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Pre-hospital treatment of patients with acute coronary syndrome: Recommendations for medical emergency teams. Expert position update 2022

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Introduction

Recommendations for medical emergency teams regarding the pre-hospital management of patients with acute coronary syndrome (ACS) have been developed in 2017 by a broad representation of Polish experts in cardiology and emergency medicine [1]. These recommendations have been updated after the publication of the 2017 European Society of Cardiology (ESC) guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation (STEMI) and the 2017 update focused on dual antiplatelet therapy (DAPT) in coronary artery disease [2–4]. The 2020 ESC guidelines for the management of ACSs in patients presenting without persistent ST-segment elevation (NSTE-ACS) introduced several significant changes in treatment strategies [5].

The current expert position update aims to put the 2020 ESC guidelines into a Polish perspective and to provide practical recommendations for medical emergency teams.

Diagnosis and logistics of ACS patients

Emergency medical teams are responsible for early diagnosis, triage, transport and treatment of ACS patients [1–6]. In order to improve the quality of care and decrease adequate treatment delay, an early working diagnosis of ACS and risk stratification should be conducted at the earliest possible moment. The efficient treatment of ACS patients requires appropriate ambulance equipment and staff competences. All medical emergency system ambulances should be equipped with electrocardiogram (ECG) recorders, defibrillators, and at least one person trained in advanced life support. All ambulance personnel should be trained to recognize clinical symptoms of acute myocardial infarction (MI), record and transmit ECG, administer oxygen when appropriate, relieve pain, and provide basic life support [1, 2, 4].

Acute coronary syndrome may be associated with a wide variety of symptoms ranging from cardiac arrest, electrical or hemodynamic instability with cardiogenic shock due to ongoing ischemia or mechanical complications such as severe mitral regurgitation, to patients who are already pain free at the time of presentation. The major trigger for the diagnostic and therapeutic actions in patients with suspected ACS is acute chest discomfort, primarily characterized as pain, pressure, tightness, and burning. Chest pain-equivalent symptoms, such as dyspnea, epigastric pain or pain in the left arm, may also occur [5].

The resting 12-lead ECG is the first-line diagnostic tool in the assessment of patients with suspected ACS. It is recommended to perform it within 10 minutes after the first contact with the emergency medical services in a pre-hospital setting and to have it immediately interpreted by a qualified physician using remote technologies [1, 2, 4, 5].

The presence of persistent ST-segment elevation in two contiguous leads is considered one of the best indicators of ongoing MI with an occluded infarct artery [2]. If the standard leads are inconclusive, recording of additional leads (V7–V9 or V3R and V4R) should be performed as they can be the only ones to reveal left circumflex artery occlusion or right ventricular MI, respectively [5]. It is recommended to manage subjects with typical clinical symptoms of ongoing myocardial ischemia and left bundle branch block (LBBB) similar to STEMI patients, regardless of whether the bundle branch block has been previously known [2, 5]. In patients with right bundle branch block the interpretation of electrocardiographic changes is more specific as ST-elevation is indicative of STEMI, while ST-segment depression in lead I, aVL, and V5–V6 is indicative of NSTE-ACS [5]. Primary percutaneous coronary intervention (PCI) strategy is also recommended in the setting of other atypical electrocardiographic presentations combined with ongoing symptoms suggestive of myocardial ischemia, including: ventricular paced rhythm (during right ventricular pacing, the ECG shows LBBB pattern), isolated posterior MI (isolated ST depression > 1 mm in leads V1–V3 and ST-segment elevation (≥ 0.5 mm) in posterior chest wall leads V7–V9), ischemia due to left main coronary artery occlusion or multivessel disease (ST-segment depression ≥ 1 mm in 6 or more surface leads, coupled with ST-segment elevation in aVR and/or V1) [2, 5]. Characteristic ECG features of NSTE-ACS include ST-segment depression, transient ST-segment elevation, and T-wave changes however, ECG may remain normal in more than 30% of patients [5].

The ECG monitoring should be applied immediately in all patients with initial diagnosis of ACS in order to detect life-threatening arrhythmias and allow prompt defibrillation, if indicated [1, 2, 4].

Acute coronary syndromes are characterized by high clinical instability, therefore patients with initial diagnosis of ACS, even those who are not candidates for immediate coronary angiography and subsequent PCI at the time of initial diagnosis, should be transported to centers with invasive cardiology facilities regardless of changes in ECG [2, 5, 7–9]. Nevertheless, teleconsultation including transmission of patients' 12-lead ECG and clinical data to the destination center should be performed at the first medical contact [1, 2, 4, 10]. Teleconsultation, apart from the preliminary diagnosis and logistics aspects, should be used to coordinate pre-hospital therapy, especially regarding antiplatelet therapy and unfractionated heparin. This strategy is aimed to reduce treatment delay leading to mortality reduction in STEMI and very high-risk NSTE-ACS patients. This allows immediate activation of the interventional team and direct transportation of patients triaged for a primary PCI strategy to the catheterization laboratory, bypassing the emergency department [1, 2, 4, 11]. Therefore, the medical emergency system dispatcher should not change the choice of the destination center, unless, in his opinion, the choice made by the emergency medical team is incorrect. In this case, the change and its justification must be documented.

In locations where there is more than one hospital with an invasive cardiology unit, the selection of the destination center should be based both on the patient's clinical status and center category depending on its level of preparation for treatment of ACS patients. Local categorization of centers should take into account the following factors: the availability of invasive cardiology and cardiac surgery in one location, the number of cath labs available, the availability of hybrid rooms and circulatory support systems, and the number of beds in the intensive coronary care unit. Generally, ACS patients qualified for the immediate invasive strategy should be transferred to the nearest PCI center, however, whenever possible, direct transport of the highest risk patients (STEMI, NSTE-ACS of very high-risk, cardiogenic shock) to centers with both invasive cardiology and cardiac surgery facilities should be considered. It should be stressed however, that preference for this category of hospitals must not cause delay of invasive diagnostics [1, 4, 12].

Centers participating in the Managed Care after Acute Myocardial Infarction (KOS-zawał) network should be preferred as the target destination for all ACS patients due to comprehensive post-hospitalization care they provide. To ensure high quality of care in ACS patients, a working diagnosis, pivotal statements, decisions, medications, and time-points should be registered and monitored. Periodic evaluation at the local level (city/voivodeship) should cover the correctness of the initial diagnosis and treatment, the duration and causes of delays related to transport, diagnosis and treatment, the quality of cooperation between the emergency medical teams and hospital staff, and the target center choice correctness [2].

Chest pain management

Coronary revascularization is the most efficient analgesic treatment in patients with acute myocardial ischemia, regardless of ACS type. Patients presenting with STEMI or NSTE-ACS with recurrent or refractory chest pain despite medical treatment should be qualified to immediate invasive strategy [2, 5]. However, even in the most developed medical emergency systems with an access to extensive network of 24/7 PCI centers, the delay between the first medical contact and coronary revascularization may reach tens of minutes contributing to a prolonging chest discomfort. In order to cover the time until the culprit vessel is treated, a potent analgesic with a quick onset of action is necessary to provide timely and effective pain blockade.

The latest ESC guidelines on the treatment of STEMI recommend to titrate intravenous opioids to relieve pain in the pre-revascularization stage in patients with ongoing chest pain. Currently this constitutes a class IIa recommendation ("should be considered") with a level of evidence C ("consensus of the opinion of the experts and/or small studies, retrospective studies, registries") [2]. Notably, this recommendation has been downgraded from class I ("is recommended") compared with the previous edition of the ESC guidelines on STEMI [2, 13]. The 2020 ESC guidelines for the management of NSTE-ACS do not contain any recommendations regarding analgesic pharmacotherapy with opioids in patients with NSTE-ACS [5]. The former edition of these guidelines also did not provide any official recommendation regarding this topic, however the authors stated, that administration of

opioids is reasonable in NSTE-ACS patients with sustained severe chest pain who are waiting for urgent coronary angiography [14]. In this group sublingual or intravenous nitrates and early initiation of beta-blocker treatment are indicated, if ischemic symptoms are ongoing [5]. On the other hand, in the acute phase of STEMI nitrates have failed to show benefit and are not recommended, unless they are required for the control of heart failure symptoms or hypertension [2, 15].

Abundant experience with the use of morphine, its analgesic potency and wide availability explain why it remains the most commonly administered analgesic in patients with MI [16]. Nevertheless, morphine may cause adverse effects, including bradycardia, hypotension, and impairment of the intestinal propulsive function or even suppression of the respiratory function [17]. Additionally, morphine leads to impaired absorption of orally administered antiplatelet drugs, delay of anti-aggregatory effect and its reduction [18]. Noteworthy, this issue not only concerns clopidogrel, but also the newer P2Y12 receptor antagonists prasugrel and ticagrelor [19–21]. Although some studies suggest that morphine use may be related to increased infarct size, reinfarction rate and mortality, data from registries are ambiguous and randomized trials on this matter are lacking [22–27]. A meta-analysis of mostly observational studies has reported no association between morphine use in patients undergoing primary PCI for STEMI and adverse short-term clinical outcomes [28].

Recently, fentanyl has been proposed as an alternative to morphine in ACS patients with chest pain. However, in the setting of PCI fentanyl, similarly to morphine, leads to impairment of ticagrelor bioavailability and delay in its antiplatelet effect suggesting a class effect regarding the opioid-P2Y12 receptor inhibitor interaction [29]. Also, there is no difference in inhibition of platelet reactivity in ACS patients during the first 2 hours after a ticagrelor loading dose, suggesting no pharmacodynamic benefit from using fentanyl instead of morphine [30]. Interestingly, intravenous acetaminophen results in a comparable extent of pain relief when compared to fentanyl before and immediately after primary PCI for STEMI [31]. Still, although this approach increases the absorption of ticagrelor in patients with STEMI compared with fentanyl-treated patients, it does not improve the early antiplatelet response (before and just after primary PCI) [31]. Additionally, acetaminophen lacks anxiolytic effect that may be advantageous in the early phase of ACS treatment.

Due to the potentially harmful effect of oxygen in uncomplicated MI patients it should be used only in hypoxic patients with arterial oxygen saturation (SaO_2) < 90% [2]. In summary, routine use of opioids in ACS should be avoided and restricted only to a selected group of patients with severe, refractory chest pain. In case analgesic treatment is needed, withdrawal from morphine use or a routine switch to either fentanyl or acetaminophen should not be recommended. **Due to reasons explained above morphine should remain the first choice analgesic in ACS. Nevertheless, it has to be underlined that administration of this opioid should be limited only to patients with severe chest pain, and that the dose should be titrated to the minimal effective dosage in order to limit potential adverse effects of the drug. The timing and dosage of administered morphine should always be recorded and communicated to the medical staff of the destination cardiology center. In order to counteract adverse effects of opioids on absorption and platelet inhibition in ACS, administration of crushed tablets of ticagrelor, prasugrel or clopidogrel should be considered due to previously demonstrated acceleration of absorption and antiplatelet effect onset of P2Y12 receptor inhibitors when given in crushed form [32–35].** Additionally, administration of intravenous metoclopramide in opioid-treated ACS patients may also be considered to enhance absorption of antiplatelet agents from the gastrointestinal tract [36].

Antiplatelet treatment in ACS patients

Dual antiplatelet therapy including acetylsalicylic acid (ASA) and one of the P2Y12 receptor inhibitors, remains a standard of care in patients with ACS [2, 3, 5, 37].

ASA therapy in patients with ACS

Acetylsalicylic acid is an irreversible inhibitor of platelet cyclooxygenase isoenzyme type 1. According to the current guidelines, administration of an oral, rapidly absorbed ASA formulation in a loading dose of 150–300 mg or 75–250 mg intravenous ASA (if oral ingestion not possible) is recommended in all ACS patients with no contraindications (class of recommendation I, level of evidence A) [2, 5, 37]. The treatment should be applied as early as possible, i.e. upon the first medical contact. Subsequently, all patients should

Table 1. Contraindications for the use of P2Y12 receptor inhibitors in patients with acute coronary syndrome.

Contraindication	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor
Hypersensitivity to the P2Y12 receptor inhibitor	X	X	X	X
Active bleeding	X	X	X	X
Severe liver disorder	X	X	X	
History of ischemic stroke	Within 7 days	X		X
History of transient ischemic attack		X		X
History of intracranial hemorrhage		X	X	X
Indication for chronic oral anticoagulation		X	X	
Prior administration of other P2Y12 receptor inhibitor		X		X

receive chronic therapy with ASA 75–100 mg q.d. [2, 3, 5, 37, 38].

Platelet P2Y12 receptor inhibitors

Currently, three platelet P2Y12 receptor inhibitors are available in Poland: clopidogrel, prasugrel, and ticagrelor. Unfortunately, cangrelor, the only intravenous rapidly acting P2Y12 receptor inhibitor recommended in the most recent ESC guidelines, is still unavailable. Clopidogrel and prasugrel are pro-drugs and require hepatic activation into active metabolites irreversibly binding to the P2Y12 receptor, whereas ticagrelor and cangrelor are active drugs, which directly and reversibly block this receptor. Prasugrel and ticagrelor are preferentially recommended over clopidogrel due to their faster, more potent, and more uniform anti-aggregation effect, translating into better clinical outcomes [2, 3, 5, 37, 38]. When starting the treatment with P2Y12 receptor inhibitors one should always be aware of contraindications for these drugs (Table 1). Both prasugrel and ticagrelor are contraindicated in patients with prior hemorrhagic stroke, severe liver disease or those requiring chronic oral anticoagulation [2, 3, 5]. Moreover, prasugrel is also contraindicated in patients with a history of ischemic stroke or transient ischemic attack, it is generally not recommended for patients above 75 years of age or with body weight below 60 kg, but, if necessary, a reduced dose of 5 mg can be applied in these patients [2, 3, 5]. When neither of these agents is available or if they are contraindicated, clopidogrel should be administered instead [2, 3, 5]. Importantly, in ACS patients who were previously treated with clopidogrel or have received a loading dose of clopidogrel a switch to ticagrelor is indicated at a loading dose of 180 mg (class of recommendation I, level of evidence B) [37, 39].

Substantial percentage of ACS patients require long-term oral anticoagulation. The concomitant use of DAPT and oral anticoagulation increases the risk of bleeding complications 2- to 3-fold when compared to anticoagulation alone [40–43]. Clopidogrel is the only P2Y12 inhibitor to be used in combination with oral anticoagulants (acenocoumarol, apixaban, dabigatran, rivaroxaban, or warfarin) [2, 3]. Use of ticagrelor or prasugrel as a part of triple therapy is not recommended (class of recommendation III, level of evidence C) [2, 3, 5]. However, patients burdened with moderate-to-severe risk of stent thrombosis, who require concomitant oral anticoagulation may benefit from dual antithrombotic therapy comprising oral anticoagulant and prasugrel or ticagrelor instead of triple therapy (class of recommendation IIb, level of evidence C) [5].

Due to its rapid onset of action cangrelor appears to be the optimal P2Y12 receptor inhibitor for ACS patients requiring urgent invasive treatment [44, 45]. This compound may be considered in patients not pre-treated with oral P2Y12 receptor inhibitors at the time of PCI or in those who are considered unable to absorb oral agents, particularly in unconscious patients, patients with post-cardiac arrest syndrome, or patients treated with mild therapeutic hypothermia, when gastrointestinal absorption of medications is impaired [2, 5, 46–48]. Unfortunately, up to date cangrelor is not available in Poland.

In conservatively treated ACS patients ticagrelor is preferred over clopidogrel (class of recommendation IIa, level of evidence C), while prasugrel is not indicated (class of recommendation III, level of evidence B) [3].

Platelet P2Y12 receptor inhibitors in the treatment of patients with STEMI

ST-segment elevation MI is usually a result of sudden and complete occlusion of a coronary artery. Such immediate interruption in oxygen supply to the heart leads to rapidly progressing myocardial necrosis. **The main goal of STEMI treatment is to salvage as much cardiac muscle as possible, and this can be obtained by expeditious reperfusion of the culprit vessel, preceded by timely diagnosis and transportation to the catheterization laboratory without unnecessary delay.** Primary PCI remains the mainstay of coronary revascularization in patients with STEMI [2]. According to the ESC guidelines pre-hospital fibrinolysis is indicated in patients presenting early when anticipated STEMI diagnosis to PCI-mediated reperfusion time is > 120 minutes [2]. Nevertheless, in the Polish reality, where the density of invasive cardiology facilities is very high and transport times are short, the probability of such a situation is negligible. Moreover, the use of fibrinolytic drugs in ambulances was not approved by the Directive of the Minister of Health of Poland [49].

In the clinical setting of STEMI both potent P2Y12 inhibitors, prasugrel or ticagrelor, are preferred over clopidogrel. The use of clopidogrel should be limited to situations when neither of the stronger P2Y12 receptor inhibitors is available or when they are contraindicated (class of recommendation I, level of evidence A) [2]. Currently there is no evidence from randomized controlled trials indicating the optimal time point for initiation of antiplatelet treatment in STEMI [2]. Nevertheless, the available data suggest early initiation of P2Y12 receptor inhibitor treatment in order to obtain effective platelet inhibition by the time of PCI, especially that administration of P2Y12 inhibitors in pre-hospital management is considered to be safe [2, 38]. **Therefore, prasugrel 60 mg loading dose or ticagrelor 180 mg loading dose should be administered directly after the STEMI diagnosis is confirmed by ECG [2].** If unavailable or contraindicated clopidogrel 600 mg should be administered instead [2]. The ATLANTIC study has shown the pre-hospital loading with ticagrelor to be safe for STEMI patients [50]. Alternatively, in P2Y12-inhibitor naive patients undergoing PCI cangrelor (intravenous bolus of 30 mg/kg with subsequent of 4 mg/kg/min infusion lasting at least 2 h or duration of procedure, whichever is longer) may be considered (class of recommendation IIb, level of evidence A) [37]. However, up to date cangrelor is not available yet in Poland. Pre-hospital administration of DAPT should be especially avoided if there is a suspicion of active bleeding, mechanical complications of MI, acute aortic dissection or any other co-morbidities requiring emergency surgical operation.

Platelet P2Y12 receptor inhibitors in the treatment of patients with NSTE-ACS

Urgent coronary reperfusion is a mainstay of treatment for patients with STEMI, while in patients with NSTE-ACS the indications and recommended timeframes for invasive diagnostics and treatment depend primarily on risk stratification [2, 5]. The available evidence indicates that a routine invasive strategy reduces the risk of the composite ischemic endpoints, particularly in high-risk patients. Nevertheless, a routine invasive strategy does not reduce all-cause mortality in the overall population of NSTE-ACS patients, and it increases the risk of periprocedural complications [5]. The results of randomized controlled trials and their meta-analyses highlight the role of risk stratification in the decision-making process and support a routine invasive strategy only in very high and high-risk patients [51–55].

According to the ESC guidelines, immediate invasive strategy (< 2 h) should be applied in very high-risk NSTE-ACS patients (i.e., with at least one very high-risk criterion) [5]. The NSTE-ACS very high-risk criteria are defined as follows:

- Hemodynamic instability;
- Cardiogenic shock;
- Recurrent/refractory chest pain despite medical treatment;
- Life-threatening arrhythmias;
- Mechanical complications of MI;
- Acute heart failure clearly related to NSTE-ACS;
- ST-segment depression > 1 mm/6 leads plus ST-segment elevation aVR and/or V1.

Early invasive strategy (< 24 h) is recommended in high-risk patients. The NSTE-ACS high-risk criteria are defined as follows:

- Established NSTEMI diagnosis;
- Dynamic or presumably new contiguous ST/T-segment changes (symptomatic or silent);
- Resuscitated cardiac arrest without ST-segment elevation or cardiogenic shock;
- GRACE risk score > 140.

Similar to STEMI, DAPT, including ASA and one of the potent P2Y12 receptor inhibitors, is also recommended in patients with NSTE-ACS, unless

contraindicated, e.g., due to excessive bleeding risk (class of recommendation I, level of evidence A) [5]. The ISAR-REACT 5 trial compared two antiplatelet strategies: prasugrel-based vs. ticagrelor-based strategy in ACS patients for whom an invasive evaluation was planned. The trial demonstrated that the prasugrel-based strategy was associated with a reduced rate of composite of death, MI, or stroke, without an increase in the rate of bleeding complications [56]. Based on this single trial, the authors of the 2020 ESC guidelines on NSTE-ACS recommended prasugrel to be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI after a diagnostic angiography was performed (class of recommendation IIa, level of evidence B) [5]. It should be highlighted, that the guidelines authors did not take into account serious limitations of the ISAR-REACT 5 trial [57–61] nor the results of the network meta-analysis of 12 randomized controlled trials by Navarese et al. [62] which clearly showed a similar reduction of ischemic events and increase of bleeding with both prasugrel and ticagrelor in comparison with clopidogrel. However, a significant mortality reduction was observed with ticagrelor only. Moreover, the meta-analysis showed that by excluding open label randomized controlled trials due to their limitations (e.g., ISAR-REACT 5), the mortality reduction with ticagrelor was strengthened without a significant increase of bleeding [62].

The 2020 ESC guidelines on NSTE-ACS suggest considering pre-treatment with a P2Y12 inhibitor in patients with NSTE-ACS who are not planned to undergo an early invasive strategy and do not have a high bleeding risk (class of recommendation IIb, level of evidence C) [5]. The same guidelines advocate against the use of routine pre-treatment with P2Y12 inhibitors in patients for whom coronary anatomy is not known and an early invasive management is planned (class of recommendation III, level of evidence A) [5].

In fact, supportive observations for a restrictive use of pre-treatment with P2Y12 receptor inhibitor are limited to prasugrel (ACCOAST trial) [63]. Therefore, prasugrel should not be administered prior to coronary angiography or when the patient is qualified for conservative treatment (class of recommendation III, level of evidence B) [37]. The prospective Swedish Coronary Angiography and Angioplasty Registry (SCAAR) [64] showed that pre-treatment of NSTE-ACS patients with P2Y12 receptor antagonists was not associated with improved clinical outcomes, but was associated with increased risk of bleeding in all consecutive patients who underwent PCI for NSTE-ACS (59894 patients with P2Y12 pre-treatment vs. 4963 patients without P2Y12 pre-treatment). However, whether pre-treatment with P2Y12 antagonists in selected high and very high-risk patients can improve clinical outcomes was not established in this study [64]. Moreover, the DUBIUS trial assessing efficacy and safety of pre-treatment vs. loading after angiography with oral P2Y12 receptor inhibitor in NSTE-ACS patients, was prematurely interrupted due to low incidence of ischemic and bleeding events and minimal numeric difference of event rates between the treatment groups [65].

According to the 2020 ESC guidelines, potent P2Y12 receptor inhibitors (ticagrelor or prasugrel) exhibit a fast onset of antiplatelet action, thereby allowing loading dose administration after diagnostic coronary angiography and directly before PCI [5]. However, the fast onset of action has been shown only in a stable setting [66–69], while in patients with MI the antiplatelet effect of both drugs was delayed, achieving satisfactory platelet inhibition in the majority of patients 2 hours after loading dose administration [17, 18, 70, 71]. Of note, even 4 hours after administration of the loading dose of ticagrelor high platelet reactivity (as assessed with VASP assay) was found in 7–37% of patients (depending on concomitant morphine administration) [17, 18, 70, 71]. Therefore, sufficient platelet inhibition at the time of PCI cannot be expected in patients in whom loading dose of ticagrelor or prasugrel was given after diagnostic coronary angiography and directly before PCI. This limitation can be overcome with cangrelor [5, 38, 44, 72, 73]. According to the ESC guidelines, due to its proven efficacy in preventing intra-procedural and postprocedural stent thrombosis cangrelor may be considered for use in P2Y12 receptor inhibitor-naive NSTE-ACS patients undergoing PCI (class of recommendation IIb, level of evidence A) [5, 37]. Unfortunately, cangrelor is still not available in Poland.

Due to conflicting evidence the routine pre-hospital administration of P2Y12 inhibitors in patients with NSTE-ACS is not recommended. However, even though early administration of P2Y12 receptor antagonists may increase the bleeding risk, the potential benefits for the selected NSTE-ACS patients may justify in-hospital administration of a ticagrelor loading dose before coronary angiography after an individual assessment. It has to be underlined though, that a decision on potential use of in-hospital pre-treatment

with ticagrelor should be left to the discretion of the treating physician.

Antiplatelet treatment after ACS

Dual antiplatelet therapy with ASA and P2Y12 receptor inhibitor should be maintained for 12 months after ACS, unless contraindications exist (class of recommendation I, level of evidence A) [2, 5]. In specific clinical scenarios, the duration of DAPT can be shortened, extended (> 12 months) or modified considering individual ischemic and bleeding risk, the occurrence of adverse events, comorbidities, and co-medications [2, 5, 62, 74–76]. Adding a second antithrombotic drug to ASA for long-term secondary prevention should be considered in patients with a high risk of ischemic events and without high bleeding risk (class of recommendation IIa, level of evidence A) — as a dual antithrombotic therapy (DATT). This strategy may be also considered in patients with at least a moderately increased risk of ischemic events and without high bleeding risk (class of recommendation IIb, level of evidence A) [5, 77]. A greater benefit in post-ACS patients may be expected with ASA and ticagrelor 60 mg b.i.d. when the therapy is continued after 12 months of DAPT without interruption or with short interruption only. On the other hand, a combination of ASA and rivaroxaban 2.5 mg b.i.d. seems to be a better option when indications for DATT appear after a longer time from ACS (more than 2 years) and/or from cessation of DAPT (more than 1 year), and in patients with multiple vascular bed atherosclerosis [78].

Conclusions

Dual antiplatelet therapy composed of ASA and a P2Y12 receptor inhibitor remains a mainstay of ACS therapy. The ESC guidelines recommend the use of potent P2Y12 inhibitors — prasugrel or ticagrelor over clopidogrel in all ACS patients, unless contraindicated, e.g., due to an excessive risk of bleeding [2, 5]. Clopidogrel is reserved for situations when prasugrel or ticagrelor are not available, cannot be tolerated or are contraindicated. Indications for ticagrelor are wider as compared with prasugrel, because ticagrelor can be used in conservatively treated ACS patients, patients pre-loaded with clopidogrel or on chronic clopidogrel therapy, as well as in those with previous ischemic stroke or transient ischemic attack, elderly (> 75 years of age) or those with low body mass (< 60 kg) [2, 3, 5]. Although, limited data on optimal timing of the P2Y12 receptor inhibitor initiation exist, there is a consistent recommendation that early administration — at the time of diagnosis — of a potent P2Y12 receptor inhibitor together with ASA and heparin is crucial in the management of all patients with STEMI [2]. In patients presenting with NSTE-ACS the latest 2020 ESC guidelines do not recommend the routine pre-treatment with a P2Y12 receptor inhibitor in patients in whom coronary anatomy is not known and an early invasive management is planned (class of recommendation III, level of evidence A) [5]. But, since the full antiplatelet effect is desired at the time of PCI and rapidly acting intravenous cangrelor is unavailable in Poland, in-hospital administration of ticagrelor loading dose before coronary angiography may be justified after an individual assessment. The use of prasugrel is not advised when the coronary anatomy is unknown what makes ticagrelor the drug of choice in the majority of ACS patients [37]. Moreover, ACS patients pre-treated with clopidogrel should be switched to ticagrelor when not contraindicated, but not to prasugrel which is recommended only in P2Y12 receptor inhibitor-naïve patients [3]. Importantly, in ACS patients undergoing coronary artery by-pass grafting procedure the use of ticagrelor provides the best safety profile, reducing the risk of adverse cardiovascular events, including death, yet not increasing the risk of coronary artery by-pass grafting-related bleeding when compared with clopidogrel [79].

Since the publication of the previous Recommendations for medical emergency teams a new Directive of the Minister of Health dated December 16, 2019 has been published [49]. Paramedics and emergency medical team members are allowed to (after ECG tele-transmission and consultation with the physician evaluating the ECG) administer as previously only clopidogrel and ticagrelor, but not prasugrel. In the periprocedural period ACS patients require anticoagulant treatment apart from DAPT, and according to the above-mentioned Directive of the Minister of Health, unfractionated heparin (70–100 U/kg) is the only anticoagulant agent that can be administered by paramedics and emergency medical team members.

This expert position is not fully in line with the recently published expert opinion of the Association of Cardiovascular Interventions and the Working Group on Cardiovascular Pharmacotherapy of the Polish Cardiac Society [80]. Nevertheless, the aforementioned expert opinion is only a summary of the 2020 ECS guidelines [5], while the present position paper is a proposal for the

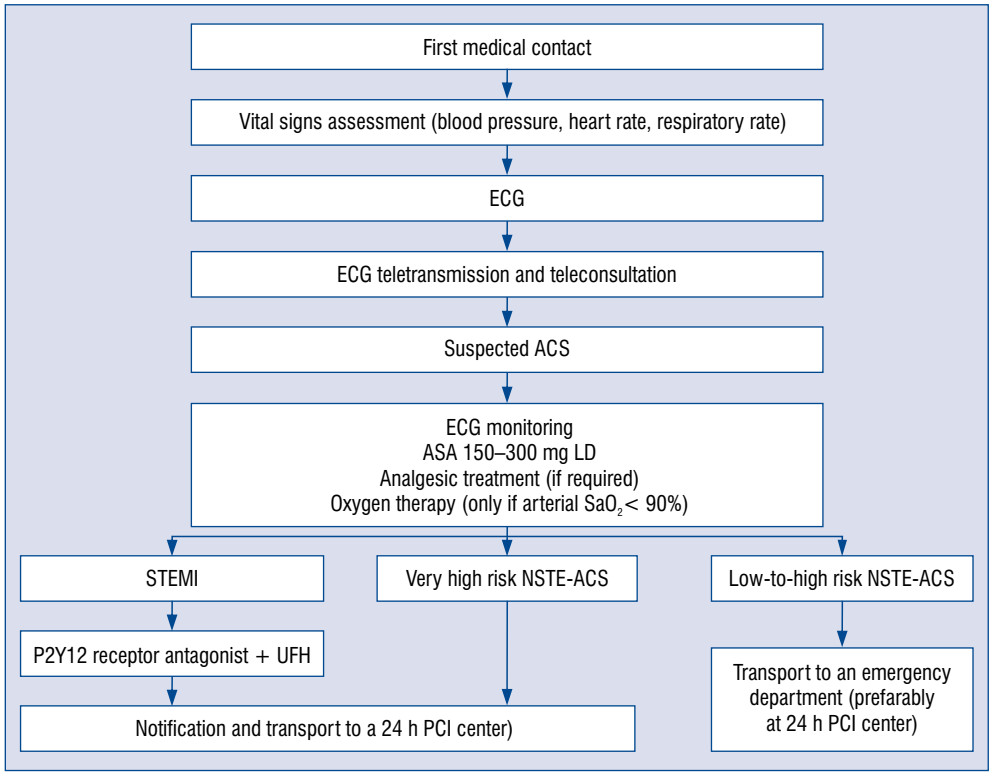

Figure 1. Algorithm for pre-hospital management of acute coronary syndromes (ACS); ASA — acetylsalicylic acid; ECG — electrocardiography; LD — loading dose; NSTE-ACS — non-ST-segment elevation acute coronary syndrome; PCI — percutaneous coronary intervention; SaO_2 — saturation of oxygen; STEMI — ST-segment elevation myocardial infarction; UFH — unfractionated heparin.

practical application of these recommendations in Polish conditions.

Pain management is an important part of the ACS emergency care. Titrated intravenous morphine remains the standard of care in STEMI patients [2]. While undertaking decision to administer morphine one should bear in mind the unwanted interaction between morphine and antiplatelet drugs as well as the fact that the most effective analgesic in ACS is urgent revascularization [17].

In the pre-hospital period patients with ACS may experience vomiting especially when given morphine. It carries the risk of loss of yet unabsorbed antiplatelet drugs. In such cases the time elapsed from drug intake to vomiting and the potential presence of tablets in the vomited content should be documented. The decision on administration of an additional dose of antiplatelet drugs should be left to the discretion of the physician at the destination hospital.

To conclude, ECG tele-transmission at first medical contact and consultation with experienced cardiologist enables pre-hospital administration of P2Y12 inhibitor loading dose added to ASA in all STEMI patients, while in NSTE-ACS patients in-hospital loading with P2Y12 inhibitor may be justified in selected patients (Fig. 1). Ticagrelor is the P2Y12 receptor inhibitor of choice in the vast majority of ACS patients.

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