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Features of antiplatelet therapy with P2Y12 receptor inhibitors in patients with myocardial infarction according to the Russian Register of Acute Myocardial Infarction REGION-MI

Aim — To study specific features of administering platelet P2Y12 receptor inhibitors to patients with myocardial infarction (MI) in real-life clinical practice; to reveal a possible inconsistency of the therapy with clinical guidelines; to evaluate the patients' compliance with the medication at the outpatient stage; and to outline major direction for improving quality of the antiplatelet treatment.

Material and methods — REGION-MI is a multicenter prospective, observational study. The observational period is divided into 3 stages: during the stay in the hospital and at 3 and 12 months following the inclusion into the registry. Information about the drug therapy (used at the time of hospitalization, administered before the hospitalization, received in the hospital, and prescribed at discharge from the hospital) was recorded in the patient's individual registration card. Information about the antiplatelet treatment at 6 months following enrollment into the study was obtain by phone.

Results — The study included 4 553 patients. Dual antiplatelet therapy was administered after MI to 94.4% patients: clopidogrel was administered to 52%, ticagrelor to 42.2%, and prasugrel to 11 patients (0.2%). Ticagrelor was administered significantly more frequently in ST segment elevation myocardial infarction (STEMI) than in NSTEMI, 45% and 33%, respectively ($p<0.001$); clopidogrel was also administered more frequently to patients with STEMI than with NSTEMI, 59% and 50%, respectively. According to ARC-HBR criteria, in MI and a high risk of bleeding, clopidogrel was administered more frequently than ticagrelor ($p<0.001$). Ticagrelor was significantly more frequently administered to patients with MI and a low risk of bleeding than to patients with a high risk ($p<0.001$). In STEMI and a low risk of bleeding, ticagrelor was administered somewhat more frequently than clopidogrel, 56% and 44%, respectively ($p<0.05$). In NSTEMI and a low risk of bleeding, clopidogrel was administered more frequently than ticagrelor, 53% and 47%, respectively ($p<0.05$). At 6 months post-MI, 94% of patients continued taking one of the P2Y12 inhibitors.

Conclusion — According to data of the REGION-MI registry, the frequency of administering P2Y12 inhibitors to patients with acute MI was high, and the patients' compliance with this therapy was high at 6 months following MI. Although ticagrelor (the most available drug of all powerful platelet P2Y12 receptor inhibitors) has been prescribed more frequently in the recent years, a definite reserve exists for increasing the frequency of its administration. This is particularly important with a low risk of bleeding and the absence of requirement for anticoagulants. Thus, the prognosis for MI patients can be considerably improved.

Keywords — Cardiovascular diseases; ischemic heart disease; acute coronary syndrome; myocardial infarction; acute myocardial infarction registry; antiplatelet therapy; dual antiplatelet therapy

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Introduction

Cardiovascular diseases (CVD) rank first among the causes of disability and mortality in the Russian Federation and most countries. Among CVD as the consequences of coronary artery disease (CAD), including myocardial infarction (MI), contribute the most to mortality, including the working-age population. The main cause of MI is the destabilization of an atherosclerotic plaque, compromised integrity of its cap (rupture, erosion), and the formation of a clot on its surface that blocks partially or completely the lumen of a coronary artery [1]. Patients with MI often have several coronary plaques with defective caps, what is why local exposure in the area of infarct-related plaque should be combined with systemic therapy aimed at reducing the likelihood of damaging other coronary plaques and clotting [1]. Platelet aggregation is a key in intracoronary clotting due to the peculiarities of the coronary arteries associated with small diameters, high flow rate, and other factors [2]. Therefore, antiplatelet therapy is the main component of management and secondary prevention in patients with a history of MI. Modern treatment approaches regulated by clinical guidelines [3–6] imply early administration of the most effective antiplatelet therapy, the standard of which is a combination of acetylsalicylic acid (ASA) and a P2Y12 receptor blocker, in any type of MI, any reperfusion strategy, or conservative treatment. Ticagrelor and prasugrel are preferable according to clinical guidelines as the most potent drugs.

The objective of this study was to analyze the peculiarities of administering P2Y12 receptor blockers in patients with MI in real-world clinical practice, identify possible non-compliance of the administered therapy with clinical guidelines, assess patients' adherence to outpatient treatment, and outline the main directions for improving the quality of antithrombotic treatment of patients with MI, based on the data of the Russian registry of acute myocardial infarction REGION-MI.

Material and methods

The Russian rEGIstry Of acute myocardial iNfarction (REGION-MI) is a multicenter prospective observational study. The registry involves 56 hospitals included in the «MI Network» in the Central, Ural, Siberian, and Far Eastern Federal Districts (a total of 39 Russian regions). The inclusion of patients began in 2020 and continues for 24 months. The registry includes all patients admitted to hospitals from day 1 to day 10 of each month with acute ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI) diagnosed according to the ESC Guidelines on Fourth Universal Definition of Myocardial Infarction (2018). Patients are included in the study after they or their representatives have signed the informed consent to participate in the study and the personal data processing consent. The study is exclusively observational. The study protocol and the informed consent form were approved by the Ethics Committee of the Academician Chazov National Medical Research Center. The study is carried out on the Quinta CRM platform. The case report form contains the following data: demographic characteristics; clinical characteristics and medical history; information on the current case of MI; findings of laboratory test and clinical examinations, coronary angiography and percutaneous coronary intervention (PCI); information on the thrombolytic therapy (TLT); drug therapy (drugs administered at the time of admission, before hospitalization, and during hospital stay); clinical outcomes of the hospital treatment. The follow-up period is divided into 3 stages: observation during hospital stay, 6 and 12 months after inclusion in the registry.

The registry was created to collect data on the diagnosis and treatment of patients with acute MI in Russian hospitals, treatment results, short-term and long-term outcomes (6 and 12 months after the diagnosis of MI) [7].

Statistical processing of the data was carried out using IBM SPSS Statistics v.24. All anamnestic, clinical, and laboratory data obtained were processed by analysis of variance. Mean values (M) and minimum (min) and maximum (max) values were determined for quantitative variables. The frequency of a sign or an event was determined for qualitative variables. The differences were statistically significant at $p<0.05$.

Results

Clinical and demographic characteristics of patients

During the period from 01.11.2020 to 30.04.2022, a total of 4,553 patients were included in the registry. The clinical and demographic characteristics of patients are provided in Table 1.

Rate of P2Y12 inhibitor administration

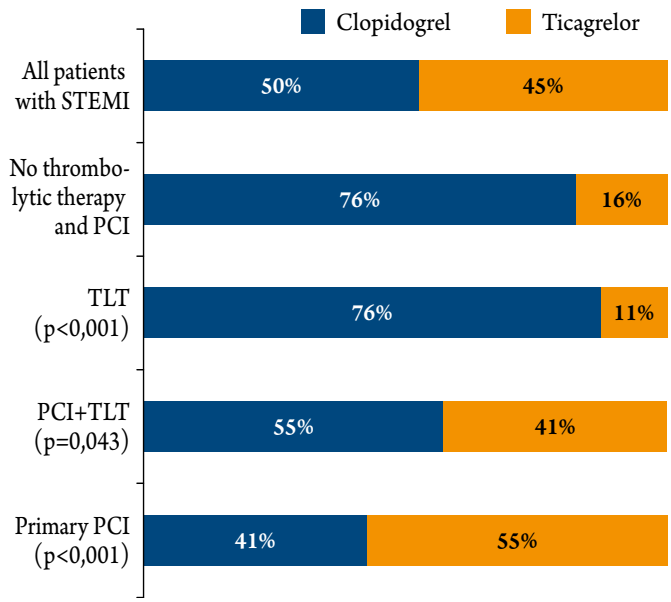
Dual antiplatelet therapy (DAPT) (ASA + a P2Y12 inhibitor) was prescribed at discharge to 94.4% of patients who had suffered MI. Clopidogrel was prescribed at discharge to 52% of patients, ticagrelor – 42.2%, and prasugrel to only 11 (0.2%) patients (10 of them were hospitalized due to STEMI).

Table 1. Clinical and demographic characteristics of the included patients (n=4,553)

Parameter	Value
Mean age of all patients, years (min–max)	63 (25–96)
Age>75 years, %	13.6
Male, %	70.1
Mean age of male patients, years (min–max)	60 (26–96)
Mean age of female patients, years (min–max)	69 (25–92)
Smokers, %	38.7
History of IS/TIA, %	7.1
Patients with arterial hypertension, %	83.1
Patients with CHF, %	22.9
History of AF, %	9.2
GFR<60 mL/min/1.73 m², %	26.1
Patients with angina pectoris, %	32.4
History of PCI/CABG, %	9.8
Patients without a history of MI, %	83.5
Patients with recurrent MI, %	16.5
STEMI, %	73.1
High risk of bleeding (ARC-HBR), %	28.3
Low risk of bleeding (ARC-HBR), %	71.7
Moderate/high/very high risk of bleeding in patients with NSTEMI (CRUSADE), %	57
Very low/low risk of bleeding in patients with NSTEMI (CRUSADE), %	43

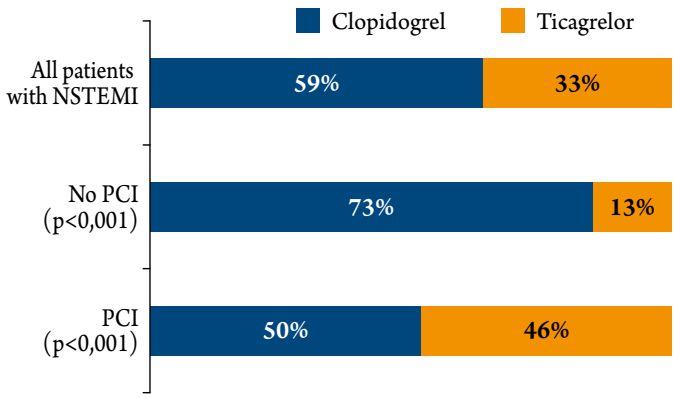
MI, myocardial infarction; CHF, chronic heart failure; IS, ischemic stroke; BMI, body mass index; CAD, coronary artery disease; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; CABG, coronary artery bypass grafting; TIA, transient ischemic attack; PCI, percutaneous coronary intervention; GFR, glomerular filtration rate; AF, atrial fibrillation.

Figure 1. Rate of P2Y12 inhibitor administration in STEMI



STEMI, ST-segment elevation myocardial infarction; TLT, thrombolytic therapy; PCI, percutaneous coronary intervention.

Figure 2. Rate of P2Y12 inhibitor administration in NSTEMI



NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention.

Table 2. Differences in the rate of clopidogrel and ticagrelor administration depending on age and the presence of comorbidities

Clopidogrel. %		p	Ticagrelor. %		p
> 75 years	< 75 years		19.7	45.8	
74.2	48.5	<0.001	History of IS/TIA	No history of IS/TIA	<0.001
History of IS/TIA	No history of IS/TIA		25.5	43.7	
67.3	50.6	<0.05	Hemoglobin>10 g/L	Hemoglobin<10 g/L	<0.001
Hemoglobin>10 g/L	Hemoglobin<10 g/L		43.3	20.5	
51.1	72.3	<0.001	History of AF. %	No history of AF	<0.001
History of AF. %	No history of AF		4.5	46.1	
85.3	48.6	<0.001	GFR<60 mL/min/1.73 m². %	GFR ≥ 60 mL/min/1.73 m². %	<0.001
GFR<60 mL/min/1.73 m². %	GFR ≥ 60 mL/min/1.73 m². %		34.3	46.1	
59.0	48.7	<0.001	34.3	46.1	<0.001

IS. ischemic stroke; TIA. transient ischemic attack; AF. atrial fibrillation; GFR. glomerular filtration rate.

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Differences in the rate of the administration of clopidogrel and ticagrelor depending on age and the presence of comorbidities are presented in Table 2. Ticagrelor was administered statistically significantly more often in patients younger than 75 years, without atrial fibrillation (AF) and a history of cerebrovascular disorders, with hemoglobin levels>10 g/dL and preserved renal function.

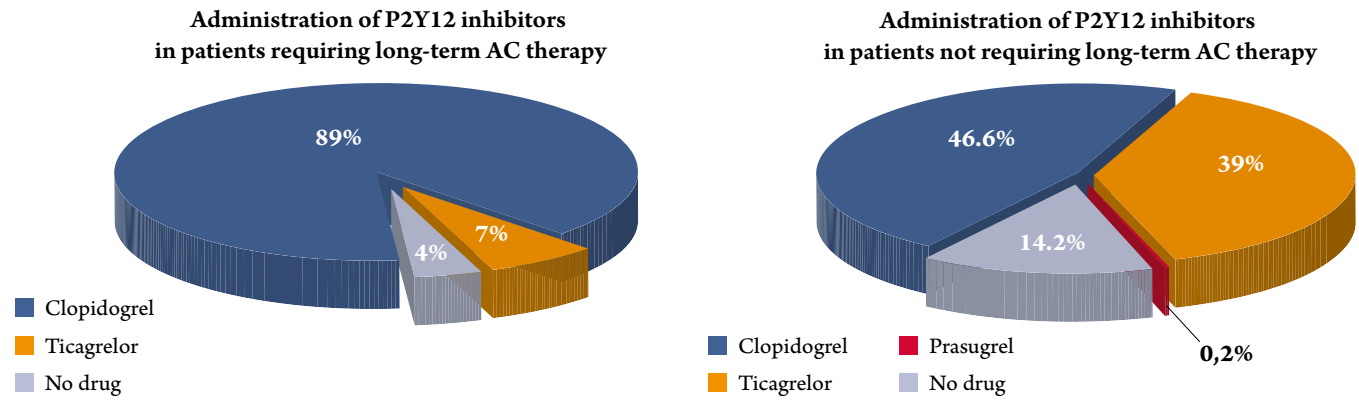
Ticagrelor was prescribed significantly more often in STEMI than in NSTEMI, 45% and 33%, respectively (p<0.001); clopidogrel was prescribed more frequently for patients with STEMI and NSTEMI, 50% and 59%, respectively (Figure 1, Figure 2).

The prescription of P2Y12 inhibitors was analyzed depending on MI treatment strategy. Patients with STEMI were divided into four groups: Ticagrelor was prescribed significantly more often to patients who had undergone primary percutaneous coronary intervention (PCI) – 55% (p<0.001). Prasugrel was administered in 9 patients. The proportion of ticagrelor in the pharmacoinvasive treatment strategy for STEMI was 41%. Clopidogrel was prescribed significantly more often during TLT or conservative therapy (Figure 1). The frequency of the administration of clopidogrel and ticagrelor was approximately the same in patients with NSTEMI after PCI, and prasugrel was prescribed to one patient. Clopidogrel was mainly used in the conservative treatment of NSTEMI (73%) (Figure 2).

The administration of P2Y12 inhibitors depending on the need for long-term anticoagulant therapy is shown in Figure 3. Prasugrel was not prescribed to patients requiring long-term anticoagulant therapy, clopidogrel was administered in the overwhelming majority of cases (89%), and ticagrelor was used in 7% of cases.

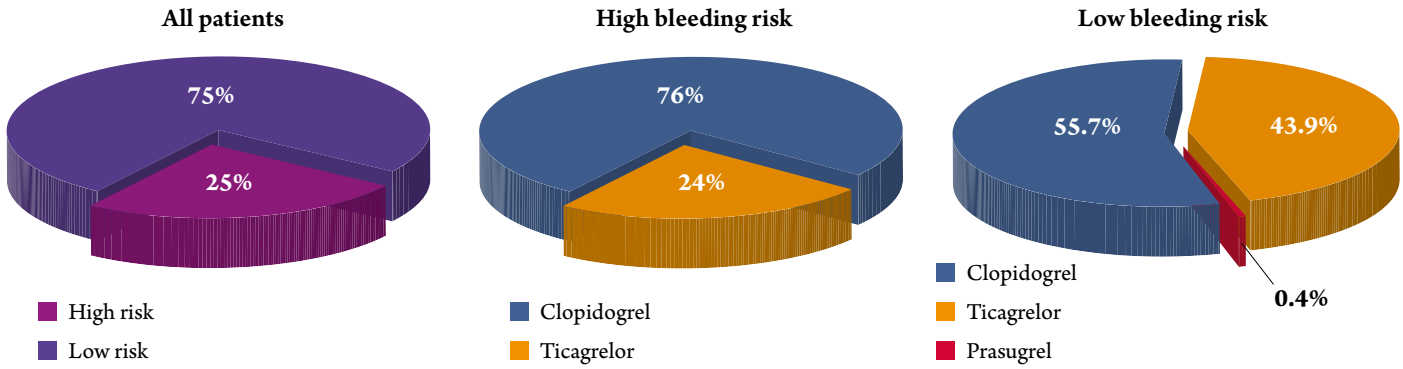
The analysis of the rate of P2Y12 inhibitor administration depending on a type of the hospital showed that the rate of the administration of clopidogrel was the same in the primary vascular departments and regional vascular centers (52%). Ticagrelor was administered relatively more often in the regional vascular centers, in the primary vascular departments – 43% and 39%, respectively. Prasugrel was prescribed to eleven patients admitted to the regional vascular

Figure 3. Administration of P2Y12 inhibitors in patients with MI depending on the need for long-term anticoagulant therapy



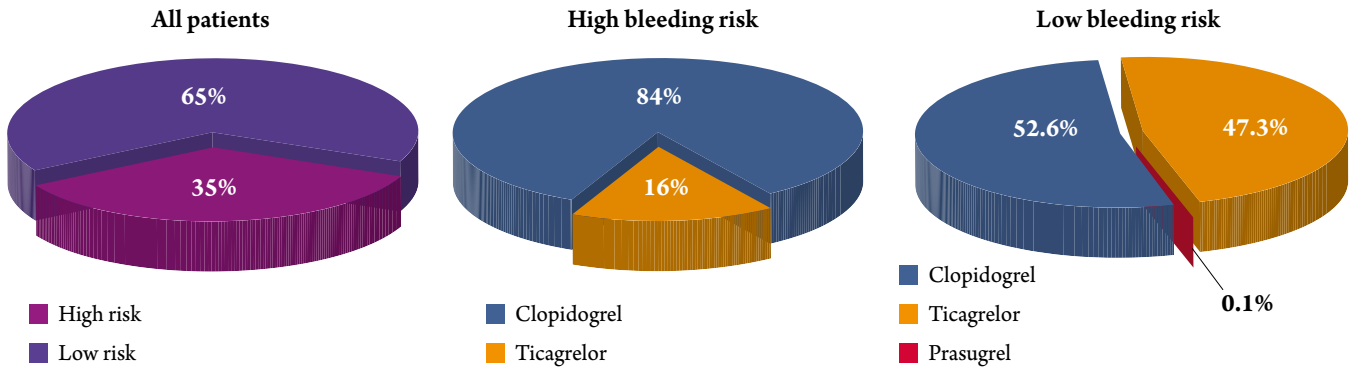
AC, anticoagulant.

Figure 4. Administration of P2Y12 inhibitors depending on a risk of bleeding in patients with STEMI according to the ARC-HBR criteria



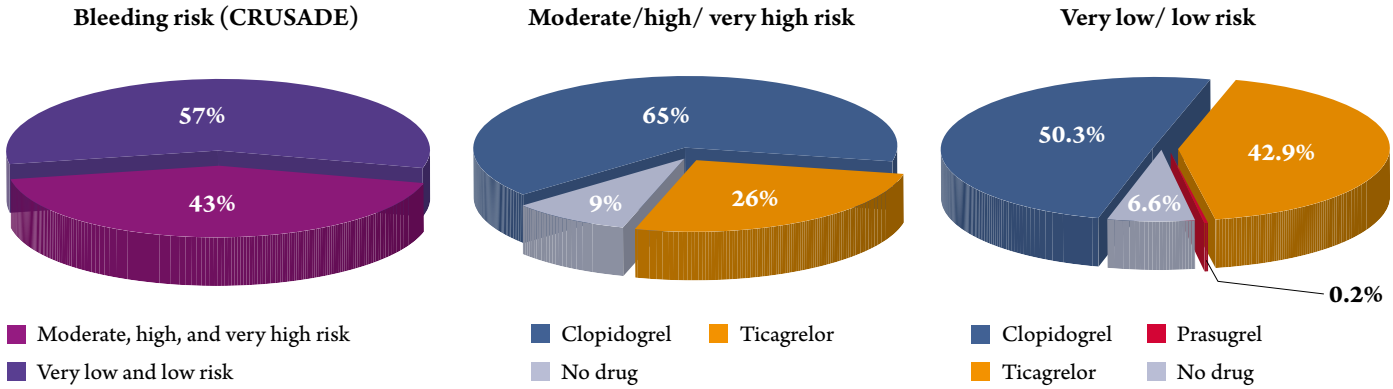
STEMI, ST-segment elevation myocardial infarction.

Figure 5. Administration of P2Y12 inhibitors depending on a risk of bleeding in patients with NSTEMI according to the ARC-HBR criteria



NSTEMI, non-ST-segment elevation myocardial infarction.

Figure 6. Administration of P2Y12 inhibitors in patients with NSTEMI depending on a risk of bleeding according to the CRUSADE score



NSTEMI, non-ST-segment elevation myocardial infarction.

centers and was not ordered in the primary vascular departments.

The analysis of the rate of P2Y12 inhibitor administration depending on the bleeding risk according to the criteria of the Academic Research Consortium for High Bleeding Risk (ARC-HBR) is provided in Figure 4 and Figure 5. Among all patients enrolled in the study, 28.3% of patients were at a high risk of bleeding as assessed by the ARC-HBR criteria, and 71.7% were at a low risk of bleeding. Clopidogrel was administered in STEMI and NSTEMI at a high risk of bleeding significantly more often than ticagrelor ($p<0.001$). Ticagrelor was prescribed significantly more frequently to patients with MI and a low risk of bleeding as assessed by the ARC-HBR criteria than patients facing a high risk of bleeding ($p<0.001$). Ticagrelor was administered in STEMI and a low bleeding risk slightly more frequently than clopidogrel, 56% and 44%, respectively ($p<0.05$). Prasugrel was prescribed to nine patients with STEMI and a low bleeding risk. Ticagrelor was prescribed in NSTEMI and a low risk of bleeding less frequently at discharge than clopidogrel (47%). Prasugel was prescribed to one patient.

Among patients with NSTEMI, 57% faced a moderate, high, and very high risk of bleeding according to the CRUSADE score (Figure 6). In this group, clopidogrel was prescribed more often (65%). Ticagrelor was administered more frequently in the very low risk and low risk group than in the moderate, high risk, and very high risk group ($p<0.05$). However, more patients at a very low and low bleeding risk received clopidogrel than ticagrelor, 50% and 43%, respectively. Prasugrel was prescribed to one patient with NSTEMI and a low risk of bleeding according to the CRUSADE score.

Adherence to antiplatelet therapy and switch of P2Y12 inhibitors

None of the patients enrolled in the study underwent escalation of antiplatelet therapy during hospitalization (switch from clopidogrel to ticagrelor or prasugrel) or its de-escalation (switch from ticagre-

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lor or prasugrel to clopidogrel). Preliminary data on antiplatelet therapy were available 6 months after MI (cut-off date April 2022). Treatment data for 1,004 patients were collected via telephone contacts. 94% of patients to whom P2Y12 inhibitors were prescribed at discharge continued taking one of the drugs 6 months after MI.

Among the patients to whom clopidogrel was prescribed at discharge, 92% continued taking the drug, 2% underwent escalation at the outpatient stage (switched to ticagrelor), 6% of patients completed treatment (42% of them discontinued the drugs on their own without a reason, 4% due to the development of side effects, and 25% stopped taking the drug on the physician's advice).

Among the patients to whom ticagrelor was prescribed at discharge, 89.5% continued taking the drug, 5% of patients were de-escalated to clopidogrel, 5.5% completed treatment (17% stopped taking the drug on their own due to low adherence, 17% due to the high cost of the drug, 6% due to the development of side effects, and 33% of patients stopped taking the drug on the physician's advice).

Discussion

Efficacy of antiplatelet therapy in patients with myocardial infarction and selection of P2Y12 inhibitor

Patients with a history of MI are at a very high risk of developing subsequent cardiovascular events. According to the APOLLO study, every fifth patient suffers an adverse cardiovascular event (cardiovascular death, MI, or stroke) within 12 months year after MI [8]. The high risk of adverse events after MI is mainly caused by recurrent thrombotic complications, which is why suppression of various pathogenetic components of clotting is one of the main directions of MI treatment and secondary prevention. Since clotting in acute coronary syndrome is mainly based on platelet adhesion and aggregation [9], modern approaches to the treatment of MI imply starting effective antiplatelet therapy as soon as possible.

Inhibition of platelet aggregation in patients with acute coronary syndrome (ACS) by targeting P2Y12 receptors has been used in clinical practice for more than 20 years. In the CURE trial, P2Y12 inhibitor clopidogrel in combination with ASA was superior to ASA monotherapy in preventing adverse events

(cardiovascular death + MI + stroke) in patients with NSTE-ACS [10, 11]. Since then, DAPT as a combination of ASA and a P2Y12 inhibitor has become a mandatory component of MI therapy.

Besides clopidogrel, two more P2Y12 inhibitors are approved in the Russian Federation: ticagrelor and prasugrel. Their efficacy in patients with MI has been demonstrated in several studies.

The efficacy and safety of ticagrelor and clopidogrel were compared in patients with MI in the PLATO trial. The trial included patients with STEMI and NSTE-ACS who underwent invasive treatment and conservative therapy in the NSTE-ACS group. Ticagrelor was superior to clopidogrel in all forms of ACS and treatment options. The rate of achieving the primary endpoint (all-cause death + MI + ischemic stroke (IS)) 12 months after the beginning of the trial was 9.8% in the ticagrelor group and 11.7% in the clopidogrel group (hazard ratio (HR) 0.84, p<0.001) [12]. The TREAT trial showed that the administration of ticagrelor soon after TLT was not associated with an increased risk of bleeding compared with clopidogrel [13]. Superiority of prasugrel over clopidogrel in invasive strategy in patients with ACS was demonstrated in the TRITON-TIMI 38 trial. Patients with STEMI and NSTEMI who underwent PCI were included in the trial. Adverse cardiovascular events occurred in 12.1% of patients receiving clopidogrel and 9.9% receiving prasugrel (HR 0.81, p<0.001). The incidence of major bleeding was higher during ticagrelor and prasugrel treatment, but the overall clinical benefit considering ischemic events and bleeding was higher than in clopidogrel group [14].

The results of the above trials were implemented in modern clinical guidelines, according to which prasugrel (in the invasive strategy) and ticagrelor (in primary PCI and conservative therapy), if not contraindicated, are the drugs of choice in the treatment of MI, as they have the most potent antiplatelet effect (class and level of recommendations of IA in STEMI and IB in NSTEMI according to the ESC guidelines; and grade of recommendation A and level of evidence 2 according to the Russian Society of Cardiology guidelines, in STEMI and NSTEMI) [3–6].

After the launch of ticagrelor and prasugrel, clopidogrel became the second line, but remains a relevant treatment. The main candidates for clopidogrel therapy are patients requiring long-term administration of anticoagulant therapy and those who cannot be treated with ticagrelor or prasugrel (high bleeding risk, contraindications, side effects during therapy) [3, 4]. Clopidogrel is the only P2Y12 inhibitor recommended to patients with STEMI before and during TLT [4].

Rate of P2Y12 inhibitor administration

At discharge, one of the P2Y12 inhibitors was prescribed to 94.4% of patients enrolled in the registry. The majority of patients received clopidogrel (52%), ticagrelor was prescribed to 42.2%, and only 11 patients received prasugrel.

According to the Austrian registry of ACS, the overall rate of clopidogrel administration was significantly lower (27.2%) than in our study, a larger number of patients (36.8%) administered ticagrelor, and 32.2% used prasugrel [15].

In our registry, the rate of clopidogrel and ticagrelor administration in STEMI was almost the same, 50% and 45%, respectively, and prasugrel was prescribed to 10 patients. According to the Russian registry RECORD-3 (from March to April 2015), the rate of ticagrelor administration in STEMI was significantly lower than in our study (only 18%) [16]. Prasugrel was not then used in the Russian Federation. We see a clear trend to increased rate of ticagrelor administration. The inclusion of the drug in the List of Vital and Essential Drugs obviously contributed to this.. The federal project Combating Cardiovascular Diseases is implemented in the Russian Federation. Under this project, five groups of patients with circulatory disorders, including those with a history of MI, take advantage of preferential provision of 23 drugs, including clopidogrel and ticagrelor. Patients can currently receive these drugs free of charge for two years after the onset of MI. Prasugrel, being a relatively expensive drug, is not included in this list, which largely explains the low administration rate. The data of the Chest Pain-Myocardial Infarction registry (USA) are consistent with our findings: the rate of clopidogrel and ticagrelor administration was 42.6% and 44%, respectively. Prasugrel was prescribed to more patients in the US registry than in our registry: 13.5% and 0.3%, respectively [17]. In the Danish MI registry, the rate of clopidogrel administration in patients with STEMI was significantly lower (24.3%) than in our study, the rate ticagrelor and prasugrel administration were, in contrast, higher: 38.6% and 37.1%, respectively [18].

The findings of the Polish PL-ACS registry were similar to ours. The rate of clopidogrel and ticagrelor administration was also approximately the same in patients with STEMI, 42.8% and 43.2%, respectively. In the PL-ACS registry, clopidogrel was administered significantly more frequently in NSTEMI (55.6%), clopidogrel was prescribed at discharge in our study to 59% of patients with NSTEMI [19]. Clopidogrel was prescribed to most patients (47.1%) in NSTEMI in the EYESHOT registry (Italy). Clopidogrel and ticagrelor were administered in STEMI in this study in

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approximately equal proportions: clopidogrel and ticagrelor in 34.9% and 34.6% of patients, respectively, and prasugrel in 25.5%. In the EYESHOT registry, like in our registry, the conservative treatment of STEMI and NSTEMI included the prescription of clopidogrel at discharge to the majority of patients despite the documented higher efficacy of ticagrelor in the conservative strategy for patients with NSTEMI [20].

In the SWEDEHEART registry (Sweden), P2Y12 inhibitors were prescribed at discharge to 97% of patients with MI. One of the most potent P2Y12 inhibitors ticagrelor was administered in more than 80% of patients with STEMI and NSTEMI [21].

In the REGION-MI registry, clopidogrel was prescribed at discharge to the majority of patients with indications for long-term anticoagulant therapy, including patients with AF. Ticagrelor was prescribed to 7% and 4.5% of patients, respectively, which is acceptable in individual cases provided that there is a high risk of ischemic events and a low risk of hemorrhagic complications.

According to the data obtained, ticagrelor is prescribed to elderly patients unreasonably rarely in the Russian Federation (only 19.6% of patients above 75 years old received ticagrelor). The safety of ticagrelor in elderly patients was demonstrated in the PLATO subanalysis [22]. Ticagrelor was more effective that clopidogrel in the older age group like in the entire patient cohort. There was unexpectedly almost no difference in bleeding rate between ticagrelor and clopidogrel in ≥75-year-old patients. Thus, older age alone should not be the cause of DAPT de-escalation.

The same can be said for the low rate of ticagrelor administration in decreased glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 (34.3%). The PLATO subanalysis [23] showed that ticagrelor was safe in patients with chronic kidney disease (there was no statistically significant increase in the incidence of bleeding in this group as compared with clopidogrel) and even more effective than in patients with preserved renal function.

When analyzing the rate of P2Y12 inhibitor administration depending on a type of the hospital, no statistically significant difference was observed, modern highly effective antiplatelet drugs are prescribed in the primary vascular departments with the same rate as in the regional vascular centers.

According to the Austrian registry [15], 55.2% of patients, to whom clopidogrel was prescribed at discharge, had no absolute contraindications to a more potent P2Y12 inhibitor. Ticagrelor was prescribed significantly more frequently in our registry to patients with MI and a low bleeding risk as assessed by the ARC-HBR criteria than patients facing a high bleeding risk. However, the high rate of clopidogrel administration is noteworthy even in the group with a low bleeding risk (44% in STEMI and 53% in NSTEMI). Thus, there is a large reserve to increase the rate of prescribing more potent and effective P2Y12 inhibitors ticagrelor and prasugrel.

Such high rate of clopidogrel administration is likely to be due to excessive alertness among physicians regarding the risk of bleeding and economic factors, because clopidogrel is available in many cheap generics.

Adherence to antithrombotic therapy 6 months after MI and inclusion in the REGION-MI registry is high: 94% of patients continue to administer one of the P2Y12 inhibitors. In our study, 92% of patients to whom clopidogrel was prescribed and 89.5% who administered ticagrelor continue taking the drugs. Adherence to clopidogrel and ticagrelor was higher than in the RECORD-3 registry. According to the RECORD-3 registry, 29% and 33% of patients discontinued clopidogrel and ticagrelor, respectively, 6 months after MI [24]. It can be said that the antiplatelet therapy situation in the Russian Federation has significantly improved in recent years. High treatment adherence can be explained by the good safety profile of the drugs, the availability of antiplatelet drugs and patients' willingness to administer them

Conclusion

The Russian registry of acute myocardial infarction REGION-MI shows the high rate of P2Y12 inhibitor prescription in patients with acute MI and high adherence to this therapy 6 months after MI. Despite the fact that ticagrelor (the most available potent P2Y12 inhibitor) has been prescribed more frequently in recent years, there is a certain reserve for higher rate of the administration, which is especially relevant in a low bleeding risk and the lack of the need for anticoagulants. Thus, the prognosis can be significantly improved in patients with MI.

Limitations

Only hospitals included in the «infarction network» participate in the registry, which excludes the analysis of cases of acute MI in non-specialized hospitals; not all regions of the Russian Federation participate in the registry program; some patients were lost to follow-up; data are collected through telephone contacts, not at appointments, which can distort the information received.

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REFERENCES

1. Shahnovich R.M. The efficacy and safety of ticagrelor in treatment of acute coronary syndrome. Emergency Cardiology. 2016;3:39–50. [Russian: Шахнович Р.М. Эффективность и безопасность тикагрелора у больных с острым коронарным синдромом. Неотложная кардиология. 2016;3:39-50]
2. Mackman N. Triggers, targets and treatments for thrombosis. Nature. 2008;451(7181):914–8. DOI: 10.1038/nature06797
3. Barbarash O.L., Duplyakov D.V., Zateischikov D.A., Panchenko E.P., Shakhnovich R.M., Yavelov I.S. et al. 2020 Clinical practice guidelines for Acute coronary syndrome without ST segment elevation. Russian Journal of Cardiology. 2021;26(4):149–202. [Russian: Барбараш О.Л., Дупляков Д.В., Затейщиков Д.А., Панченко Е.П., Шахнович Р.М., Явелов И.С. и др. Острый коронарный синдром без подъема сегмента ST электрокардиограммы. Клинические рекомендации 2020. Российский кардиологический журнал. 2021;26(4):149-202]. DOI: 10.15829/1560-4071-2021-4449
4. Averkov O.V., Duplyakov D.V., Gilyarov M.Yu., Novikova N.A., Shakhnovich R.M., Yakovlev A.N. et al. 2020 Clinical practice guidelines for Acute ST-segment elevation myocardial infarction. Russian Journal of Cardiology. 2020;25(11):251–310. [Russian: Аверков О.В., Дупляков Д.В., Гиляров М.Ю., Новикова Н.А., Шахнович Р.М., Яковлев А.Н. и др. Острый инфаркт миокарда с подъемом сегмента ST электрокардиограммы. Клинические рекомендации 2020. Российский кардиологический журнал. 2020;25(11):251-310]. DOI: 10.15829/29/1560-4071-2020-4103
5. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H 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). European Heart Journal. 2018;39(2):119–77. DOI: 10.1093/eurheartj/ehx393
6. Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021;42(14):1289–367. DOI: 10.1093/eurheartj/ehaa575
7. Boytsov S.A., Shakhnovich R.M., Erlikh A.D., Tereschenko S.N., Kukava N.G., Rytova Yu.K. et al. Registry of Acute Myocardial Infarction. REGION-MI – Russian Registry of Acute Myocardial Infarction. Kardiologiia. 2021;61(6):41–51. [Russian: Бойцов С.А., Шахнович Р.М., Эрлих А.Д., Терещенко С.Н., Кукава Н.Г., Рытова Ю.К. и др. Регистр острого инфаркта миокарда. РЕГИОН–ИМ – Российский рЕГИстр Острого иНфаркта миокарда. Кардиология. 2021;61(6):41-51]. DOI: 10.18087/cardio.2021.6.n1595
8. Jernberg T, Hasvold P, Henriksson M, Hjelm H, Thuresson M, Janzon M. Cardiovascular risk in post-myocardial infarction patients: nationwide real world data demonstrate the importance of a long-term perspective. European Heart Journal. 2015;36(19):1163–70. DOI: 10.1093/eurheartj/ehu505
9. Libby P. Current Concepts of the Pathogenesis of the Acute Coronary Syndromes. Circulation. 2001;104(3):365–72. DOI: 10.1161/01.CIR.104.3.365
10. Erlikh A.D. Place of ticagrelor in the new recommendations for the management of patients with acute coronary syndrome. Atherothrombosis. 2015;2:58–65. [Russian: Эрлих А.Д. Место тикагрелора в новых рекомендациях по лечению пациентов с острым коронарным синдромом. Атеротромбоз. 2015;2:58-65]
11. Yusuf S, Fox KA, Tognoni G, Mehta SR. Effects of Clopidogrel in Addition to Aspirin in Patients with Acute Coronary Syndromes without ST-Segment Elevation. New England Journal of Medicine. 2001;345(7):494–502. DOI: 10.1056/NEJMoa010746
12. Lindholm D, Varenhorst C, Cannon CP, Harrington RA, Himmelmann A, Maya J et al. Ticagrelor vs. clopidogrel in patients with non-ST-elevation acute coronary syndrome with or without revascularization: results from the PLATO trial. European Heart Journal. 2014;35(31):2083–93. DOI: 10.1093/eurheartj/ehu160
13. Berwanger O, Nicolau JC, Carvalho AC, Jiang L, Goodman SG, Nicholls SJ et al. Ticagrelor vs Clopidogrel After Fibrinolytic Therapy in Patients With ST-Elevation Myocardial Infarction: A Randomized Clinical Trial. JAMA Cardiology. 2018;3(5):391–9. DOI: 10.1001/jamacardio.2018.0612
14. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S et al. Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes. New England Journal of Medicine. 2007;357(20):2001–15. DOI: 10.1056/NEJMoa0706482
15. Tscharre M, Egger F, Machata M, Rohla M, Michael N, Neumayr M et al. Contemporary use of P2Y12-inhibitors in patients with acute coronary syndrome undergoing percutaneous coronary intervention in Austria: A prospective, multi-centre registry. PLOS ONE. 2017;12(6):e0179349. DOI: 10.1371/journal.pone.0179349
16. Barbarash O.L., Kashtalap V.V., Kochergina A.M., Leonova V.O., Erlikh A.D. Management of patients with ST-segment elevation acute coronary syndrome in interventional cardiology units: RECORD-3 registry data. Fundamental and Clinical Medicine. 2016;1(3):6– 13. [Russian: Барбараш О.Л., Кашталап В.В., Кочергина А.М., Леонова В.О., Эрлих А.Д. Ведение пациентов с острым коронарным синдромом с подъемом сегмента ST в инвазивных стационарах. Результаты регистрового исследования РЕКОРД-3. Фундаментальная и клиническая медицина. 2016;1(3):6-13]. DOI: 10.23946/2500-0764-2016-1-3-6-13
17. Faridi KF, Garratt KN, Kennedy KF, Maddox TM, Secemsky EA, Butala NM et al. Physician and Hospital Utilization of P2Y12 Inhibitors in ST-Segment–Elevation Myocardial Infarction in the United States: A Study From the National Cardiovascular Data Registry's Research to Practice Initiative. Circulation: Cardiovascular Quality and Outcomes. 2020;13(3):e006275. DOI: 10.1161/CIRCOUTCOMES.119.006275
18. Jacobsen MR, Engstrøm T, Torp-Pedersen C, Gislason G, Glinge C, Butt JH et al. Clopidogrel, prasugrel, and ticagrelor for all-comers with ST-segment elevation myocardial infarction. International Journal of Cardiology. 2021;342:15–22. DOI: 10.1016/j.ijcard.2021.07.047
19. Tubek S, Kuliczkowski W, Gąsior M, Gierlotka M, Kubica J, Budaj A et al. Antiplatelets in acute coronary syndrome in Poland – from guidelines to clinical practice. Advances in Interventional Cardiology. 2021;17(2):141–54. DOI: 10.5114/aic.2021.107492
20. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. The New England Journal of Medicine. 2009;361(11):1045–57. DOI: 10.1056/NEJMoa0904327
21. SWEDEHEART. Annual report 2021. Av. at: https://www.ucr.uu.se/swedeheart/dokument-sh/arsrapporter-sh/1-swedeheart-annual-report-2021-english/viewdocument/3384. 2022.
22. Husted S, James S, Becker RC, Horrow J, Katus H, Storey RF et al. Ticagrelor Versus Clopidogrel in Elderly Patients With Acute Coronary Syndromes: A Substudy From the Prospective Randomized PLATelet Inhibition and Patient Outcomes (PLATO) Trial. Circulation: Car-

ISSN 0022-9040. Kardiologiia. 2022;62(9). DOI: 10.18087/cardio.2022.9.n2278

diovascular Quality and Outcomes. 2012;5(5):680–8. DOI: 10.1161/CIRCOUTCOMES.111.964395
23. James S, Budaj A, Aylward P, Buck KK, Cannon CP, Cornel JH et al. Ticagrelor Versus Clopidogrel in Acute Coronary Syndromes in Relation to Renal Function: Results From the Platelet Inhibition and Patient Outcomes (PLATO) Trial. Circulation. 2010;122(11):1056–67. DOI: 10.1161/CIRCULATIONAHA.109.933796
24. Erlikh A.D. Six-month outcomes in patients with acute coronary syndrome included in the Russian register RECORD-3. Russian Journal of Cardiology. 2017;22(11):8–14. [Russian: Эрлих А.Д. Шестимесячные исходы у пациентов с острым коронарным синдромом, включенных в Российский регистр РЕКОРД-3. Российский кардиологический журнал. 2017;22(11):8-14]. DOI: 10.15829/1560-4071-2017-11-8-14