https://doi.org/10.31925/farmacia.2021.5.14 **ORIGINAL ARTICLE**

ORAL ANTIPLATELET THERAPY IN ACUTE CORONARY SYNDROMES, CLINICAL EXPERIENCE IN AN EMERGENCY HOSPITAL WITH PERCUTANEOUS CORONARY INTERVENTION FACILITIES

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Abstract

Antiplatelet is a first line medical therapy in acute coronary syndrome (ACS) management. Although current antiplatelet therapy is highly effective in preventing atherothrombotic complications, a significant number of patients continue to experience ischemic events. Due to increasing research efforts this drug class continues to evolve as novel agents with increasingly antiplatelet actions are identified. Dual antiplatelet therapy (DAPT) with clopidogrel and acetylsalicylic acid (ASA) was the backbone of antiplatelet therapy in ACS for over a decade. The third generation P2Y12-receptor inhibitors prasugrel and ticagrelor have a faster acting, more potent and more predictable antiplatelet effect than clopidogrel which translates into improved clinical outcomes. The aim of the study was exploring the current patterns of oral antiplatelet drug administration and adherence to guideline recommendations in real world clinical practice in patients admitted for ACS in an Emergency County Hospital with percutaneous coronary intervention (PCI) facilities.

Rezumat

Antiagregantele reprezintă terapia de bază în sindromul coronarian acut. Deşi terapia antiagregantă actuală are o eficienţă dovedită în prevenirea evenimentelor aterotrombotice, un număr semnificativ de pacienţi continuă să prezinte complicaţii ischemice. Aceasta clasă de medicamente a continuat să evolueze descoperindu-se agenţi noi cu acţiune antiagregantă crescută. Terapia antiagregantă dual cu clopidogrel şi acid acetilsalicilic (ASA) a constituit baza terapeutică în sindromul coronarian acut în ultimul deceniu. A treia generaţie de inhibitori ai receptorilor P2Y12, prasugrel şi ticagrelor au o acţiune mai rapidă, mai potentă şi mai predictibilă decât clopidogrelul ceea ce rezultă în îmbunătăţirea rezultatelor clinice. Scopul acestui studiu a fost de a explora terapia antiplachetară orală şi aderenţa la ghidurile actuale în practica clinică la pacienţii spitalizaţi cu diagnosticul de sindrom coronarian acut într-un spital clinic judeţean de urgenţă cu facilităţi de angioplastie coronariană percutană.

Keywords: acute coronary syndrome, antiplatelet, therapy

Introduction

Acute coronary syndrome (ACS) is the term used to define patients with unstable angina (UA) and myocardial infarction with (STEMI) or without ST segment elevation (NSTEMI) on electrocardiography (ECG). Atherosclerotique plaque rupture or erosion promotes activation and aggregation of the platelets with pathological thrombus formation that may occlude coronary arteries [29]. Depending on the degree and nature of the blockage the patient will develop stable, UA or myocardial infarction (MI) with myocardial cell necrosis. Antiplatelets represent a first line medical therapy in ACS management and this drug class continues to evolve as novel agents with increasingly antiplatelet actions are identified. Antiplatelet drugs are focused on the inhibition of three key platelet activation pathways: thromboxane A2 generation *via* cyclooxygenase-1; adenosine diphosphate mediated activation of the P2Y12 receptor and thrombin mediated activation of protease activated receptor-1 [1, 5]. Acetylsalicylic acid (ASA) remains the first line treatment of ACS. ASA irreversibly inhibits COX -1 enzymes, so thromboxane A2 induced platelet activation and aggregation are blocked [7, 25]. The antiplatelet effect of ASA occurs rapidly [17] and true pharmacological resistance to ASA is rare [13, 14]. The co-administration of ASA and P2Y12 inhibitors provides additive inhibition of platelet activation [12, 24]. Clopidogrel is a second generation of P12Y12 inhibitors that selectively and irreversibly prevent binding of adenosine diphosphate ADP to the P2Y12 receptor and is the most widely prescribed drug in the thienopyridine class. Clopidogrel is a prodrug requiring hepatic activation *via* cytochrome

P450 (CYP), so the onset of action can take 2 - 8 hours [15]. Genetic polymorphism in CYP enzymes and/or concomitant administration of drugs that competitively inhibit its activation *via* CYP enzymes such as proton-pump inhibitors (PPI) may diminish clopidogrel responsiveness [2, 19]. Approximatively 25% of patients are clopidogrel non-responders according to ADP-aggregation testing [9]. For more than 10 years, dual antiplatelet therapy (DAPT) with ASA and clopidogrel has remained the cornerstone of treatment for patients with ACS. The novel oral P2Y12-receptor inhibitors prasugrel and ticagrelor were developed to resolve these issues: slow onset of action and heterogeneous inhibiting properties of clopidogrel. Ticagrelor, unlike clopidogrel is a cyclo-pentyl-triazolopyrimidine ADP antagonist that reversibly inhibits the P2Y12 receptor by blocking ADP induced signal transduction [20]. Ticagrelor is a direct acting agent which not requires metabolic activation so it has a faster onset of action in 30 min - 4 h [15]. In Platelet Inhibition and Patient Outcomes (PLATO) trial, DAPT with ticagrelor and ASA in patients with ACS significantly reduced the rate of cardiovascular death, MI and stroke compared to clopidogrel and ASA. Results were persistent in patients managed with percutaneous coronary intervention (PCI) procedures, but also in medically managed patients [6, 16, 21, 30, 34]. Prasugrel is an oral thienopyridine prodrug that is hydrolysed by esterase to an inactive metabolite that is activated *via* CYP enzymes to the active metabolite that irreversibly binds to the platelet P2Y12 receptor and inhibits platelet function [20]. In the trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in MI 38 (TRITON-TIMI 38) prasugrel was more effective than clopidogrel in reducing ischemic events in ACS patients undergoing PCI [36], but it was not superior to medically managed patients [27]. This antiplatelet drug is not available in Romania.

The aim of the study was to explore the current patterns of oral antiplatelet drug administration and adherence to guideline recommendations in real world clinical practice in patients admitted for ACS.

Materials and Methods

Study group and methods

We performed a retrospective observational descriptive study on patients admitted with the diagnosis of ACS in the Emergency County Clinical Hospital Oradea, Romania, Cardiology Department in 2018. The main inclusion criterion was the diagnosis of ACS: UA, STEMI or NSTEMI. Patients were divided in three groups according to antiplatelet drugs administered at discharge: the group with DAPT ASA and ticagrelor; the group with DAPT ASA and clopidogrel and a group with monotherapy: ASA, clopidogrel or ticagrelor alone. Demographic data, clinical characteristics, risk factors, treatment modalities, interventions performed and medication administered during admission and at discharge were recorded. Data were obtained from patient s medical records and from the hospital informatics system. The diagnosis of ACS was made if ischemic symptoms (prolonged angina chest pain at rest, new onset angina, *crescendo* angina, post myocardial infarction angina and dyspnoea as angina equivalent) and one or more of the following were reported: cardiac biomarkers of myocardial necrosis elevated, new ST-T changes on ECG, new left bundle branch block, new pathological Q waves on ECG, new imaging echo evidence of regional wall motion abnormality.

Statistical analysis

Statistical analysis was performed using SPSS statistical package. Results are presented as mean ± SD for continuous variables and percentage for categorical variables. Intergroup comparisons were performed using both parametric test one-way ANOVA method and *posthoc* multiple comparison Tukey test or nonparametric tests Kruskal Wallis with Bonferroni correction for multiple tests to evaluate if the differences between the three groups were statistically significant. The correlations between the studied parameters were evaluated by calculating the Pearson correlation coefficient. A $p < 0.05$ was considered statistically significant.

The study has been conducted in accordance with ethical principles set out by Helsinki declaration and Good Clinical Practice and was approved by the hospital Ethics Committee.

Results and Discussion

There were a number of 936 patients admitted in Clinical Emergency Hospital, Department of Cardiology, Oradea, Romania, in 2018 with the diagnosis of ACS. The mean age of the patients admitted for ACS was 65.64 ± 11.794 years and male prevalence was high (64.1%). From the 936 patients admitted with ACS, 442 patients had UA (47.22%), 113 patients were diagnosed with NSTEMI (12.1%) and 381 patients were with STEMI (40.70%). A number of 87 patients died during hospital admission (9.29%). From 849 discharged alive a number of 13 patients (1.53%) were without antiplatelet therapy: 12 patients with oral anticoagulant therapy due to other associated diseases, most frequently atrial fibrillation (5 with antivitamin K and 7 with non-antivitamin K), and one patient with gastric ulcer and a severe haemorrhagic event during hospitalization. These 13 patients without antiplatelet therapy at discharge were not included in study.

The rest of 836 patients (98.47%) were treated with at least one antiplatelet drug. They were divided in three groups according to type of antiplatelet prescribed

at discharge: ASA and ticagrelor, ASA and clopidogrel or monotherapy. The most prescribed antiplatelet therapy prescribed at discharge was DAPT consisting in ASA and ticagrelor in 410 patients (48.29%) and ASA and clopidogrel in 232 patients (27.32%). Monotherapy was prescribed only in 194 patients (22.85%).

Demographic and clinical characteristics of ACS patients according to the antiplatelet treatment (Table I)

Patients treated with the association ASA and ticagrelor were significantly younger. Male prevalence was higher in all three groups compared to female and there were significantly more male in the group treated with DAPT compared to the group treated with monotherapy. Cardiovascular medical past history (documented coronary artery disease, angina or old myocardial infarction, atrial fibrillation, hypertension, heart failure) was more frequent in the group of patients treated with ASA-clopidogrel and monotherapy. Smokers were more prevalent in the group of ACS patients treated with ASA-ticagrelor. The body mass index (BMI) and the prevalence of hypertension were similar in the three groups.

Cholesterol level was significantly higher and dyslipidaemia was more frequent in the group treated with ASA-ticagrelor. There were no statistically significant differences regarding the prevalence of diabetes in the three groups.

Creatinine level was significantly higher in patients treated with ASA-clopidogrel. Haemoglobin (Hb) level was significantly lower in patients with prescription of ASA-clopidogrel and in patients treated with monotherapy. Glycaemia was significantly higher in the group treated with ASA-ticagrelor. Thrombocytes number was significantly lower in patients treated with monotherapy compared to patients treated with ASA-ticagrelor. Left ventricular ejection fraction (LVEF) was significantly lower in ACS patients treated with ASA-clopidogrel compared to the other two groups. There were significantly more patients with the diagnosis of UA in the group treated with monotherapy compared with the groups treated with DAPT. The patients with STEMI were more frequent in the group treated with ASA-ticagrelor.

Table I

Demographic and clinical characteristics of ACS patients according to antiplatelet treatment

Antiplatelet therapy		**ASA + Ticagrelor 410**	**ASA + Clopidogrel 232**	**Monotherapy 194**	**p**
Age (mean ±SD)		61.99 ±11.055	67.93 ± 11.491	67.13 ± 11.246	< 0.001
Sex (Male %)		297 (72.44%)	152 (65.51%)	104 (53.61%)	< 0.05
Cardiovascular medical history		265 (64.63%)	186 (80.17%)	146 (75.25%)	< 0.05
Risk factors	**Smoking**	124 (30.24%)	46 (19.82%)	39 (20.10%)	< 0.05
	Body mass index	30.876 ± 5.250	31.207 ± 5.221	31.304 ± 5.570	0.63
	Cholesterol	182.51 ± 46.360	174.03 ± 50.038	172.42 ± 47.537	< 0.05
	Hypertension	279 (68.04%)	161 (69.39%)	145 (74.74%)	0.75
	Diabetes	121 (29.51%)	77 (33.18%)	61 (31.44%)	0.65
	Dyslipidaemia	226 (55.12%)	95 (40.94%)	83 (42.78%)	< 0.05
Laboratory data	**Creatinine**	–	1.129 ± 0.772	1.086 ± 0.667	< 0.05
	Haemoglobin	14.101 ± 1.688	13.620 ± 1.760	13.339 ± 1.828	< 0.01
	Thrombocytes	230.797 ± 69.973	225.155 ±74.749	216.363 ± 67.036	0.057
	Glycaemia	98.103 ± 13.788	92.501 ± 10.901	95.406 ± 12.781	< 0.05
LVEF (%)		47.60 ± 7.894	45.77 ± 9.542	47.61 ± 8.852	< 0.05
UA		155 (37.80%)	111 (47.84%)	159 (81.95%)	< 0.05
NONSTEMI		45 (10.97%)	37 (15.94%)	19 (9.79%)	0.08
STEMI		210 (51.21%)	84 (36.20%)	16 (8.24%)	< 0.001

Myocardial infarction with (STEMI) or without ST segment elevation (NSTEMI); Left ventricular ejection fraction (LVEF); unstable angina (UA)

For the patients with NSTEMI it was no statistically significant difference between the three groups.

Antiplatelet therapy according to diagnosis

In the group of patients with diagnosis of UA, 37.41% were treated with monotherapy, the rest were on DAPT: 36.70% on ASA-ticagrelor and 25.88% on ASA-clopidogrel ($p < 0.05$ between groups). In the group of patients with NSTEMI, 37.62% were on DAPT with ASA-clopidogrel and 43.56% with ASA-ticagrelor, the rest of 18.81% were on monotherapy ($p = 0.08$).

In the group of patients with STEMI, DAPT was predominant, 67.74% of patients were on ASA-ticagrelor and 27.09% were on ASA-clopidogrel ($p < 0.001$). Monotherapy was prescribed in only 5.16% of patients ($p < 0.001$) (Figure 1).

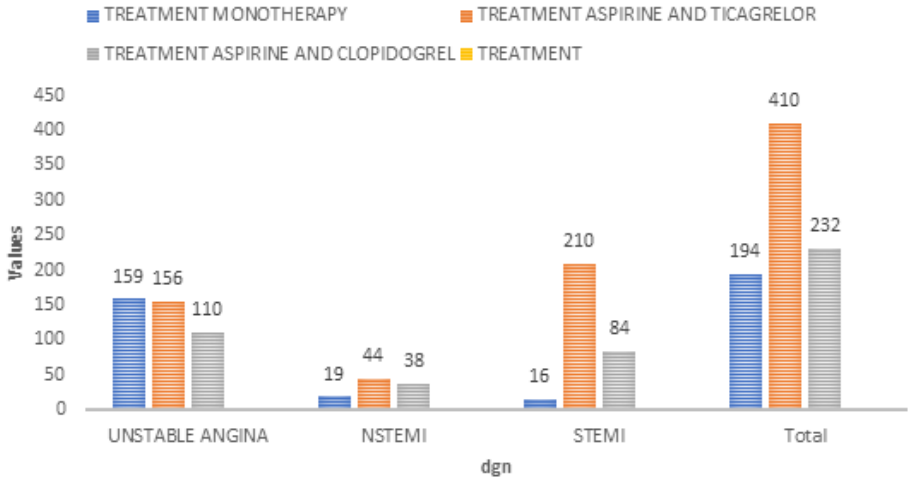

Figure 1.
Antiplatelet therapy according to diagnosis

Antiplatelet therapy according to the type of treatment
The majority of patients, 57.29% were treated with PCI respectively angioplasty and coronary stenting. A number of 33.13% patients were medically managed only with drugs and 9.56% performed coronary artery bypass (CABG).
In the group with PCI, DAPT was predominant being prescribed in 98.12% of the patients. The preferred therapy was ASA-ticagrelor in 80.58% *vs*. ASA-clopidogrel in 17.53% ($p < 0.001$). Monotherapy was prescribed only in 1.87% patients with PCI ($p < 0.001$). In the medically managed group, most of the patients, 61.01% were on monotherapy *vs*. 34.29% on ASA-clopidogrel ($p < 0.001$) and only 4.69% were on ASA-ticagrelor ($p < 0.001$). Patients with ACS undergoing CABG were more frequently treated with DAPT ASA-clopidogrel, 66.25% *vs*. only 20% on monotherapy ($p < 0.001$). Only 13.75% of patients send to CABG were on ASA-ticagrelor ($p < 0.05$ *vs*. monotherapy) (Figure 2).

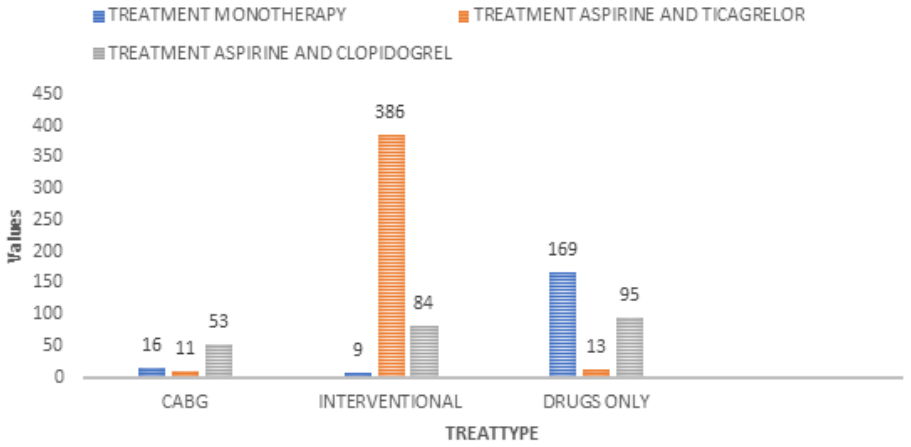

Figure 2.
Antiplatelet therapy according to type of treatment

Antiplatelet therapy according to diagnosis and the type of treatment can be found in Table II. In patients with UA treated only with drugs, the most frequent antiplatelet therapy was monotherapy, followed by DAPT with ASA-clopidogrel.
Patients with UA undergoing PCI procedure are most frequently treated with DAPT consisting from ASA-ticagrelor, followed by DAPT with ASA-clopidogrel, and only a few patients were on monotherapy. Patients with UA referred for CABG were most often treated with DAPT with ASA-clopidogrel.
NSTEMI patients were most frequently treated with PCI and the preferred antiplatelet therapy in this situation was dual consisting from ASA-ticagrelor.
NSTEMI patients treated only with medical therapy were most frequently treated with monotherapy and ASA-clopidogrel. NSTEMI patients referred for CABG were most frequently on DAPT with ASA-clopidogrel.
STEMI patients were usually treated with PCI therapy in emergency (81.93% patients) and the most used was DAPT with ASA-ticagrelor.

Table II

Antiplatelet therapy according to diagnosis and type of treatment

Diagnostic	Treatment	n	ASA + Ticagrelor n = 410	ASA + Clopidogrel n = 232	Monotherapy n = 194	p
UA	DRUGS	204	8	52	144	< 0.001
	PCI	172	144	26	2	< 0.001
	CABG	49	4	32	13	< 0.001
NSTEMI	DRUGS	33	1	16	16	< 0.001
	PCI	53	42	10	1	< 0.001
	CABG	15	1	12	2	< 0.001
STEMI	DRUGS	40	4	27	9	< 0.001
	PCI	254	200	48	6	< 0.001
	CABG	16	6	9	1	< 0.05

Myocardial infarction with (STEMI) or without ST segment elevation (NSTEMI); Left ventricular ejection fraction (LVEF); unstable angina (UA); Percutaneous coronary intervention (PCI); Performed coronary artery bypass (CABG)

Drug therapy alone was used in only 12.90% of patients with STEMI, usually patients who refused coronary angiography, died before revascularization attempt or coronary anatomy was not suitable for interventional revascularization. In this subgroup the most prescribed was DAPT with ASA-clopidogrel and monotherapy. Only 5.16% of patients with STEMI were referred for CABG, and were most frequently treated with the DAPT ASA-clopidogrel.

Drugs associated with antiplatelet therapy (Table III).

The most frequently prescribed associated therapy was statin therapy in 755 patients (89.2%), followed by therapy with renin angiotensin system blockers (angiotensin converting enzyme inhibitors-ACEI or angiotensin receptor blockers-ARB) 637 patients (75.3%), beta-blockers in 597 patients (70.6 %) and PPIs in 522 patients (61.7%).

Table III

Associated therapy

Associated treatment	ASA + Ticagrelor n = 410	ASA + Clopidogrel n = 232	Monotherapy n = 194	p
Beta-blockers	315 (76.82%)	146 (62.93%)	126 (64.94%)	< 0.01
ACEI/ARB	332 (80.97%)	162 (69.82%)	135 (69.58%)	< 0.01
Statins	387 (94.39%)	213 (91.81%)	148 (76.28%)	< 0.001
PPIs	277 (67.56)	149 (64.22%)	89 (45.87%)	< 0.01
Nitrates	59 (14.39%)	81 (34.91%)	38 (19.58%)	< 0.001
Diuretics	171 (41.70%)	136 (58.62%)	115 (59.27%)	< 0.001
Omega 3 fatty acids	9 (2.19%)	13 (5.6%)	10 (5.15%)	0.11
NOAC	5 (1.21%)	12 (5.17%)	21 (10.82%)	< 0.05
Vit K antagonists	12 (2.92%)	17 (7.32%)	29 (14.94%)	< 0.01

Regarding the associated drug therapy in the three groups' beta-blocker therapy was more frequently prescribed in the group treated with ASA-ticagrelor.

ACEI and ARB were more frequently prescribed in the group treated with ASA-ticagrelor. Statins were significantly most frequently prescribed in the group treated with ASA-ticagrelor and ASA-clopidogrel. ACS patients treated with ASA-ticagrelor and ASA-clopidogrel received significantly most often PPI. Despite the presence in the literature of data regarding the negative association between clopidogrel/ticagrelor and PPI [4] almost 70% of patients with DAPT were prescribed PPI due to concerns about the risk of gastrointestinal bleeding.

Nitrates were most frequently prescribed in the group treated with ASA-clopidogrel. Diuretics were most often prescribed in the group treated with mono-therapy and in the group treated with ASA-clopidogrel.

A number of 96 patients (11.48%) were discharged with associated antiplatelet and anticoagulant therapy mainly due to atrial fibrillation, (38 patients on NOAC and 58 patients on vitamin K antagonists). Anti-coagulants were prescribed mainly in the group with monotherapy. A number of 29 patients were on DAPT with ASA-clopidogrel and associated anticoagulant therapy (12 on NOAC and 17 on vitamin K antagonists), 26 of them treated with PCI revascularization procedure. A number of 17 patients were on DAPT with ASA-ticagrelor and associated anticoagulant therapy (5 on NOAC and 12 on vitamin K antagonists), all of them were treated with PCI therapy and stent implantation. The current ESC guidelines recommend DAPT with ASA and a P2Y12 antagonist for all patients with ACS [31]. Ticagrelor is recommended over clopidogrel irrespective of the initial management strategy. Indications for clopidogrel remained: patients with contraindications to ticagrelor, patients who need concomitant oral anticoagulation or those treated with fibrinolysis agents [26].

The majority of patients with ACS in our study were discharged with at least one antiplatelet drug (98.47%). The most prescribed antiplatelet therapy at discharge was DAPT consisting in ASA-ticagrelor (48.29%), but DAPT with ASA-clopidogrel is yet prescribed in a significant number of patients with ACS (27.32%). In the subgroup of patients treated with PCI, 98.12% were on DAPT. In the subgroup of medically managed patients only 38.98% were on DAPT.

Other studies revealed poorer results regarding antiplatelet therapy with a considerable proportion of patients remaining without antiplatelet treatment after an ACS event [2, 8, 22]. Cimmimiello *et al*. in an observational retrospective study performed in Italy, observed that after an ACS, 23% did not receive any antiplatelet drug during the first month after discharge. DAPT in the subgroup of patients undergoing PCI was prescribed in 79.2% of cases and to 46.1% of medically managed patients [8].

The study performed by Maggioni *et al*. [22] also highlights that the prescription of antiplatelet therapy, specifically DAPT is suboptimal. From 26834 patients discharge after an ACS, 77% were on antiplatelet therapy. Among patients undergoing PCI, 90% received antiplatelet agents. DAPT was prescribed in 49.6% of the total population and in 68.5% of those with PCI, significantly less than in our study.

The first choice in our study was DAPT with ASA-ticagrelor, but DAPT with ASA-clopidogrel continued to be used in a significant proportion of ACS patients, although ESC guidelines recommend ticagrelor regardless of the initial treatment strategy including patients pre-treated with clopidogrel [31]. Although ticagrelor was preferred over clopidogrel it is still underutilised in ACS. A possible explanation is the economical reason since DAPT with ASA-ticagrelor is on free prescription only in patients with PCI procedure.

Widimsky *et al*. in two complementary ACS registries organised between 2013 and 2015 in the Czech Republic on 1967 patients observed that discharge medication included ASA in 93%, clopidogrel in 73%, ticagrelor in 14% and prasugrel in 4%. Of the cases Clopidogrel preference over ticagrelor lead to the conclusion that the use of modern guidelines recommended treatment with novel antiplatelet agents was surprisingly reduced and it was not limited by economic restrictions [35]. The TRANSLATE ACS enrolled 12,365 patients with MI treated with PCI. In the first year after MI 11% patients had recurrent ischemic events. At the time of the recurrent ischemic event 62.5% were taking clopidogrel, 21.9% were taking prasugrel and only 3.2% were taking ticagrelor [10]. Different results more adapted to ESC guidelines were observed in our study. STEMI patients were usually treated with PCI therapy in emergency cases (81.93% patients). Most often in patients with STEMI treated with PCI was prescribed DAPT with ASA-ticagrelor (78.74%) patients. Significantly less patients with STEMI treated with PCI received DAPT with ASA-clopidogrel (18.89%, $p < 0.001$), and only a few patients were on monotherapy (2.36%, $p < 0.001$). Similar results to ours were observed by Anastasius *et al*. in a study performed in australian hospitals regarding antiplatelet therapy in ACS. They observed that between 2009 and 2016 from 8,939 patients, 70.04% were on DAPT, 24.1% on single antiplatelet therapy and 5.5% were on no antiplatelet therapy [3]. Marcucci *et al*. in the prospective observational registry carried out in seven Italian cardiology institutions on patients admitted for ACS observed that the DAPT most prescribed was ASA-ticagrelor (47.9%) and ASA-clopidogrel (32.1%) similar results with those observed in our study [23].

In the study performed by Kim *et al*. on 66,335 subjects who underwent PCI (between 2009 and 2013), the authors observed that the use of clopidogrel decreased from 100% to 65%. The use of new agents as oppose to use of clopidogrel was associated with younger age (< 65 years), male gender, diagnosis of STEMI. Condition increasing mortality and risk of cardiovascular complications were associated with higher odds of using clopidogrel [18]. Similar results were observed in our study. The dual therapy ASA-ticagrelor was preferred in younger patients, patients with STEMI and interventional treatment. The dual therapy ASA-clopidogrel was prescribed in patients with more severe medical condition with lower LVEF, with higher creatinine level and in older patients.

The group of patients treated with DAPT ASA-ticagrelor were the best treated group regarding associated therapy in line with literature data and ESC guidelines [33, 34]. They received associated therapy with beta-blockers (76.82%), ACEI/ARB (80.97%) and statin therapy (94.39%). Similar results were observed in the study performed by Farmakis *et al*. A combination of statin, dual antiplatelet therapy and beta-blockers were prescribed to 79.6% of patients with ACS upon discharge. An ACEI/ARB was prescribed to 67.3% of patients [11].

Although anticoagulant therapy was mainly prescribed in the group with antiplatelet monotherapy, in patients with ACS and indication for anticoagulant therapy (mainly for atrial fibrillation) undergoing stent implantation DAPT in addition to oral anticoagulant therapy was indicated. While the use of triple antithrombotic therapy may reduce the risk of cardiac ischemic events the risk of bleeding is significantly increased so optimal antithrombotic therapy in this group of patients represents a clinical challenge. In every patient the ischemic risk (complexity of the treated coronary artery disease, residual coronary artery lesions, technical considerations regarding stent implantation and results) and the bleeding risk (assessed with HASBLED or ABC score) must be evaluated. ESC guidelines recommend in these patients

the triple therapy with ASA-clopidogrel and an oral anticoagulant for up to 6 months if the ischemic risk is high due to ACS and other anatomical or procedural characteristics [31, 32]. In our study the majority of patients undergoing interventional procedure on DAPT and with concomitant indication for anticoagulation were treated with ASA-clopidogrel as recommended in ESC guidelines (60.47%). There were also a number of 17 patients (39.53%) treated with DAPT ASA-ticagrelor and associated anticoagulant therapy all of them revascularized with stent implantation and with ischemic risk evaluated to be high by the prescribing physician. ESC guidelines do not recommend the use of ticagrelor as a part of triple therapy due to high haemorrhagic risk and the absence of safety and efficacy data from randomised controlled trials [31].

In patients taking vitamin K antagonists and DAPT the INR should be monitored closely and kept between the 2 to 2.5 range and when NOAC is used the lowest dose approved to be effective in stroke prevention should be considered.

Despite DAPT, 10% of ACS patients experience recurrent major adverse cardiovascular events over the subsequent 30 days driving the quest for more effective inhibition of thrombotic pathways [28]. Increased antithrombotic efficacy improves outcomes post ACS, but carries the price of increased bleeding risk, the challenge for the future is to better predict the benefit risk ratio in individual patients so that intensity of antiplatelet therapy can be optimised on a personalised basis [20].

Conclusions

The most prescribed antiplatelet therapy in patients with ACS was DAPT with ASA and ticagrelor (48.29%), but ASA and clopidogrel is still utilised in a significant number of patients (27.32%). Only 22.85% were on antiplatelet monotherapy and a few patients were discharged without antiplatelet therapy (1.53%). The dual antiplatelet therapy ASA ticagrelor is still underutilized mainly due to economic reasons. In the group of patients treated with interventional revascularization dual antiplatelet therapy was prescribed in the majority of patients (98.12%). The preferred combination used was ASA and ticagrelor in 80.58% of the patients.

Dual therapy with ASA and ticagrelor is preferred in patients with STEMI, interventional revascularization and in younger patients. Dual therapy with ASA and clopidogrel was used more often in patients undergoing CABG, in medically managed patients and in patients with more frailty: lower ejection fraction, higher creatinine level, older patients. Monotherapy was used more often in patients with UA, medically managed patients and patients treated concomitantly with oral anticoagulant drugs.

Conflict of interest

The authors declare no conflict of interest.

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