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MYOCARDIAL REVASCULARIZATION IN RUSSIAN FEDERATION FOR ACUTE CORONARY SYNDROME IN 2016-2020

<i>Aim</i>	To analyze the number of cases of acute coronary syndrome (ACS) [ST segment elevation myocardial infarction (STEMI), non-ST elevation acute coronary syndrome (nSTEACS)] and results of myocardial revascularization for ACS as a part of the monitoring performed by the Ministry of Health Care of Russia*. This analysis allows, on one hand, providing control of morbidity and mortality of patients with socially significant pathologies and, on the other hand, monitoring the effectivity of treatments to identify and correct their shortcomings. Time-related changes in results of myocardial revascularization performed for ACS patients in the Russian Federation in 2020 were analyzed and compared with the values of 2016–2019 based on data of the Russian Ministry of Health Care monitoring.
<i>Material and Methods</i>	Yearly absolute, relative, and calculated indices of revascularization for ACS were analyzed and compared based on data of the Russian Ministry of Health Care monitoring in 2016–2020.
<i>Results</i>	In the Russian Federation in 2020, the lowest number of hospitalizations for ACS (403, 931) was recorded with an unprecedented ratio of 1/1.8 for STEMI/nSTEACS, respectively. In Russia in 2020, the proportion of primary percutaneous coronary interventions (pPCI) for STEMI continued growing; it reached 44% and peaked to the maximum for 2016–2020. At the same time, the thrombolytic therapy (TLT) remained essential in the structure of reperfusion strategies during those years (24.0–27.3% of all STEMI cases). Total death rate of admitted patients with STEMI in Russia was stable at the level of 13.1–14.6%. In 2020, there were no significant differences in quality indexes of the treatment for STEMI from the previous period (2016–2019). A yearly relative increase in the number of PCIs for STEACS (from 16% in 2016 to 30% in 2020 and from 30% to 46% for high-risk nSTEACS) was observed. In 2020, a significant increase in death rate was observed for nSTEACS as a whole (to 4.1%) and for individual subgroups (high-risk nSTEACS, to 4.5%; after PCI for nSTEACS, to 1.8%; and after PCI for high-risk nSTEACS, to 2.8%) whereas mean death rate values in these subgroups in 2016–2019 were 2.75%, 3.45%, 1.5%, and 2.3%, respectively.
<i>Conclusion</i>	The analysis of revascularization indexes in ACS patients based on the Ministry of Health Care of Russia monitoring performed in 2016–2020 showed a number of positive trends, including an increase in the total number of revascularization procedures; a decrease in the time from the disease onset to the endovascular treatment; an increase in the availability of stenting for severe ACS; and general stabilization of the mortality. On the other hand, the Russian Federation is considerably behind European countries in several qualitative and quantitative parameters of health care in ACS, such as pPCI availability, symptom-to-balloon time, total mortality of all hospitalized STEMI patients, and revascularization for nSTEACS. Despite the gradual improvement of relative quantitative indexes of myocardial revascularization for ACS, negative changes in the absolute number of myocardial revascularizations for various forms of ACS and a notable increase in the death rate in nSTEACS were observed in 2020, including patients after PCI. There is no doubt that the negative results of myocardial revascularization in Russia in 2020 were due to the effect of the COVID-19 pandemic.
<i>Keywords</i>	COVID-19; acute coronary syndrome; myocardial reperfusion; percutaneous coronary intervention; the Stent – Save a Life initiative; Russian Federation
<i>For citations</i>	Alekyan B.G., Boytsov S.A., Manoshkina E.M., Ganyukov V.I. Myocardial revascularization in Russian Federation for acute coronary syndrome in 2016-2020. <i>Kardiologiya</i> . 2021;61(12):4–15. [Russian: Арлекин Б.Г., Бойцов С.А., Маношкина Е.М., Ганюков В.И. Реваскуляризация миокарда в Российской Федерации при остром коронарном синдроме в 2016-2020 гг. <i>Кардиология</i> . 2021;61(12):4–15]
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* monitoring of measures to reduce the mortality from ischemic heart disease (letters of the Ministry of Health Care of the Russian Federation of 13.03.2015 # 17–6/10/1–177 and of 24.07.2015 # 17–9/10/2–4128), which includes monthly collection of data on the Federal Research Institute for Health Organization and Informatics portal, the Automated System for Monitoring of Medical Statistics, at <http://asmms.mednet.ru>.

Introduction

In 2018, the Russian Federal Project «Combating Cardiovascular Diseases» was launched. The aims of the project include reducing myocardial infarction mortality (up to 30.6 per 100,000 people by 2024) and increasing the number of X-ray-endovascular interventions for treatment purposes (up to 332,300 by 2024) [1].

Acute coronary syndrome (ACS), which represents the most threatening manifestation of coronary artery disease (CAD), has two main patterns: ST-elevation ACS and non-ST elevation ACS (NSTEMI-ACS). Since the former results in myocardial infarction in most cases, the term ST-elevation myocardial infarction (STEMI) will be used. The annual incidence of STEMI and NSTEMI-ACS varies in European countries between 430–1,440 [2] and 900–2,610 per million people, respectively [3–5].

Percutaneous coronary intervention (PCI) is the principal method of myocardial revascularization in ACS [2–4]. Quantitative and qualitative targets for effective treatment identified for patients with STEMI are mainly associated with PCI accessibility [2, 3, 6]. While patient heterogeneity precludes such clear unifying criteria for treatment efficacy in NSTEMI-ACS, myocardial revascularization is achieved in this group of patients with ACS at a total of 60–75% (coronary artery bypass grafting/PCI – 8–12%/50–60%) [4, 5].

According to Fox et al. [7], five-year mortality in patients with a history of ACS is as high as 20%. However, there is no difference in the long-term mortality between patients with STEMI and NSTEMI-ACS. However, most fatalities (up to 95%) in NSTEMI-ACS occur after discharge from the hospital. In 2020, the quantitative and qualitative indicators of outcomes in patients with ACS changed worldwide due to the COVID-19 pandemic [8–11].

Objective

To analyze the trends in the myocardial revascularization indicators in patients with ACS in the Russian Federation for 2020 and compare them with the indicators for 2016–2019 using the monitoring data of the Ministry of Health of Russia.

Material and Methods

The analysis includes annual monitoring data of the Ministry of Health of Russia [Monitoring of measures to reduce coronary artery disease mortality; correspondence of the Ministry of Health of Russia nos. 17–6/10/1–177 dated 03/13/2015 and 17–9/10/2–4128 dated 07/24/2015]. The data on ACS were collected monthly in the web portal of the Russian Research Institute of Health – Automated System of Monitoring of Medical

Statistics (<http://asmms.mednet.ru>). A total of 546,934 hospitalizations due to ACS were registered in the Russian Federation in 2016; the corresponding figures for 2017, 2018, 2019 and 2020 were 550,609, 531,019, 501,238 and 403,931, respectively. All patients with ACS were divided into two groups: STEMI and NSTEMI-ACS. After dividing each group into subgroups, annual rates were analyzed for 2016–2020.

In the STEMI group, the study involved the following subgroups: patients hospitalized within 12 hours after the onset of symptoms; patients who underwent primary PCI (pPCI) (PCI for symptom-related stenosis performed within 12 hours after the onset of STEMI symptoms in patients who did not receive preliminary thrombolytic therapy (TLT); patients who underwent PCI more than 12 hours after the onset of symptoms; patients who received TLT; patients who underwent performed PCI within 24 hours after TLT.

In the NSTEMI-ACS group, the following subgroups were evaluated: patients hospitalized due to high-risk NSTEMI-ACS; patients who underwent PCI; patients with high-risk NSTEMI-ACS who underwent PCI.

After comparing absolute, relative, and calculated annual rates between groups and subgroups for 2016–2020, the trends of indicators were analyzed. Here, the main parameters of interest were the absolute and relative volumes of groups and subgroups, mortality in groups and subgroups, as well as the total number of patients who received and did not receive reperfusion therapy in the STEMI group. Particular attention was paid to the comparison of the rates for 2020 and 2016–2019.

The data were processed using descriptive statistics; the variables were presented as absolute values and/or percentages. The statistical significance of the differences was not assessed.

Results of monitoring of myocardial revascularization in ACS by the Ministry of Health of Russia in 2016–2020

Trends in the number of ACS cases in Russia in 2016–2020

In terms of the absolute number of patients hospitalized with ACS in the Russian Federation in 2016–2019, there were slightly more than 500 thousand cases a year (Figure 1). The largest and the smallest numbers of hospitalized patients with ACS were 550,609 patients in 2017 and 403,931 patients in 2020 (by 26.6%), respectively. In these years, the total hospitalization rates per million people were 3,745 and 2,748, respectively (Table 1). In 2020, the ratio of patients with STEMI/NSTEMI-

Table 1. Trends in the numbers of hospitalized patients with various patterns of ACS per million people in the Russian Federation in 2016–2020

Patterns of ACS	Year analyzed				
	2016	2017	2018	2019	2020
All patterns of ACS	3720	3745	3612	3410	2748
NSTE-ACS	2612	2711	2610	2370	1771
High risk NSTE-ACS	789	889	881	789	621
STEMI	1097	1033	1003	1040	975
STEMI < 12 hours after the onset of symptoms	712	679	670	738	700

ACS – acute coronary syndrome; NSTE-ACS – non-ST segment elevation acute coronary syndrome; STEMI – ST elevation myocardial infarction.

ACS varied from 1/2.6 in 2018 to 1/1.8, respectively. Although the number of patients hospitalized with STEMI remained significantly unchanged to average about 150,000 cases a year (from 161,399 in 2016 to 143,381 in 2020), the mean number of patients with NSTE-ACS (~380,000 cases) decreased significantly in 2020 to 260,350 patients. In 2019, there was a decrease in the number of hospitalizations for ACS by 5.6% and for NSTE-ACS by 9.2% (including patients with high-risk NSTE-ACS by 10.4%) as compared to 2018, whereas the incidence of hospitalizations for STEMI increased by 3.7% (Figure 1).

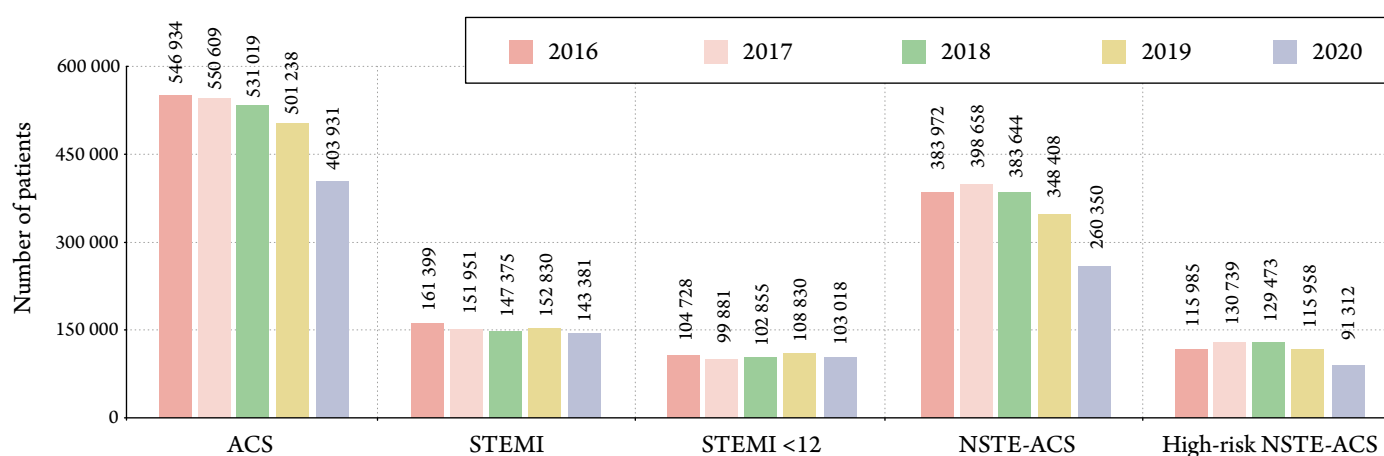
The number of patients with STEMI hospitalized within 12 hours after the onset of symptoms gradually increased from 64.9% in 2016 to 71.8% in 2020. NSTE-ACS with an unfavorable prognosis – that is, high-risk NSTE-ACS – was observed on average in about 32% of all hospitalized patients with NSTE-ACS. In 2020, the percentage of patients with high-risk NSTE-ACS increased to 35.1%; at the same time, the number

of hospitalized patients with NSTE-ACS decreased significantly (Figure 1). Trends of the numbers of hospitalized patients with various patterns of ACS per 1 million people in the Russian Federation are presented in Table 1.

Trends in the number of revascularization procedures in ACS in Russia in 2016–2020

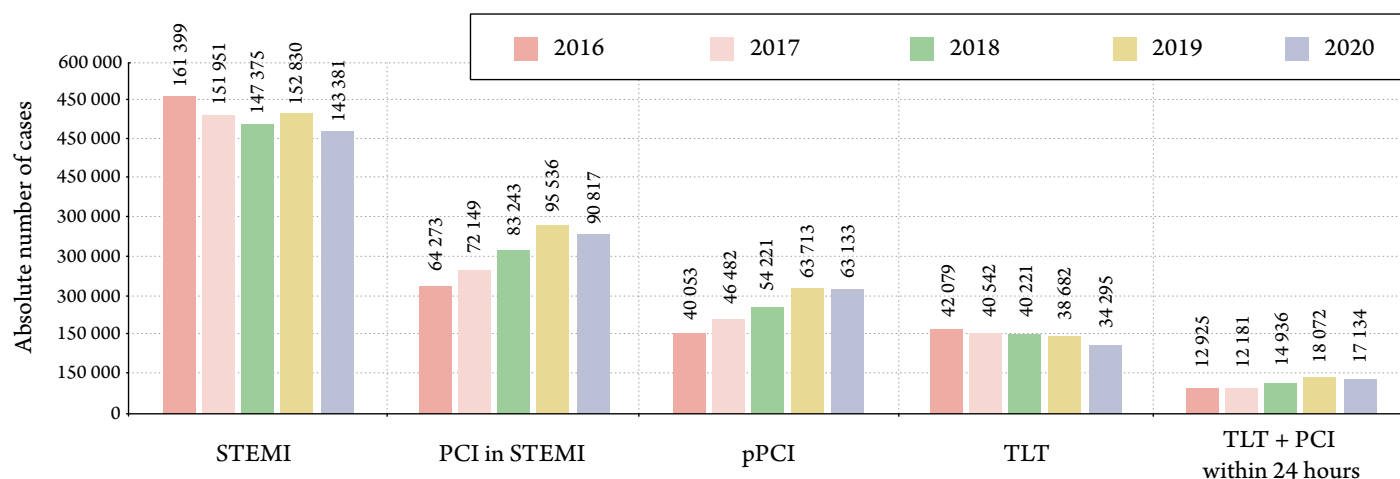
While the total annual number of PCIs in patients with STEMI gradually increased from 64,273 interventions in 2016 to 95,536 in 2019 (by 48.6%) (Figure 2), the number decreased to 90,817 in 2020 (by 4.9% compared to 2019) in the context of the COVID-19 pandemic. The absolute number of primary PCIs (pPCI) – that is, PCI for symptom-related stenosis performed within 12 hours after the onset of symptoms of STEMI in a patient who had not received preliminary TLT – increased by 59.1% from 40,053 in 2016 to 63,713 in 2019. Patients with STEMI who had undergone PCI within the period from 12 to 48 hours after the onset

Figure 1. Absolute number of patients with various patterns of ACS hospitalized annually in the Russian Federation in 2016–2020



ACS – number of cases of any pattern of acute coronary syndrome; STEMI – number of cases of ST elevation myocardial infarction; STEMI <12 – number of cases of ST elevation myocardial infarction hospitalized within 12 hours after the onset of symptoms; NSTE-ACS – number cases of non-ST elevation acute coronary syndrome; high-risk NSTE-ACS – number of cases of high-risk non-ST elevation acute coronary syndrome.

Figure 2. Absolute annual number of cases of various types of reperfusion therapy in STEMI in the Russian Federation in 2016–2020



STEMI – number of cases of ST elevation myocardial infarction; PCI in STEMI –total number of PCIs for STEMI; pPCI – PCI for symptom-related stenosis performed within 12 hours after the onset of STEMI symptoms in a patient who had not received preliminary TLT (patients with STEMI who had undergone PCI within 12–48 hours after the onset of symptoms were excluded from the pPCI group in this study). It is difficult to allocate this group of patients as it is small and not analyzed within the monitoring by the Ministry of Health of Russia).

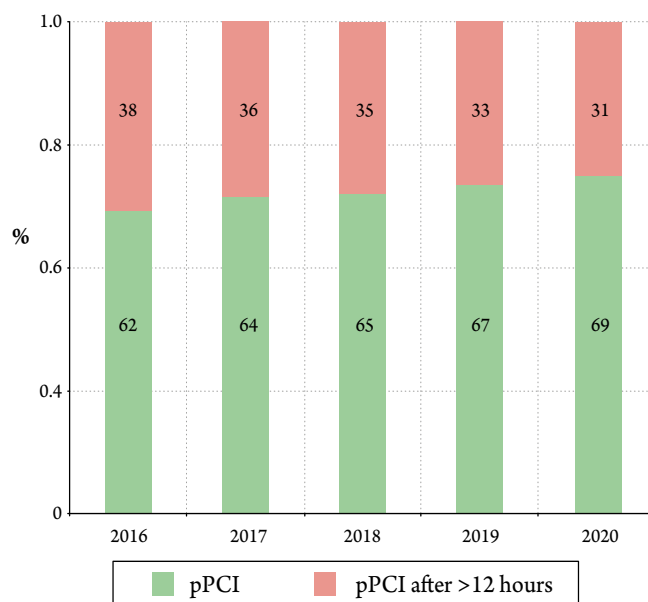
of symptoms were excluded from the pPCI group in this study. This was due to difficulty of allocating such a small group of patients, which has not been analyzed within the monitoring by the Ministry of Health of Russia.

In 2020, the number of pPCI performed was only 580 less than in 2019. Being the most effective treatment for STEMI, primary PCI was performed in only 24.8% (40,053 pPCIs per 161,399 patients with STEMI) of patients hospitalized with STEMI in 2016, compared to 44% in 2020 (63,133 pPCIs per 143,381 patients with STEMI) (the target is more than 70% according to the Stent Save a Life initiative [6]). Other than pPCI, 24,220 (37.7%) (64,273 PCIs for STEMI minus 40,053 pPCIs) and 27,684 (30.5%) (90,817 PCIs for STEMI minus 63,133 pPCIs) PCIs, respectively, were performed in patients hospitalized with STEMI 12 hours following the onset of symptoms in the same years.

Thus, two subgroups of STEMI patients without preliminary TLT who underwent PCI (100%) can be allocated as follows: subgroup 1 (pPCI performed as a timely treatment in 62.3–69.5% of the total number of PCIs for STEMI) and subgroup 2 (PCI performed more than 12 after the onset of STEMI, i.e., late PCI, in 37.7–30.5% of the total number of PCIs for STEMI) (Figure 3).

From 2016 to 2019, there was a slight decrease in the rates of TLT from 42,079 to 38,682 patients with STEMI, which was 26.1% (42,079 cases of TLT in 161,399 patients with STEMI) and 25.3% (38,682 cases of TLT in 152,830 patients with STEMI) of all hospitalized patients with STEMI (Figure 2 and Figure 5). In 2020,

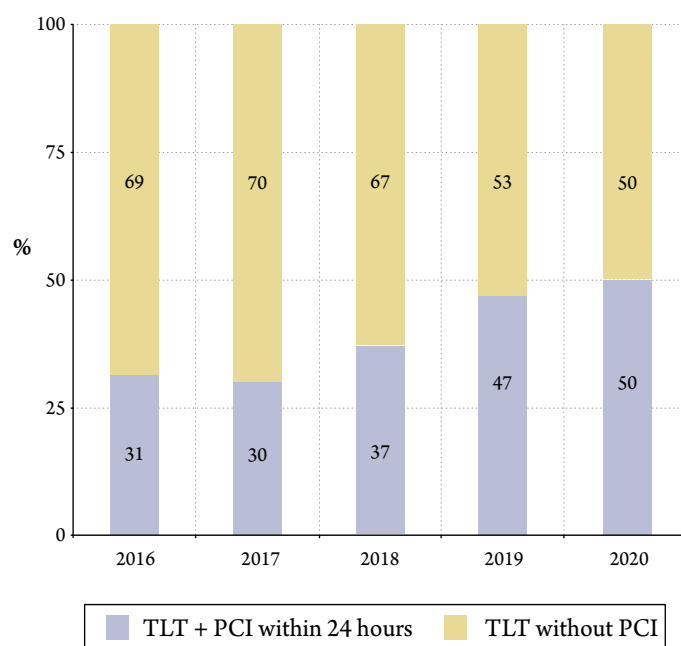
Figure 3. Correlation between pPCI (lower parts of the columns) and late revascularization (upper parts of the columns) in STEMI in the Russian Federation in 2016–2020



pPCI – percentage of PCIs for symptom-related stenosis performed within 12 hours after the onset of STEMI symptoms in a patient who had not received preliminary TLT of the total number of PCIs for STEMI; PCI after >12 hours –percentage of PCIs in STEMI performed more than 12 hours after the onset of symptoms of the total number of PCIs in STEMI; indicators are rounded to integer values.

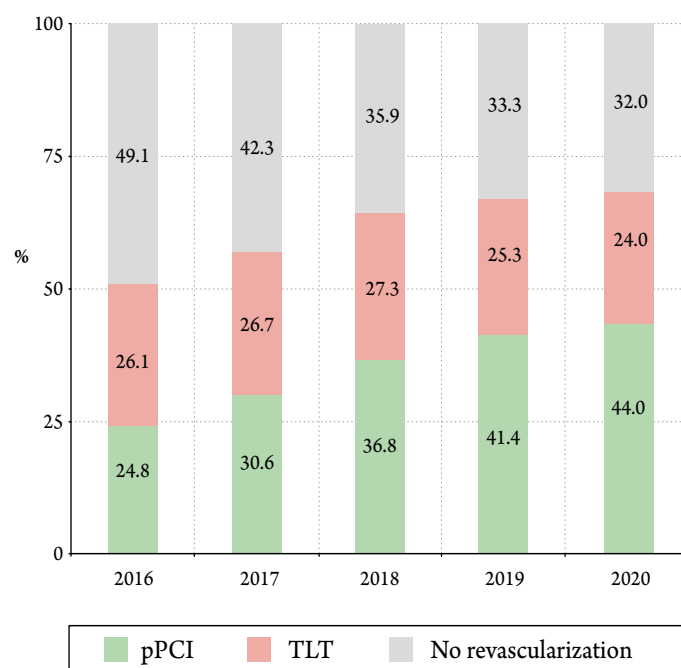
the number of patients who received TLT decreased to 23.9% (34,295 of 143,381 STEMI patients received TLT). The pharmacoinvasive approach (PCI within 24 hours after TLT) was implemented only in 30.7% (12,925 cases of TLT + PCI within 24 hours versus 42,079 cases of TLT) of patients in 2016, but 46.7% (18,072 cases of

Figure 4. Outcomes of thrombolytic therapy (TLT) in the Russian Federation in 2016–2020



TLT+PCI within 24 hours – TLT and PCI completed within 24 hours (pharmacoinvasive approach) after the onset of STEMI (lower part of the graph); TLT without PCI – TLT without PCI (upper part of the graph) within 24 hours; indicators are rounded to integer values.

Figure 5. Reperfusion treatment in STEMI in the Russian Federation in 2016–2020



The lower part of the graph represents the percentage of pPCIs of the total number of STEMI cases, the middle part is the percentage of isolated TLT, and the upper part is the percentage of patients who had not received any reperfusion treatment. STEMI, ST elevation myocardial infarction; TLT, thrombolytic therapy; pPCI, primary percutaneous coronary intervention.

TLT + PCI within 24 hours versus 38,682 cases of TLT) in 2019. The pharmacoinvasive approach was even more applied in 2020 when its frequency increased to 49.9% (17,134 cases of TLT+PCI within 24 hours versus 34,295 cases of TLT), while the total number of cases of TLT decreased by 4,387 (11.3%) compared to 2019 (Figure 4). Here, the frequency of TLT+PCI, which should ideally approach 100%, is insufficient.

Over the 5-year study period, the number of pPCIs increased from 24.8% to 44%, while the relative number of patients with STEMI who did not undergo revascularization (PCI and/or TLT) decreased from 49% in 2016 to 33.3% in 2019 and 32% in 2020 (Figure 5). The relative rates of cases of TLT, including as a part of the pharmacoinvasive approach, were within 27–24% in 2016–2020, with a minimum in 2020.

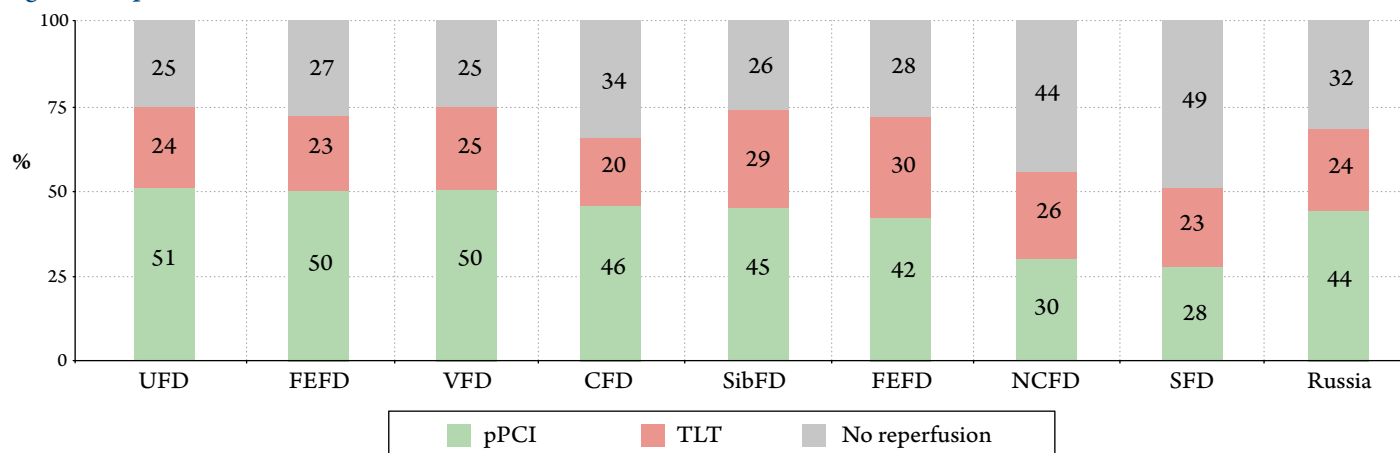
The accessibility of revascularization in STEMI varies considerably throughout Russia (Figure 6). In 2020, the largest percentage of pPCI (51%) was registered in the Ural Federal District, while the largest percentage of pPCI + TLT (75%) was registered in the Ural and Volga Federal Districts.

It is disappointing that the lowest percentage of pPCI was registered in the Southern Federal District (28%), with its high population density and easy access to transport. Data of the European Register on the rates of pPCI and TLT in STEMI in several European countries for 2011 are presented for comparison and to demonstrate the accessibility of revascularization in the Russian Federation (Figure 7) [6].

The total mortality rate in STEMI in the Russian Federation in 2016–2019 was naturally higher in all hospitalized patients compared to the patients who underwent pPCI (Figure 8). A positive trend of decreasing mortality in STEMI should be noted from 14.6% in 2016 to 13.1% in 2019 (by 10.3%). In 2020, the total mortality increased to 14.5% in this group by 10.7% compared to 2019. Mortality increased in the pPCI group from 5.8% in 2019 to 6.2% in 2020. The highest (16.4%) and the lowest (12.4%) mortality rates in STEMI was recorded in 2020 in the Siberian Federal District and the Ural Federal District, respectively (Figure 9).

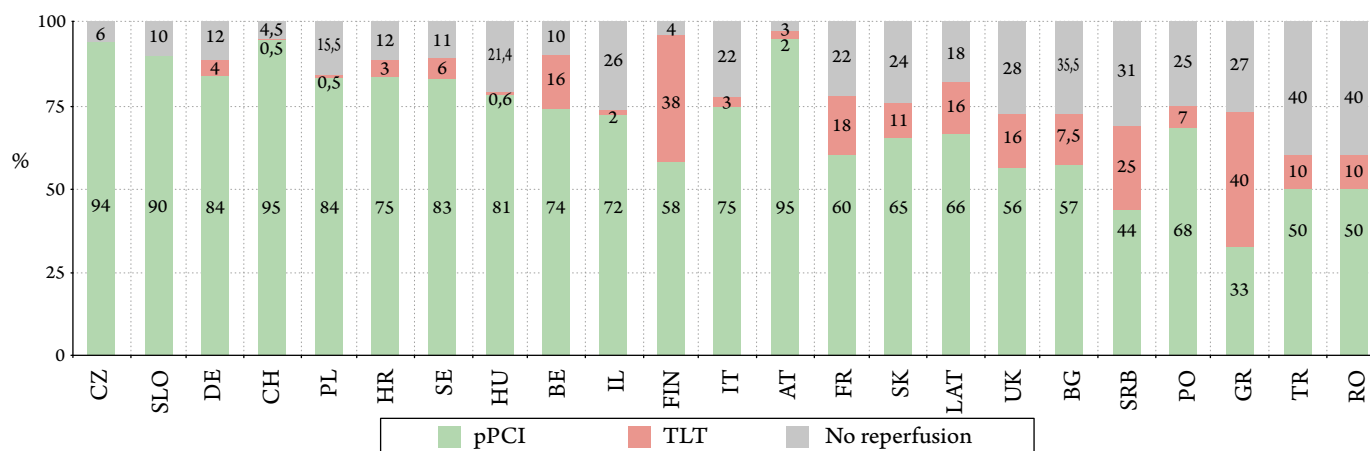
According to symptom-to-balloon time, comprising an indirect indicator of management quality in STEMI, while the trends are not very pronounced in the period of time being analyzed, they are overall positive. In the period from 2016–2020, symptom-to-balloon time decreased from 257 to 231 minutes in the Russian Federation. It should be noted that, while symptom-to-call time (time of the patient's responsibility), which is the first component of symptom-to-balloon time, hardly

Figure 6. Reperfusion treatment in STEMI in the Russian federal districts in 2020



The lower part of the graph represents the percentage of pPCIs of the total number of STEMI cases, the middle part is the percentage of TLT, while the upper part is the percentage of patients who had not received any reperfusion treatment. FEFD – Far Eastern Federal District; VFD – Volga Federal District; NWFD – Northwestern Federal District; NCFD – North Caucasian Federal District; SibFD – Siberian Federal District; UFD – Ural Federal District; CFD – Central Federal District; SFD – Southern Federal District.

Figure 7. Reperfusion therapy in STEMI in Europe in 2010–2011 according to Kristensen et al. [6]



The lower part of the graph represents the percentage of pPCIs of the total number of STEMI cases, while the middle part is the percentage of TLT, while the upper part is the percentage of patients who had not received any reperfusion treatment. CZ – Czech Republic; SLO – Slovenia; DE – Germany; CH – Switzerland; PL – Poland; HR – Croatia; SE – Sweden; HU – Hungary; BE – Belgium; FIN – Finland; IT – Italy; AT – Austria; FR – France; SK – Slovakia; LAT – Latvia; UK – United Kingdom; BG – Bulgaria; SRB – Serbia; PO – Portugal; GR – Greece; RO – Romania.

changed (122, 140, 122, and 123 minutes in 2016, 2017, 2019 and 2020, respectively), a gradual decrease in the second component call-to-balloon time (time of the responsibility of the health system) was recorded (134, 138, 114 and 108 minutes, respectively).

Trends in the number of revascularization procedures in NSTEMI-ACS in Russia in 2016–2020

The absolute annual number of PCIs in NSTEMI-ACS increased in the Russian Federation from 61,001 to 91,429 from 2016 to 2019 (from 16% to 26% of the total number of hospitalized patients with NSTEMI-ACS, respectively) (Figure 10 and Figure 11). In 2020, the absolute number of PCIs in NSTEMI-ACS was 78,481 (30% of all hospitalized patients), representing a 14% decrease as compared to 2019. Here, it should

Figure 8. Mortality in STEMI in the general group and in pPCI in the Russian Federation in 2016–2020

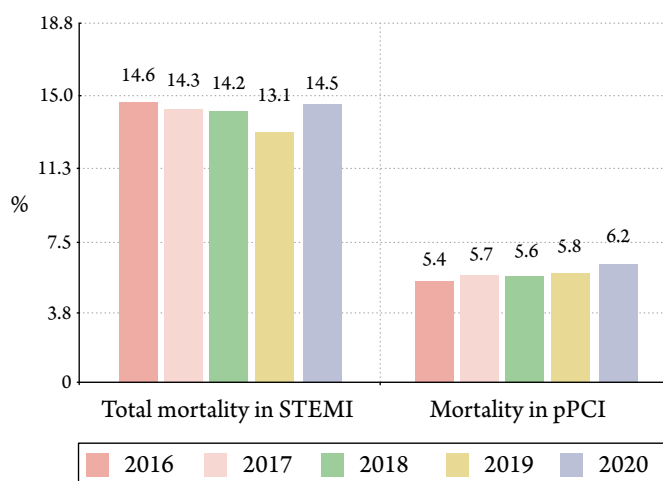
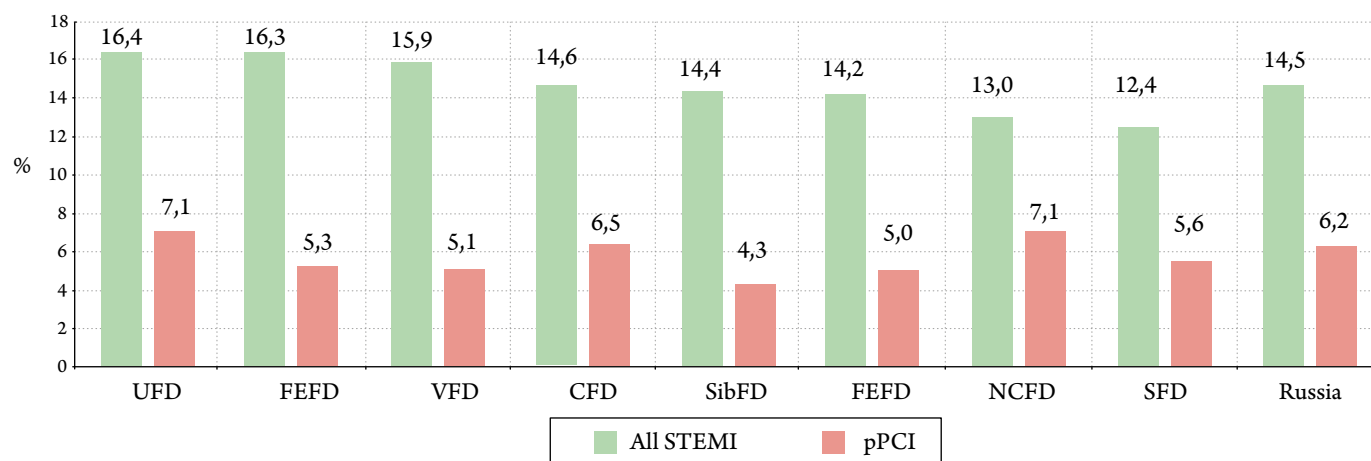
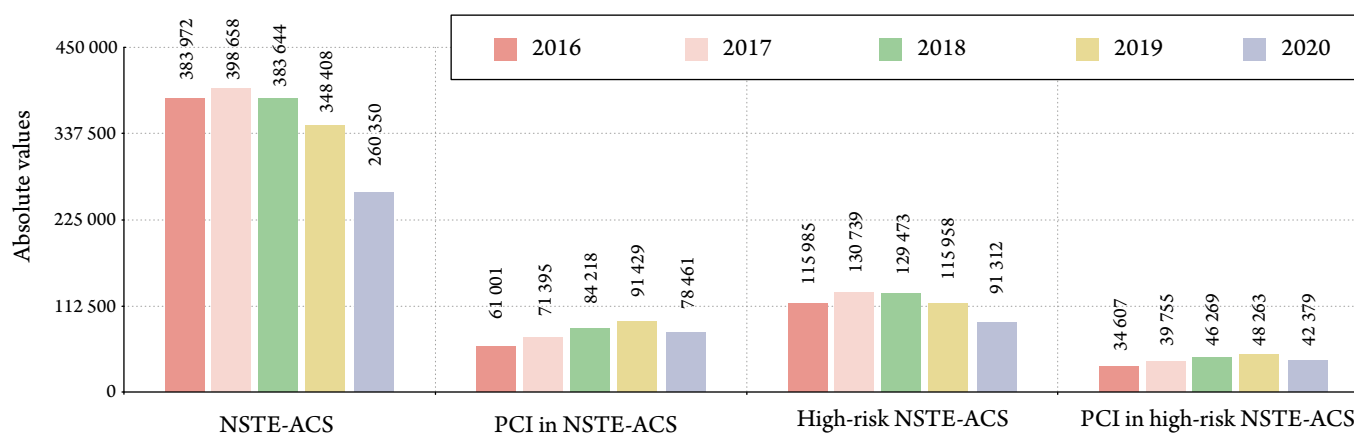


Figure 9. Mortality in STEMI in the general group and in pPCI in 2020 in the Russian federal districts



FEFD is the Far Eastern Federal District; VFD, the Volga Federal District; NWFD, the Northwestern Federal District; NCFD, the North Caucasian Federal District; SibFD, the Siberian Federal District; UFD, the Ural Federal District; CFD, the Central Federal District; SFD, the Southern Federal District.

Figure 10. Myocardial revascularization in NSTEMI-ACS in the Russian Federation in 2016–2020 (absolute values)



NSTEMI-ACS – number of hospitalizations for non-ST elevation acute coronary syndrome within a year; PCI in NSTEMI-ACS – number of percutaneous interventions in patients hospitalized with non-ST elevation acute coronary syndrome; high-risk NSTEMI-ACS – number of patients hospitalized with high-risk non-ST elevation acute coronary syndrome; PCI in high-risk NSTEMI-ACS – number of percutaneous interventions in non-ST elevation acute coronary syndrome.

be emphasized that the decrease in the number of PCIs was significantly smaller in 2020 than a decrease in the number of hospitalized patients with NSTEMI-ACS (25.3%). The absolute number of PCIs in high-risk NSTEMI-ACS increased from 34,607 to 48,263 in 2016 to 2019 (from 30% to 42% of the total number of hospitalized patients with high-risk NSTEMI-ACS). The absolute number of endovascular interventions in high-risk NSTEMI-ACS decreased by 12% in 2020 compared to 2019, amounting to 42,379 (46% of all patients with high-risk NSTEMI-ACS hospitalized in 2020). It should be noted that most of all PCIs in NSTEMI-ACS were performed in patients with high-risk NSTEMI-ACS in the Russian Federation in 2016–2020.

The mortality trends of hospitalized patients with various patterns of NSTEMI-ACS who had and had not

undergone PCI in the Russian Federation in 2016–2020 are presented in Figure 12. In 2016–2019, mortality rates ranged from 2.7% to 2.9% in all hospitalized patients with NSTEMI-ACS, from 3.2% to 4.2% in patients with high-risk NSTEMI-ACS, compared with 1.4% to 1.8% and 2.1% to 2.6%, respectively. In 2020, these indicators increased significantly to 4.1%, 4.5%, 1.8% and 2.8%, respectively.

Discussion

Analysis of quantitative, qualitative, and target indicators of reperfusion for STEMI in the Russian Federation in 2016–2020

The European Society of Cardiology and the European Association of Percutaneous Cardiovascular



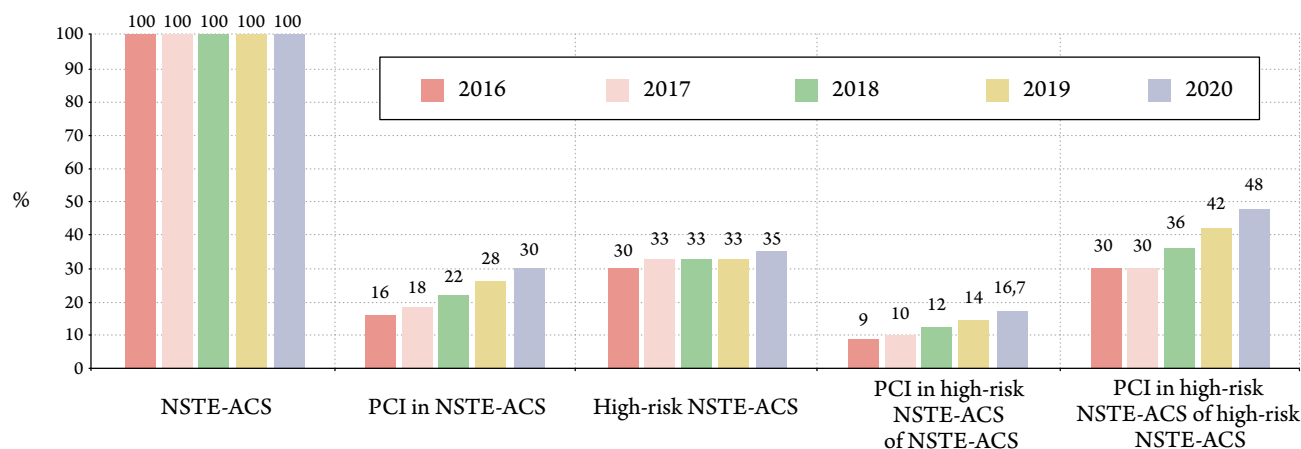
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- Снижению частоты госпитализаций по поводу фатального и нефатального инфаркта миокарда¹
- Снижению числа госпитализаций в связи с усилением симптомов течения ХСН¹

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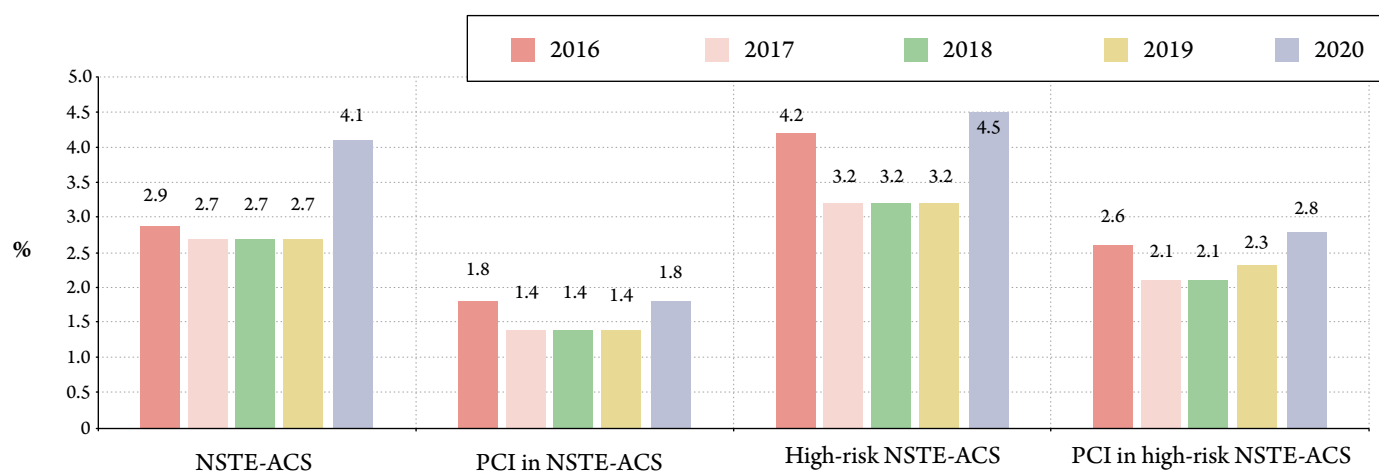
Состав. Таблетки, покрытые оболочкой, содержащие каждая 5 мг или 7,5 мг ивабрадина в виде ивабрадина гидрохлорида. Содержит лактозу в качестве вспомогательного вещества. **Фармакотерапевтическая группа.** Антиангинальное средство. **Показания к применению.** Стабильная стенокардия у пациентов с нормальным синусовым ритмом: при переносимости или наличии противопоказаний к применению бета-адреноблокаторов; в комбинации с бета-адреноблокаторами при неадекватном контроле стабильной стенокардии на фоне оптимальной дозы бета-адреноблокатора. Хроническая сердечная недостаточность: для снижения частоты развития сердечно-сосудистых осложнений (смертность от сердечно-сосудистых заболеваний и госпитализации в связи с усилением симптомов ХСН) у пациентов с синусовым ритмом и ЧСС не менее 70 уд/мин. **Способ применения и дозы.** Кораксан® следует принимать внутрь 2 раза в сутки, утром и вечером во время приема пищи. Стабильная стенокардия. Рекомендуемая начальная доза препарата составляет 10 мг в сутки (по 1 таблетке 5 мг 2 раза в сутки). В зависимости от терапевтического эффекта через 3-4 недели применения суточная доза препарата может быть увеличена до 15 мг (по 1 таблетке 7,5 мг 2 раза в сутки). Если на фоне терапии препаратом Кораксан® ЧСС в покое урежается до значений менее 50 уд/мин или у больного возникают симптомы, связанные с брадикардией, необходимо уменьшить дозу препарата Кораксан® (например, до 2,5 мг по 1/2 таблетки по 5 мг 2 раза в сутки). Если при снижении дозы препарата Кораксан® ЧСС остается менее 50 уд/мин или сохраняются симптомы выраженной брадикардии, то прием препарата следует прекратить. **Противопоказания.** Повышенная чувствительность к ивабрадину или любому из вспомогательных веществ препарата; брадикардия (ЧСС в покое менее 60 уд/мин (до начала лечения)); кардиогенный шок; острый инфаркт миокарда; тяжелая артериальная гипотензия (систолическое АД менее 90 мм рт.ст. и диастолическое АД менее 50 мм рт.ст.); тяжелая печеночная недостаточность (более 9 баллов по шкале Чайлд-Пью); синдром слабости синусового узла; синоатриальная блокада; нестабильная или острая сердечная недостаточность; наличие искусственного водителя ритма; нестабильная стенокардия; атриовентрикулярная (AV) блокада III степени; одновременное применение с мощными ингибиторами изоферментов системы цитохрома P450 3A4 (кетоназол, итраконазол), антибиотиками группы макролидов (кларитромицин, эритромицин для приема внутрь, джозамицин, телитромицин), ингибиторами ВИЧ-протеазы (нефенавир, ритонавир) и нефазодон; беременность и период кормления грудью; женщины детородного возраста, не использующие соответствующих средств контрацепции (см. раздел «Применение при беременности и в период лактации»); возраст до 18 лет (эффективность и безопасность применения препарата в данной возрастной группе не изучались); дефицит лактазы, непереносимость лактозы, синдром глюкозо-галактозной мальабсорбции. **С осторожностью.** Препарат не рекомендуется пациентам с фибрилляцией предсердий (мерцательной аритмией) или другими типами аритмий, связанными с функцией синусового узла; во время терапии следует проводить клиническое наблюдение за пациентами на предмет выявления фибрилляции предсердий (пароксизмальной или постоянной). Пациенты с хронической сердечной недостаточностью и нарушениями внутрижелудочковой проводимости (блокада левой или правой ножки пучка Гиса) и желудочковой диссинхронией должны находиться под пристальным контролем; Кораксан® противопоказан, если до начала терапии ЧСС в покое составляет менее 60 уд/мин (см. раздел «Противопоказания»). Если на фоне терапии ЧСС в покое урежается до значений менее 50 уд/мин или у пациента возникают симптомы, связанные с брадикардией (такие как головокружение, повышенная утомляемость или артериальная гипотензия), необходимо уменьшить дозу препарата. Если при снижении дозы препарата ЧСС остается менее 50 уд/мин или сохраняются симптомы, связанные с брадикардией (такие как головокружение, повышенная утомляемость или артериальная гипотензия), необходимо прекратить прием препарата. Если при снижении дозы препарата ЧСС остается менее 50 уд/мин или сохраняются симптомы, связанные с брадикардией, то прием препарата следует прекратить. Умеренно выраженная печеночная недостаточность (менее 9 баллов по шкале Чайлд-Пью); тяжелая почечная недостаточность (КК менее 15 мл/мин); врожденное удлинение интервала QT; однократный прием лекарственных средств, удлиняющих интервал QT; однократный прием умеренных ингибиторов изоферментов цитохрома CYP3A4 и грейфрутового сока; бессимптомная дисфункция левого желудочка; хроническая сердечная недостаточность IV функционального класса по классификации NYHA; атриовентрикулярная блокада II степени; недавно перенесенный инсульт; пигментная дегенерация сетчатки глаза (retinitis pigmentosa); артериальная гипотензия; одновременное применение с блокаторами кальциевых каналов (БМКК), урежающими ЧСС, такими как верапамил или дилтиазем. При возможности отсрочить плановую электрическую кардиоверсию прием препарата Кораксан® следует прекратить за 24 часа до ее проведения. При изменении гипотензивной терапии у пациентов с хронической сердечной недостаточностью, принимающих Кораксан®, требуется мониторинг АД через соответствующие интервалы времени. **Взаимодействие с другими лекарственными средствами.** Противопоказано: с сильными ингибиторами изофермента CYP3A4, антибиотиками группы макролидов (кларитромицин, эритромицин для приема внутрь, джозамицин, телитромицин), ингибиторами ВИЧ-протеазы (нефенавир, ритонавир) и нефазодон. Не рекомендуется: с лекарственными средствами, удлиняющими интервал QT, умеренными ингибиторами изофермента CYP3A4 (дилтиазем или верапамил). **С осторожностью:** умеренные ингибиторы изофермента CYP3A4, индукторы изофермента CYP3A4, грейфрутовый сок. Беременность и период лактации. Препарат Кораксан® противопоказан для применения при беременности и кормлении грудью. Влияние на способность управлять транспортными средствами и выполнять работы, требующие высокой скорости психомоторных реакций. Возможное возникновение временного изменения световосприятия должно приниматься во внимание при управлении автомобилем или другими механизмами при резком изменении интенсивности света, особенно в ночное время. **Побочное действие.** Очень часто: изменение световосприятия (протопсия). Часто: нечеткость зрения, брадикардия, AV-блокада I степени; желудочковая экстрасистолия, головная боль, головокружение, кратковременное повышение АД. Не часто: ощущение сердцебиения, наджелудочковая экстрасистолия, тошнота, запор, диарея, одышка, вертиго, спазмы мышц, гиперурикемия, эозинофилия, повышение концентрации креатинина в плазме крови, выраженное снижение АД. Очень редко: фибрилляция предсердий, AV-блокада II и III степени, синдром слабости синусового узла. Неучтенной частоты: обмороч, кожная сыпь, зуд, эритема, ангионевротический отек, крапивница, астеня, повышенная утомляемость, недомогание, дислипидия, ухудшение зрения. **Передозировка.** Фармакологическое действие. Действие Кораксана основано исключительно на снижении ЧСС, благодаря селективному и специфическому ингибированию ионных токов I-ригусового узла. Снижение ЧСС приводит к нормализации потребления кислорода тканями сердца. Кораксан® дозозависимо снижает ЧСС и обеспечивает высокую антиишемическую и антиангинальную эффективность. Форма выпуска. Таблетки, покрытые пленочной оболочкой, 5 мг и 7,5 мг. По 14 таблеток в блистер (ПВХ/Ал). По 1, 2 или 4 блистера с инструкцией по медицинскому применению в пачку картонную. При расфасовке (упаковке) на российском предприятии ООО «Сервье»: по 14 таблеток в блистер (ПВХ/Ал). По 1, 2 или 4 блистера с инструкцией по медицинскому применению в пачку картонную. ¹ Для получения полной информации, пожалуйста, обратитесь к инструкции по медицинскому применению лекарственного препарата Кораксан®. Регистрационный номер: ЛС-000885 от 13.04.2018.

Figure 11. Myocardial revascularization in NSTEMI-ACS in the Russian Federation in 2016–2020



NSTEMI-ACS – percentage of hospitalizations for non-ST elevation acute coronary syndrome within a year; PCI in NSTEMI-ACS – percentage of percutaneous interventions of the total number of hospitalizations for non-ST elevation acute coronary syndrome; high-risk NSTEMI-ACS – percentage of hospitalizations for high-risk non-ST elevation acute coronary syndrome of the total number of patients with non-ST elevation acute coronary syndrome; PCI in high-risk NSTEMI-ACS of NSTEMI-ACS – percentage of percutaneous interventions for non-ST elevation acute coronary syndrome of the total number of cases of non-ST elevation acute coronary syndrome; PCI in high-risk NSTEMI-ACS of high-risk NSTEMI-ACS – percentage of percutaneous interventions for non-ST elevation acute coronary syndrome of the total number of patients with high-risk non-ST elevation acute coronary syndrome.

Figure 12. Total mortality in patients with NSTEMI-ACS and in patients with NSTEMI-ACS who underwent PCI in the Russian Federation in 2016–2020



NSTEMI-ACS – mortality in the general group of patients hospitalized for non-ST elevation acute coronary syndrome; PCI in NSTEMI-ACS – mortality in patients who underwent percutaneous interventions for non-ST elevation acute coronary syndrome; high-risk NSTEMI-ACS – mortality in patients with high-risk non-ST elevation acute coronary syndrome; PCI in high-risk NSTEMI-ACS – mortality in patients who underwent percutaneous interventions in high-risk non-ST elevation acute coronary syndrome.

Interventions launched the Stent for Life initiative in 2009, which has now been succeeded by the Stent – Save a Life! initiative [12]. The priority in the treatment of STEMI is given to pPCI in the project papers, and the target quantitative values for pPCI are determined to be achieved in at least 70% of all patients with STEMI, or in the absolute number of more than 600 pPCIs per million people at the national level [3, 6, 12].

The introduction of a program for establishing vascular centers in the Russian Federation in 2008, which has been implementing the Federal Project ‘Combating Cardiovascular Diseases’ since 2018, led

to significant improvements in the accessibility of endovascular management for patients with ACS.

The percentage of pPCIs in patients with STEMI continued to increase to reach 44% in 2020 (Figure 5). Although this is the highest level achieved within the period of 2016–2020, it remains significantly lower than the European target level. The provision of pPCI to 90% of patients in Moscow is an outstanding example of the achieved success. At the same time, the absolute number of pPCIs per million people was almost the same in 2020 as in 2019. The accessibility of reperfusion treatment for STEMI (pPCI and TLT) gradually increases in the

Russian Federation: while 49% of patients with STEMI did not receive reperfusion therapy in 2016, by 2020, the figure had improved to 32% (Figure 5). At the same time, TLT remains a significant part in the reperfusion strategies (24–27.3% of all STEMI cases). In European countries, the main treatment method is pPCI, with TLT being used in no more than 5% of STEMI cases (Figure 7) [5, 6]. Given the large territory of the Russian Federation (remoteness of a PCI-center from the place of residence for a part of the population) and the insufficient number of pPCIs (44%), it is necessary to continue implementing measures to increase the accessibility of pPCI-centers (new PCI-centers, logistics of patient routing, early diagnosis of MI). However, while pPCI remains partially inaccessible, the pharmacoinvasive approach should be key in reperfusion: pre-hospital TLT (in-hospital TLT is possible only if MI develops in hospital) with PCI within 24 hours after successful thrombolysis [13, 14]. The pharmacoinvasive approach is applied when the time from diagnosis of STEMI to PCI is expected to be more than 120 minutes. The trends for the pharmacoinvasive approach (performing PCI within 24 hours after TLT) were positive in the Russian Federation in the period of interest (2016–2020). While TLT followed by PCI within 24 hours from the onset of MI was performed in only 31% of patients in 2016, by 2020 this had improved to 50%. However, this value should ideally approach 100%.

The reasons for the low accessibility of revascularization in the North Caucasian and Southern Federal Districts should be analyzed separately; here 44% and 49% of patients with STEMI did not receive quality care in 2020, with pPCI being performed only in 30% and 28% of patients, respectively (Figure 6).

In the Russian Federation, qualitative indicators of STEMI management (mortality, time from symptom onset to revascularization) are significantly worse than the mean European values [5, 6]. The total mortality of hospitalized patients with STEMI does not exceed 10% in Europe, while, in the Russian Federation, the comparable figure varies between 13.1–14.6% (Figure 8). These inconsistencies with the European reference levels are likely to be due to the relatively low rate of pPCI in the Russian Federation (44% with the target value of >70% [6]) and the long time to revascularization (symptom-to-balloon time was within 231–278 minutes in the Russian Federation in different years of the period of interest, as compared with the European target indicator of 170 minutes [5]). However, while the symptom-to-balloon time gradually decreases due to the call-to-balloon time, the symptom-to-call time remained stable at ~ 120 minutes over the

5-year period. Thus, the medical care system is gradually improving, but the problem persists that people are too slow to seek medical attention when MI symptoms occur. In general, no significant differences were found in the qualitative indicators of STEMI treatment in the Russian Federation in 2020 compared to the previous period (2016–2019).

Analysis of quantitative, qualitative, and target indicators of myocardial revascularization for NSTEMI-ACS in the Russian Federation in 2016–2020

The myocardial revascularization in NSTEMI-ACS is mainly performed using the endovascular approach in the Russian Federation.

The annual rate of coronary artery bypass grafting in patients with NSTEMI-ACS has not been evaluated in monitoring carried out by the Ministry of Health of Russia since 2017. In 2016 alone, 2,281 coronary artery bypass grafting interventions were performed, which was 2% of the total amount of hospitalized patients with NSTEMI-ACS, with only 1,026 (0.9%) surgeries performed within 72 hours from hospitalization.

A favorable trend for the endovascular treatment in patients with NSTEMI-ACS is the annual relative increase in the number of PCIs in NSTEMI-ACS from 16% in 2016 to 30% in 2020 and from 30% to 46% in high-risk NSTEMI-ACS (Figure 11). In 2016–2019, mortality rates ranged from 2.7% to 2.9% in all hospitalized patients with NSTEMI-ACS, from 3.2% to 4.2% in patients with high-risk NSTEMI-ACS, compared with 1.4% to 1.8% and 2.1% to 2.6%, respectively, which is consistent with the mean European mortality rates in NSTEMI-ACS.

When comparing the results of myocardial revascularization for NSTEMI-ACS with Sweden, an insufficient amount of revascularization procedures is evident in the Russian Federation (30% vs. 70%) with comparable mortality (3–4%) [5].

Analysis of the peculiarities of managing patients with ACS in the Russian Federation in 2020

In 2020, the quantitative and qualitative indicators of outcomes in patients with ACS changed worldwide, including in the Russian Federation, due to the COVID-19 pandemic [8–11].

In the Russian Federation, the number of hospitalized patients for ACS decreased by ~ 24% in 2020 compared to the mean number of hospitalized patients in the previous four years (Figure 1). This decrease was mainly due to hospitalizations for NSTEMI-ACS, which were dramatically reduced by ~ 31% in 2020 as compared with the mean level of the previous years. Here, it should

be noted that the main decrease in hospitalizations for NSTEMI/ACS involved patients with milder symptoms; for patients with high-risk NSTEMI/ACS, the comparable figure was only ~ 10%.

Given the comparable number of hospitalized patients with STEMI in 2020 as compared with the previous years, a serious positive trend in the STEMI/NSTEMI/ACS ratio (1/1.8) was registered in the Russian Federation for the first time, which averaged 1/2.4 in previous years. Foreign data also show that the number of hospitalizations for ACS disproportionately involves patients with NSTEMI/ACS [10, 11].

In 2020, the growth in the number of revascularizations for STEMI ceased for the first time in the past 5 years in the Russian Federation: both pPCI for and TLT and the pharmacoinvasive approach (Figure 2). This is particularly clear for the total number of PCIs for STEMI, in which case the annual increase was 8,000–12,000 in 2016–2019, decreasing by 4,719 interventions in 2020 as compared to 2019. However, the positive trend of decreasing numbers of late PCIs after STEMI continued throughout this period to reach a minimum value in 2020, when PCI was performed later than 12 hours after the onset of MI in 31% of patients (Figure 3). Another positive trend can be seen in the increasing number of PCIs performed within 24 hours after TLT, with a maximum value of 50% being achieved in 2020 (Figure 4).

The decrease in the absolute number of PCIs for NSTEMI/ACS by 14% and high-risk NSTEMI/ACS by 12% in 2020 is associated with the direct and indirect effects of the COVID-19 pandemic. This can also help to explain the significant increase in mortality in NSTEMI/ACS in general (up to 4.1%) and in individual subgroups (up to 4.5% in high-risk NSTEMI/ACS, up to 1.8% after PCI for NSTEMI/ACS, and up to 2.8% after PCI for high-risk NSTEMI/ACS) in 2020, whereas in 2016–2019 the mean mortality rates in the above subgroups were 2.75%, 3.45%, 1.5%, and 2.3%, respectively (Figure 12). In addition to the more severe condition of NSTEMI/ACS patients with COVID-19, who tend to be older and have more comorbidities, higher mortality can also be associated with the indirect effects of the COVID-19 pandemic (refusal of patients with mild NSTEMI/ACS from hospitalization due to the risk of COVID-19 infection; reduced accessibility of emergency medical care). The relative number of high-risk

NSTEMI/ACS patients in the NSTEMI/ACS group who were hospitalized in 2020 increased to 35%, which was higher than in 2016–2019.

Limitations

The presented analysis is limited by the relative accuracy and low reproducibility of some indicators used for the monitoring by the Ministry of Health of Russia. This is particularly true of the accuracy of symptom-to-balloon times in STEMI, which appear unrealistic in some Russian regions.

Conclusion

Thus, the analysis of myocardial revascularization indicators in patients with ACS according to the monitoring by the Ministry of Health of Russia in 2016–2020 shows several positive trends: increased total number of revascularization procedures; decreased time from the onset to endovascular treatment; increased accessibility of stenting in severe ACS; mostly stable mortality. On the other hand, the Russian Federation continues to trail behind the European countries in terms of several target quantitative and qualitative indicators of medical care in ACS: accessibility of pPCI, symptom-to-balloon time, total mortality of hospitalized patients with STEMI, revascularization for NSTEMI/ACS.

In 2020, a minimum number of hospitalizations of patients with ACS ($n = 403,931$) was registered in the Russian Federation with an unprecedented STEMI/NSTEMI/ACS ratio of 1/1.8 over the past five years. However, despite gradually improving relative quantitative rates of myocardial revascularization in ACS, there was a negative trend in the absolute number of myocardial revascularizations in various patterns of ACS in 2020, translating into a clear increase in NSTEMI/ACS mortality, including in patients who underwent PCI. The negative outcomes of myocardial revascularization in the Russian Federation in 2020 can be confidently attributed to the COVID-19 pandemic.

No conflict of interest is reported.

The article was received on 12/10/2021

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