [45].

An analysis of domestic and foreign literature sources [23, 39, 41], as well as the results of large-scale sociological surveys conducted in our country, showed extremely low awareness of the population about CVD risk factors, MI signs and symptoms, as well as measures to prevent it. All of the above mean the need for a large-scale educational campaign to increase public awareness of the main IM symptoms, the importance of fast call to EMC, as well as increasing adherence to a healthy lifestyle among the population.

An example of such campaigns is the social project "Act Fast! Save life!", implemented in the Samara region as part of the European Stent for Life initiative [7]. Also there are a number of social and educational programs "Pulse of Life", "Health Index of the Future", implemented in Russia by joint efforts of medical workers, media, involving administrative and other resources. Various events are considered as the main project tool (including on-site seminars, outdoorsy events, conferences, TV shows), aimed primarily at reducing cardiovascular mortality by increasing awareness of the importance of early sought treatment for MC in case of ACS symptoms.

In our opinion, the results of the Swedish study (820 patients) are interesting. In this research authors study characteristics of the MI symptoms and changes of the time interval from the onset of the symptoms to FMC in the primary and repeated MI in the same patient [46]. It was noteworthy that a small number of patients (10% of men and 16,2% of women) reported a different characteristics of symptoms in primary and repeated MI. Moreover, patients with a pre-hospital delay of $\geqslant$2 h with primary MI were more likely to have similar temporary indicators of pre-hospital delay with repeated MI. Researchers concluded that according to the patient's behavior during primary MI, they can predict how they will lead yourself with repeated MI. Therefore, in the development of preventive action algorithms in ACS, a personalized approach is necessary, taking into account certain prognostic factors (for example, old age, concomitant diseases, etc.) and sociological characteristics [38].

One of the extremely important aspects that deserves special attention is the oligosymptomatic and asymptomatic MI course. In a study by O'Donnell S, et al. (2014) it was noted that with the development of atypical MI variants, most patients have difficulties in interpreting their clinical status, which leads to an increase in the time from the onset of symptoms to treatment for MC [11]. Given the above data, it is necessary to consider the need to include information on certain variants of MI to educational events.

Conclusion

The delay in applying for MC for patients with ACS/MI is currently a significant factor in determining the effectiveness of the treatment of these diseases. Over the past decades, modern methods of treatment, clear recommendations from the health system have been developed. Meaningful progress has been made in reducing the time from calling the EMC to receiving treatment, especially in developed countries.

With regard to the behavior of patients, that is, the time from the onset of symptoms to treatment for MC progress is significantly less. Many patients require more than two hours to make a decision about calling an ambulance, which significantly reduces the probability of effective treatment. A number of modified and non-modified factors associated with the decision making speed of patients are demonstrated. A significant factor is the medical literacy of the population, that is, awareness of the symptoms and the ability to recognize them and seek help in time.

In the world and in Russia, experience in conducting interventions at the population level has been accumulated. It aimed at improving the literacy of the population in terms of symptoms of MI/ACS and the importance of timely treatment for MC.

Today, there is no doubt that, along with organizational measures aimed at fight against CVD (improving the MC quality, increasing the coverage of dispensary care, optimizing the system of ambulance care), enhancement the awareness of the population about the ACS symptoms and the course of urgent action should be considered as one of priority areas.

Conflicts of interest: nothing to declare.

References

1. Boytsov SA, Shalnova SA, Deev AD. Cardiovascular mortality in the Russian Federation and possible mechanisms of its changes. Zh Nevrol Psikhiatr Im S S Korsakova. 2018;118(8):98-103. (In Russ.) doi:10.17116/jnevro201811808198.
2. The Demographic Yearbook of Russia. 2017: Statistical Handbook. Rosstat. M., 2017. p. 263. (In Russ.) ISBN 978-5-89476-447-4.
3. Wilkins E, Wilson L, Wickramasinghe K, et al. European Cardiovascular Disease Statistics 2017. European Heart Network, Brussels. http://www.ehnheart.org/images/CVD-statistics-report-August-2017 (05 Feb 2019).
4. Kontsevaya AV, Drapkina OM, Balanova YA, et al. Economic Burden of Cardiovascular Diseases in the Russian Federation in 2016. Rational Pharmacotherapy in Cardiology 2018;14(2):156-66. (In Russ.) doi:10.20996/1819-6446-2018-14-2-156-166.
5. Sagaydak OV, Oschepkova EV, Popova YV, et al. Approaches to optimization of ACS patients care timing characteristics in Federal ACS Registry system and Russian Ministry of Health monitoring system. Kardiologicheskii vestnik. 2017;12(4):82-7. (In Russ.)
6. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39(2):119-77. doi:10.1093/eurheartj/ehx393.
7. Ganyukov VI, Protopopov AV, Bashkireva AL, et al. European initiative "Stent for life" in Russia. Russian Journal of Cardiology. 2016;(6):68-72. (In Russ.) doi:10.15829/1560-4071-2016-6-68-72.
8. Park Y, Kang G, Song B, et al. Factors related to pre-hospital time delay in acute ST-segment elevation myocardial infarction. J Korean Med Sci. 2012;27(8):864-9. doi:10.3346/jkms.2012.27.8.864.
9. Mackay M, Ratner P, Nguyen M, et al. Inconsistent measurement of acute coronary syndrome patients' pre-hospital delay in research: a review of the literature. Eur J Cardiovasc Nurs. 2014;13(6):483-93. doi:10.1177/1474515114524866.
10. Saczynski J, Yarzebski J, Lessard D, et al. Trends in Pre-hospital Delay in Patients with Acute Myocardial Infarction (From The Worcester Heart Attack Study). Am J Cardiol. 2008;102(12):1589-94. doi:10.1016/j.amjcard.2008.07.056.
11. O'Donnell S, McKee G, Mooney M, et al. Slow-onset and fast-onset symptom presentations in acute coronary syndrome (ACS): new perspectives on pre-hospital delay in patients with ACS. J Emerg Med. 2014;46(4):507-15. doi:10.1016/j.jemermed.2013.08.038.
12. McKee G, Mooney M, O'Donnell S, et al. Multivariate analysis of predictors of pre-hospital delay in acute coronary syndrome. Int J Cardiol. 2013;168(3):2706-13. doi:10.1016/j.ijcard.2013.03.022.
13. Nilsson G, Mooe T, Söderström L, et al. Pre-hospital delay in patients with first time myocardial infarction: an observational study in a northern Swedish population. BMC Cardiovasc Disord. 2016;16:93. doi:10.1186/s12872-016-0271-x.
14. Kalla K, Christ G, Karnik R, et al. Implementation of Guidelines Improves the Standard of Care. The Viennese Registry on Reperfusion Strategiesin ST-Elevation Myocardial Infarction (Vienna STEMI Registry). Circulation. 2006;113:2398-405.
15. Goldberg R, Spencer F, Fox K, et al. Pre-hospital delay in patients with acute coronary syndromes (from the Global Registry of Acute Coronary Events [GRACE]). Am J Cardiol. 2009;103:598-603. doi:10.1016/j.amjcard.2008.10.038.
16. Mandelzweig L, Battler A, Boyko V, et al. The second Euro Heart Survey on acute coronary syndromes: Characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J. 2006;27(19):2285-93. doi:10.1093/eurheartj/ehl196.
17. Order of the Ministry of Health of the Russian Federation of February 27, 2016 No. 132n "On the requirements for the placement of medical organizations of the state health care system and the municipal health care system based on the needs of the population." Ministry of Health of the Russian Federation: URL: www.rosminzdrav.ru. (In Russ.) URL: www.rosminzdrav.ru. (24 Apr 2019).
18. O'Gara P, Kushner F, Ascheim D, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127(4):362-425. doi:10.1161/CIR.0b013e3182742cf6.
19. Sullivan A, Beshansky J, Ruthazer R, et al. Factors associated with longer time to treatment for patients with suspected acute coronary syndromes: a cohort study. Circ Cardiovasc Qual Outcomes. 2014;7(1):86-94. doi:10.1161/CIRCOUTCOMES.113.000396.
20. ACCESS Investigators. Management of acute coronary syndromes in developing countries: acute coronary events-a multinational survey of current management strategies. Am Heart J. 2011;162(5):852-9. doi:10.1016/j.ahj.2011.07.029.
21. Xavier D, Pais P, Devereaux P, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet. 2008;371(9622):1435-42. doi:10.1016/S0140-6736(08)60623-6.
22. Erlikh AD, Gratsianskii NA on behalf of participants RECORD-3 registers. Registry of Acute Coronary Syndromes «RECORD-3». Characteristics of patients and treatment until discharge during initial hospitalization. Kardiologiya. 2016;4:16-24. (In Russ.) doi:10.18565/cardio.2016.4.16-24.
23. Bulakhova IY. Effect of delayed application for medical help on the clinical course of myocardial infarction. Klin Med. 2009;87(4):63-7. (In Russ.)
24. Ginzburg ML, Kutishenko NP, Martsevich SY, et al. The analysis of factors influencing the terms of hospital admission in patients with acute coronary syndrome (according to the LIS study data — Lyubertsy study on mortality rate in patients after acute myocardial infarction). Rational Pharmacother. Card. 2012;8(2):141-8. (In Russ.) doi:10.20996/1819-6446-2012-8-2-141-148.
25. Shevchenko II, Erlikh AD, Islamov RR, et al. Comparison of data from registries of acute coronary syndromes record and record-2: Management of patients and its results in noninvasive hospitals. Kardiologiya. 2013;53(8):4-10. (In Russ.)
26. Kosyagina DO, Zavyrilina PN, Sedih DY, et al. Factors associated with delays in seeking medical care in myocardial infraction. Complex Issues of Cardiovascular Diseases. 2017;(3):104-12. (In Russ.) doi:10.17802/2306-1278-2017-6-3-104-112.
27. Perkins-Porras L, Whitehead D, Strike P, et al. Pre-hospital delay in patients with acute coronary syndrome: factors associated with patient decision time and home-to-hospital delay. Eur J Cardiovasc Nurs. 2009;8(1):26-33. doi:10.1016/j.ejcnurse.2008.05.001.
28. Nguyen H, Saczynski J, Gore J, et al. Age and sex differences in duration of pre-hospital delay in patients with acute myocardial infarction: a systematic review. Circ Cardiovasc Qual Outcomes. 2010;3:82-92. doi:10.1161/CIRCOUTCOMES.109.884361.
29. Zhang Z, Fang J, Gillespie C, et al. Age-specific gender differences in in-hospital mortality by type of acute myocardial infarction. Am J Cardiol. 2012;109(8):1097-103. doi:10.1016/j.amjcard.2011.12.001.
30. Efremova OA, Semikopenko IS, Rybasova TA, et al. Epidemiological characteristic of non-typical form of myocardial infarction in Belgorod region. Scientific bulletin BelSU. Medicine Pharmacy. 2015;22(32):104-6. (In Russ.)
31. Ladwig K, Fang X, Wolf K, et al. Comparison of Delay Times Between Symptom Onset of an Acute ST-elevation Myocardial Infarction and Hospital Arrival in Men and Women <65 Years Versus ⩾65 Years of Age.: Findings From the Multicenter Munich Examination of Delay in Patients Experiencing Acute Myocardial Infarction (MEDEA) Study. Am J Cardiol. 2017;120(12):2128-34. doi:10.1016/j.amjcard.2017.09.005

32. Moser D, McKinley S, Dracup K, et al. Gender differences in reasons patients delay in seeking treatment for acute myocardial infarction symptoms. Patient Educ Couns. 2005;56:45-54.
33. Ting H, Bradley E, Wang Y, et al. Factors associated with longer time from symptom onset to hospital presentation for patients with ST-elevation myocardial infarction. Arch Intern Med. 2008;168(9):959-68. doi:10.1001/archinte.168.9.959.
34. Lovlien M, Schei B, Hole T. Pre-hospital delay, contributing aspects and responses to symptoms among Norwegian women and men with first time acute myocardial infarction. Eur J Cardiovasc Nurs. 2007;6(4):308-13. doi:10.1016/j.ejcnurse.2007.03.002.
35. Fathi M, Rahiminiya A, Zare M, et al. Risk factors of delayed pre-hospital treatment seeking in patients with acute coronary syndrome: A prospective study. Turk J Emerg Med. 2016;15(4):163-7. doi:10.1016/j.tjem.2015.06.001.
36. Mozer D, Kimble L, Alberts M, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Council on cardiovascular nursing and stroke council. Circulation. 2006;114:168-82.
37. Xie L, Huang S-F, Hu Y-Z. Factors influencing pre-hospital patient delay in patients with acute myocardial infarction. Chinese Nursing Research. 2015;2:75-9. doi:10.1016/j.cnre.2015.04.002.
38. Bunde J, Martin R. Depression and pre-hospital delay in the context of myocardial infarction. Psychosom Med. 2006;68:51-7. doi:10.1097/01.psy.0000195724.58085.f0.
39. Thuresson M, Jarlöv M, Lindahl B, et al. Thoughts, actions, and factors associated with pre-hospital delay in patients with acute coronary syndrome. Heart Lung. 2007;36(6):398-409. doi:10.1016/j.hrtlng.2007.02.001.
40. Dracup K, McKinley S, Moser D. Australian patients' delay in response toheart attack symptoms. Med J Aust. 1997;166(5):233-6.
41. Farshidi H, Rahimi S, Abdi A, et al. Factors Associated With Pre-hospital Delay in Patients With Acute Myocardial Infarction. Iran Red Crescent Med J. 2013;15(4):312-6. doi:10.5812/ircmj.2367.
42. Kontsevaya AV, Myrzamatova AO, Kashirin AK. Cardiovascular risk factors among inhabitants of rural areas by the epidemiological data: review article Cardiovascular Therapy and Prevention. 2016;15(6):66-71. (In Russ.) doi:10.15829/1728-8800-2016-6-66-71.
43. Timonin S, Kontsevaya A, McKee M, et al. Reducing geographic inequalities inaccess times for acute treatment of myocardial infarction in a large country: the example of Russia. Int J Epidemiol. 2018;47(5):1594-602. doi:10.1093/ije/dyy146.
44. Dracup K, McKinley S, Riegel B, et al. A randomized clinical trial to reduce patient pre-hospital delay to treatment in acute coronary syndrome. Circ Cardiovasc Qual Outcomes. 2009;2(6):524-32. doi:10.1161/CIRCOUTCOMES.109.852608.
45. Wright R, Kopecky S, Timm M, et al. Impact of community-based education on health care evaluation in patients with acute chest pain syndromes: the Wabasha Heart Attack Team (WHAT) project. Fam Pract. 2001;18(5):537-9.
46. Strömbäck U, Engström Å, Lundqvist R, et al. The second myocardial infarction: Is there any difference in symptoms and pre-hospital delay compared to the first myocardial infarction? Eur J Cardiovasc Nurs. 2018;17(7):652-9. doi:10.1177/1474515118777391.