

Comparison of Platelet Function Guided Versus Unguided Treatment With P2Y₁₂ Inhibitors in Patients With Acute Myocardial Infarction (from the Hungarian Myocardial Infarction Registry)



András Komócsi, MD, DSc^{a,*}, Dániel Aradi, MD, PhD^{b,c}, Tibor Szűk, MD, PhD^d, Gergely György Nagy, MD, PhD^e, Ebrahim Noori, MD^f, Zoltán Ruzsa, MD, PhD^{c,g}, Róbert G. Kiss, MD, PhD^h, Péter Andrásy, MD, PhDⁱ, Lajos Nagy, MD, PhD^j, Ferenc Tamás Nagy, MD, PhD^k, Géza Lupkovics, MD^l, Zsolt Kőszegi, MD, PhD^m, Csaba András Dézsi, MD, PhDⁿ, Előd Papp, MD, PhD^o, Zsolt Molnár, MD^o, Péter Kupó, MD^a, Péter Ofner, MD^p, Béla Merkely, MD, DSc^c, and András Jánosi, MD, DSc^p

Evidence is conflicting regarding the clinical benefits of selecting P2Y₁₂ inhibitors based on platelet function testing (PFT). Between March 1, 2013 and March 1, 2014, we collected clinical characteristics and platelet function data in a nationwide acute myocardial infarction (AMI) registry from 15 interventional cardiology centers in Hungary. The risk of all-cause mortality at 1 year were compared after propensity score (PS) matching between patients receiving PFT-guided and unguided P2Y₁₂-inhibitor therapies. High platelet reactivity on clopidogrel (HPRoC) was uniformly defined with the Multiplate assay. A total of 5,583 patients with AMI and coronary intervention were registered. After exclusion of cases with contraindication to prasugrel, propensity matching resulted in a sample of 2,104 patients with well-adjusted characteristics. Clopidogrel was the dominant P2Y₁₂ inhibitor in both groups (unguided: 96% vs PFT guided: 85%, $p < 0.001$). In the PFT-guided group, 19% of patients had HPRoC and 77% of them were switched to prasugrel. According to the adjusted analysis, all-cause mortality at 1 year was significantly lower in the PFT-guided compared with the unguided group (hazard ratio 0.57 [95% confidence interval 0.43 to 0.77], $p < 0.001$). Although prasugrel treatment was not associated with lower all-cause mortality in the overall cohort, patients with HPRoC who switched to prasugrel had significantly lower mortality when compared with those continuing clopidogrel (hazard ratio 0.33 [95% confidence interval 0.12 to 0.92], $p < 0.05$). In conclusion, in patients with AMI, PFT-guided treatment with a high rate of switchover to prasugrel was associated with a lower risk of mortality. Prasugrel was a predictor of lower mortality in patients with HPRoC but not in the overall cohort of AMI. © 2018 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). (Am J Cardiol 2018;121:1129–1137)

Inhibition of platelet aggregation is one of the major therapeutic targets in patients with an acute myocardial infarction (AMI). Among platelet P2Y₁₂-receptor inhibitors, prasugrel and ticagrelor are the preferred choices for patients with AMI.^{1,2} Due to contraindications, financial restrictions, and regulatory reasons, the availability of prasugrel and ticagrelor is not

uniform across countries, whereas the use of clopidogrel and switching between P2Y₁₂ inhibitors is frequent.^{3–5} High platelet reactivity on clopidogrel (HPRoC) is an independent predictor of stent thrombosis and myocardial infarction.^{6–8} However, current guidelines discourage the routine use of platelet function testing (PFT) due to lack of evidence on the ability

^aHeart Institute, Medical School, University of Pécs, Pécs, Hungary; ^bHeart Centre, Balatonfüred, Hungary; ^cHeart and Vascular Center, Semmelweis University, Budapest, Hungary; ^dDepartment of Cardiology and Cardiac Surgery, University of Debrecen, Debrecen, Hungary; ^eBorsod-Abaúj-Zemplén County Hospital, Department of Cardiology, Miskolc, Hungary; ^fCounty Hospital Fejér, Szent György Hospital, Székesfehérvár, Hungary; ^gInvasive Cardiology Department, Bács-Kiskun County Hospital, Kecskemét, Hungary; ^hMilitary Hospital, Budapest, Hungary; ⁱBajcsy Hospital, Budapest, Hungary; ^jMarkusovszky University Teaching Hospital, Szombathely, Hungary; ^k2nd Department of Internal Medicine and Cardiology Center, University of Szeged, Szeged, Hungary; ^lZala County Saint Raphael Hospital, Zalaegerszeg, Hungary; ^mAndrás Jóna University Teaching Hospital,

Nyiregyháza, Hungary; ⁿPetz Aladár County Teaching Hospital, Győr, Hungary; ^oMór Kaposi University Teaching Hospital, Kaposvár, Hungary; and ^pHungarian Myocardial Infarction Registry, György Gottsegen Hungarian Institute of Cardiology, Budapest, Hungary. Manuscript received December 1, 2017; revised manuscript received and accepted January 25, 2018.

¹The authors contributed equally to the article.

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*Corresponding author: Tel: 0036302355639; fax: 003672536399.

E-mail address: komocsi.andras@pte.hu (A. Komócsi).

of PFT-based P2Y₁₂ therapy to improve outcomes.^{1,2} Local reimbursement regulations in Hungary mandate PFT on clopidogrel, and prasugrel is reimbursed for patients with HPRoC. This policy resulted in a high penetration of PFT across invasive centers. We sought to evaluate the clinical impact of PFT guidance based on a nationwide registry of patients with AMI who were treated with coronary intervention.

Methods

The Hungarian Myocardial Infarction Registry is a prospective, Internet-based registry collecting clinical data on consecutive patients treated for an event of AMI in Hungary, a country with 9.8 million residents. At the time of the conduction of the present study, the registry operated on a voluntary basis, capturing 51% of AMI cases treated countrywide.^{9–11} The protocol of the study is in accordance with the Declaration of Helsinki and was reviewed by the ethical board. All patients recorded in the registry gave written informed consent.

Between March 1, 2013 and March 1, 2014, all patients with AMI (both with ST segment elevation and without) were eligible for enrollment if intervention was performed successfully with stent implantation and there was no contraindication to treatment with a P2Y₁₂ inhibitor for 1 year. Data of patients treated in 15 centers of invasive cardiology collaborating with providing and monitoring platelet function data were analyzed.

Patients with an indication of chronic oral anticoagulation, with a history of stroke or transient ischemic attack, who are aged older than 75 years, who weigh less than 60 kg, or who have had an administration of P2Y₁₂ inhibitors other than clopidogrel or prasugrel before or during intervention were excluded. Thienopyridins were supplemented with low-dose aspirin, typically 100 mg with an optional loading dose of 300 to 500 mg. The use of perioperative anticoagulation and the administration of platelet IIb/IIIa inhibitors were allowed according to the local protocols.

Generally, P2Y₁₂-inhibitor treatment before intervention comprised clopidogrel, usually given in a loading dose of 600 mg but left to the decision of the treating physicians. After intervention, both prasugrel and clopidogrel were available for long-term treatment. However, although clopidogrel use was not restricted by any reimbursement rule, prasugrel was reimbursed at 70% only if PFT results confirmed HPRoC. Importantly, it was left to the discretion of the treating physicians whether to perform PFT and make the choice based on PFT (PFT-guided group) or make a clinical decision without PFT (unguided group).

All participating centers used a homogeneous method for PFT, which was the Multiplate analyzer (Roche Diagnostics GmbH, Rotkreuz, Switzerland). PFT was performed at least 6 hours after the intervention or at least 24 hours after platelet IIb/IIIa inhibitor treatment cessation.¹² HPRoC was defined as an adenosine diphosphate test level >46 U.¹² The choice of P2Y₁₂ inhibitor in patients with HPRoC was also left to the treating physician: either switch to prasugrel, or high (150 mg/day) or conventional doses (75 mg) of clopidogrel were allowed.

The primary efficacy end point was all-cause mortality within 1 year after the index procedure. Secondary end points

included the composite of cardiovascular death, recurrent myocardial infarction, and stroke as well as transfusion and the individual elements of the composite end point. Overall mortality was obtained from the patient vital status in the database of the Hungarian Central Statistical Office and the National Health Insurance Fund, including the date and the cause of death. In patients who died, the cause of death was assessed by qualifying deaths related to infection, malignancy, and trauma as noncardiovascular. Data related to recurrent hospitalization for AMI, for stroke, as well as for bleeding event leading to transfusion were extracted from the database of the National Health Insurance Fund.

Variables are presented as means \pm SD or as frequencies and percentages. Unpaired *t* tests were used for comparisons of continuous variables between groups. Categorical variables were compared using chi-square or Fisher's exact test as appropriate. As eligible patients were not randomly assigned to PFT-guided or unguided treatments, we intended to balance the groups to reduce potential bias associated with treatment selection. For this aim we built a propensity score (PS)-matched cohort with comparable chance for either strategy by adjusting for differences in baseline characteristics. PS was computed by using a logistic regression model for PFT-guided versus unguided groups. Patient characteristics at presentation and clinical factors from the medical history with potential influence on the decision regarding PFT (listed in Table 1) were used as predictors in calculating PS. In the PS-matching procedure, we first randomly selected a patient in the unguided group and matched him or her with a patient from the PFT-guided group with the closest estimated PS value. We performed a 1-to-1 matched analysis without replacement with a match tolerance of <0.01. Unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were determined in univariate Cox proportional models, and then a multivariable Cox proportional hazards model was used to determine independent predictors of all-cause mortality. As a sensitivity exercise, PFT-guided and unguided patients were compared also in the PS-unmatched study population with Cox regression analyses. All reported *p* values are 2-sided, and *p* values of <0.05 were considered to indicate statistical significance. This analysis was conducted using the SPSS 22 statistical package.

Results

From March 1, 2013 to March 1, 2014, data of 6,795 patients hospitalized in the participating centers for an event of AMI were entered in the registry. Of these, 5,583 patients (82.2%) were treated with coronary intervention and stenting. In 3,715 cases (66.5%), long-term P2Y₁₂-inhibitor treatment was chosen based on PFT results (PFT-guided group), whereas PFT was not performed in 1,868 cases (unguided group 33.5%). After excluding 29% of patients with absolute or relative contraindications to prasugrel, an unmatched patient pool of 3,974 cases was obtained (Figure 1). As expected, there were numerous differences in baseline characteristics between the groups. To adjust for these differences, PS matching was performed that resulted in a matched population of 2,104 patients (Table 1).

Among the 2,901 subjects of the PFT-guided group, 554 (19%) had HPRoC. Seventy percent of them were switched

Table 1
Characteristics of the patient population before and after propensity score matching

Clinical characteristics	Entire cohort (n = 3974)			Propensity matched cohort (n = 2104)		
	PFT-guided (n = 2901)	Unguided treatment (n = 1073)	p value	PFT-guided (n = 1052)	Unguided treatment (n = 1052)	p value
Age, (years) *	58.9 ± 9.6	60.5 ± 9.2	<0.001	60.5 ± 9.0	60.5 ± 9.1	0.926
Men *	69.3 %	65.7 %	0.035	65.3 %	66.1 %	0.748
Medical history						
Hypertension	64.6 %	71.2 %	<0.001	68.41 %	70.6 %	0.297
Diabetes mellitus	24.8 %	29.2 %	0.006	27.8 %	28.4 %	0.734
- insulin	1.6 %	1.6 %	1.000	1.0 %	1.5 %	0.324
Hyperlipidemia *	11.1 %	5.1 %	<0.001	3.7 %	5.2 %	0.113
Smoker (current/past/never)	35.2/1.6/63.3 %	36.1/2.1/61.9 %	0.458	36.2/1.8/62.0 %	36.2/1.9/61.8 %	0.950
Prior myocardial infarction	15.8 %	27.4 %	<0.001	26.6 %	26.0 %	0.771
Prior coronary intervention*	4.6 %	7.3 %	0.001	7.1 %	7.4 %	0.867
Prior of coronary bypass operation *	1.8 %	1.0 %	0.113	0.8 %	1.0 %	0.646
Peripheral artery disease *	5.3 %	11.6 %	<0.001	10.2 %	10.4 %	0.943
Presentation						
ST segment elevation myocardial infarction *	64.1 %	51.0 %	<0.001	55.1 %	51.7 %	0.126
Culprit artery (LM/LAD/ Cx/RCA/VSG)	2.8/46.7/23.0/35.8/1.2 %	3.3/44.1/25.9/35.8/1.1 %	0.3461	2.9/46.7/24.4/34.3/1.2 %	2.9/44.2/25.5/36.0/1.0 %	0.734
Heart rate (bpm)	79.8 ± 17.1	80.6 ± 18.1	0.236	81.4 ± 18.0	80.5 ± 18.1	0.250
Systolic blood pressure (mm Hg)*	137.9 ± 24.2	136.6 ± 25.7	0.191	138.6 ± 24.8	136.5 ± 25.7	0.054
Diastolic blood pressure (mm Hg)*	70.0 ± 24.7	68.7 ± 25.0	0.168	67.9 ± 26.1	68.8 ± 25.1	0.440
Adenosin diphosphate reactivity	32.5 ± 19.5	-	NA	32.5 ± 19.9	-	NA
High platelet reactivity	19.1 %	-	NA	18.6 %	-	NA
Medications						
Clopidogrel 75 mg daily	50.6 %	74.3 %	<0.001	43.6 %	74.2 %	<0.001
Clopidogrel 150 mg daily	34.4 %	21.6 %		40.2 %	21.8 %	
Prasugrel	15.0 %	4.1 %		16.2 %	4.0 %	
Aspirin	71.1 %	81.0 %	<0.001	80.9 %	79 %	0.547
β-blocker	84.1 %	90.6 %	<0.001	88.5 %	90.4 %	0.176
Statin	81.0 %	91.8 %	<0.001	91.6 %	91.7 %	0.579

Data are presented as percentages or as mean ± standard deviation. Asterisk marks parameters associated to the invasive therapy in binary logistic model.

* p value < 0.1.

LM = left main coronary artery; LAD = left anterior descending artery; Cx = left circumflex artery; RCA = right coronary artery; SVG = saphenous vein graft.

to prasugrel, whereas 30% continued clopidogrel (14% high-dose and 16% standard-dose clopidogrel). In patients without HPROc (no HPROc group), use of prasugrel was low (2%), resulting in an overall high proportion of patients continuing clopidogrel based on PFT guidance. Among unguided patients, prasugrel was prescribed only in 4%, whereas low-dose clopidogrel was quite frequent (74%). Treatment allocation patterns in the PS-matched cohort remained similar with 77% switchover to prasugrel in patients with HPROc (Figure 2).

During the follow-up period, 200 patients died from the PS-matched cohort, resulting in a 1-year all-cause mortality rate of 9.5%, in this unselected, high-risk cohort. PFT-guided subjects had a highly significant, 43% lower hazard for all-cause mortality compared with the unguided group. Similar to this, cardiovascular mortality was also reduced by 39% (Figure 3 and Table 2). In the unmatched total cohort including 3,974 patients, similar results were observed for all-

cause and cardiovascular mortality without a significant difference in the risk of stroke or repeat myocardial infarction (Table 2). As the use of prasugrel was higher in the PFT-guided than in the unguided group (16% vs 4%, $p < 0.001$), its potential impact on survival was calculated in the overall analysis populations. Prasugrel treatment, however, was not associated with lower risk of mortality in the PS-matched (HR 0.65 [0.38 to 1.11], $p = 0.116$) or in the unmatched cohorts (HR 0.75 [0.51 to 1.11], $p = 0.145$).

As a prespecified analysis, the clinical impact of prasugrel and clopidogrel were tested on all-cause mortality within subgroups of PFT-guided and unguided therapy, and across HPROc groups. Within the PFT-guided group of PS-matched patients, clopidogrel use was associated with significantly worse survival compared with prasugrel in case of HPROc. Among clopidogrel-treated patients with HPROc, high-dose clopidogrel was associated with a numerically lower risk of mortality than standard-dose clopidogrel (8.7% vs 21.7%),

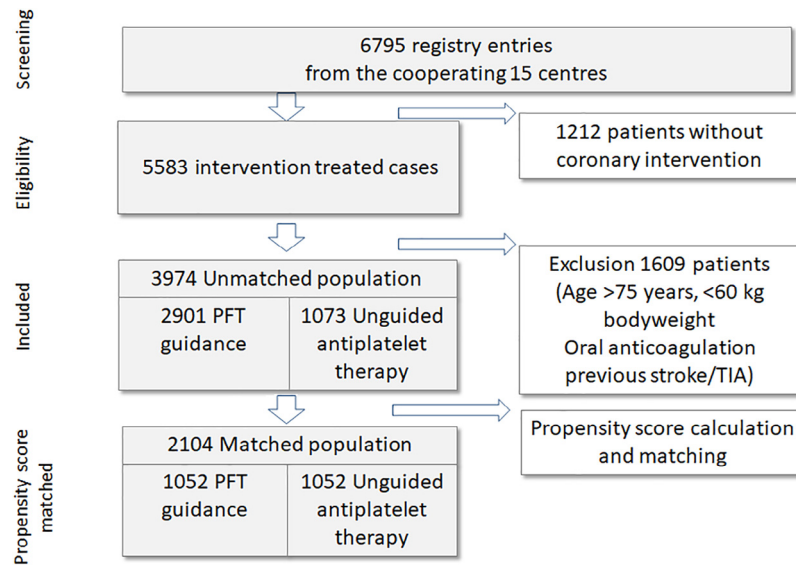


Figure 1. Flowchart of patient selection. TIA = transient ischemic attack.

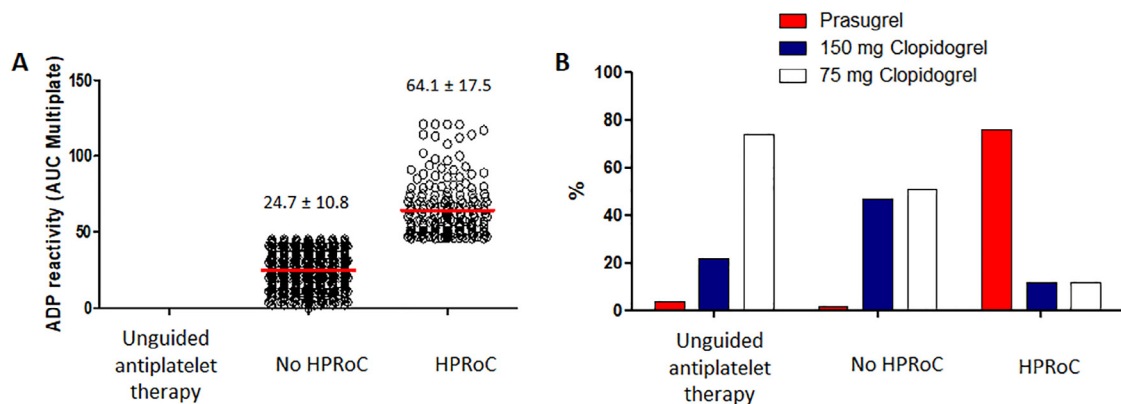


Figure 2. Results of the platelet function tests (A) and P2Y₁₂ antagonist therapy in the platelet function test results defined groups of the propensity-adjusted sample (B). ADP = adenosine diphosphate; AUC = area under the curve.

but this difference did not reach the level of statistical significance (HR 0.37 [95% CI 0.07 to 1.88], $p = 0.228$). In the unguided group and in patients without HPRoC of the guided cohort, prasugrel versus clopidogrel therapy was not a significant predictor of survival (Figures 4 and 5).

To separate and analyze the potential role of PFT on mortality independently from other potentially relevant determinants, univariate and multivariate models were generated. In the multivariate model, beyond known risk factors including age, smoking, history of peripheral artery disease, hypertension, diabetes, high heart rate or low arterial pressures at presentation, and left main coronary involvement, PFT guidance remained a significant, independent predictor of lower all-cause mortality, whereas prasugrel therapy was not associated with an improved overall survival (Table 3).

Discussion

Our analysis of a large, prospective, unselected database of patients treated with coronary intervention due to an event

of AMI showed improved survival in patients with PFT-guided antiplatelet treatment compared with an unguided strategy. Explorative analyses demonstrated that the results of PFT had an important impact on the selected P2Y₁₂-inhibitor therapy as patients without PFT guidance were more frequently kept on clopidogrel, whereas those in the PFT-guided group harboring HPRoC were mostly switched over to prasugrel. Importantly, prasugrel therapy was not a predictor of lower mortality in the overall cohort, but it was associated with a reduction in all-cause death only in patients with HPRoC. These findings may explain why PFT-guided P2Y₁₂-inhibitor treatment selection, but not prasugrel therapy, prevailed as an independent predictor of improved survival in the multivariate analysis. These results were confirmed both in the overall and in the PS-matched cohorts.

Prasugrel and ticagrelor showed a significant reduction in the risk of ischemic end points in AMI patients.^{13,14} However, both potent P2Y₁₂ inhibitors were associated with a higher risk of major bleeding, and in case of prasugrel, no apparent benefit in patients over 75 years of age or with low body

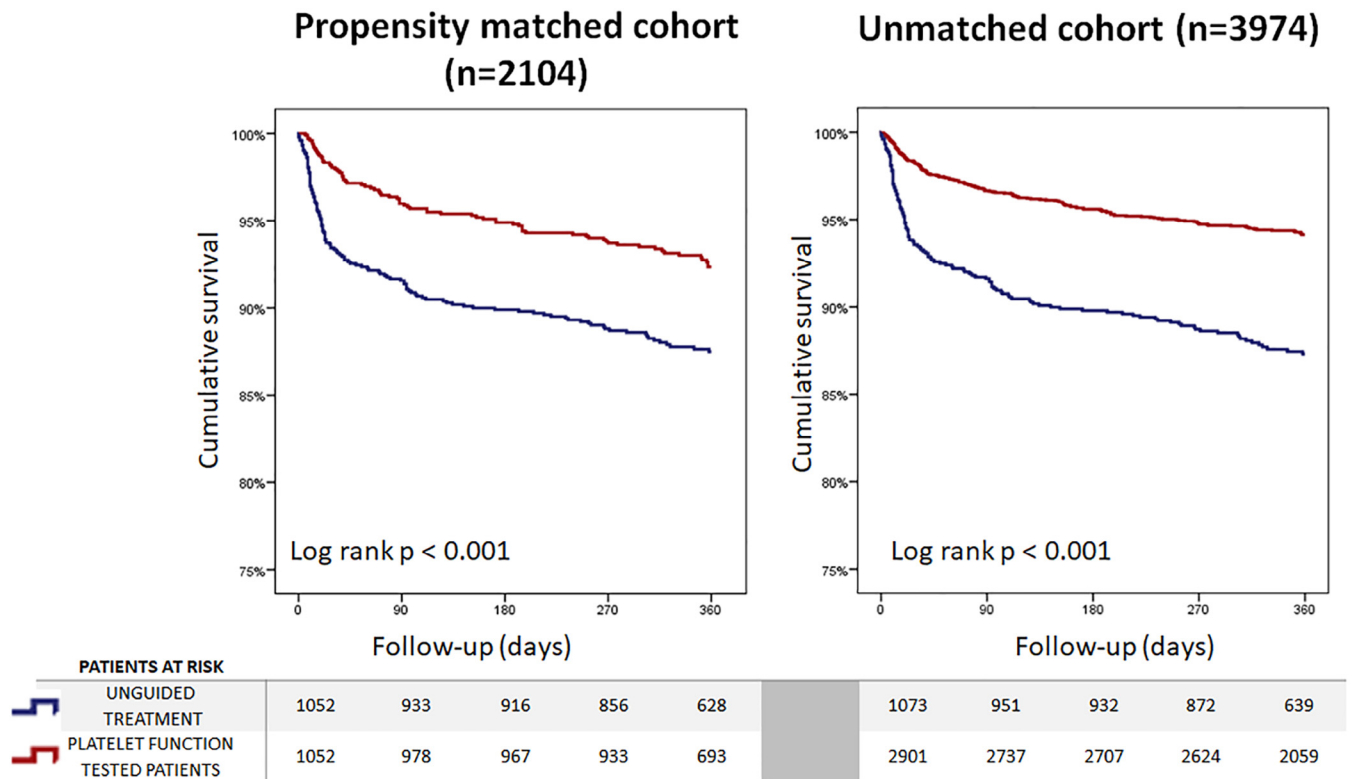


Figure 3. Kaplan–Meier curves of survival comparing platelet function test–guided versus unguided treated myocardial infarction cases assessed in the PS-adjusted sample and in the whole cohort.

Table 2
Clinical outcomes of platelet function test guided versus unguided patients

A. Propensity matched cohort (n = 2104)

	Nr. of patients (%)		Hazard Ratio [95% Confidence interval]
	Platelet function guided treatment (n = 1052)	Unguided treatment (n = 1052)	
Death from any cause	75 (7.1 %)	125 (11.9 %)	0.57 [0.43–0.77]***
Death from cardiovascular causes	66 (6.3 %)	104 (9.9 %)	0.61 [0.45–0.83]**
Repeated myocardial infarction	29 (2.8 %)	20 (1.9 %)	1.38 [0.78–2.44]
Stroke	8 (0.8 %)	8 (0.8 %)	0.95 [0.36–2.54]
Major adverse cardiac events (cardiovascular death, myocardial infarction, or stroke)	97 (9.2 %)	126 (12.0 %)	0.74 [0.57–0.96]*
Transfusion	74 (7.0 %)	67 (6.4 %)	1.01 [0.73–1.41]

B. Unmatched cohort (n = 3974)

	Platelet function guided treatment (n = 2901)	Unguided treatment (n = 1073)	Hazard Ratio [95% Confidence interval]
Death from any cause	163 (5.6 %)	129 (12.0 %)	0.44 [0.35–0.56]***
Death from cardiovascular causes	139 (4.8 %)	107 (10.0 %)	0.45 [0.35–0.58]***
Repeated myocardial infarction	71 (2.4 %)	20 (1.9 %)	1.22 [0.74–2.01]
Stroke	23 (0.8 %)	8 (0.7 %)	0.99 [0.44–2.21]
Major adverse cardiac events (cardiovascular death, myocardial infarction, or stroke)	218 (7.5 %)	129 (12.0 %)	0.59 [0.47–0.73]***
Transfusion	131 (4.5 %)	70 (6.5 %)	1.03 [0.92–1.64]

Data from Cox-regression analyses are presented as hazard ratio [95% Confidence interval], asterisks marks comparisons with p value * < 0.05, ** < 0.01, and *** < 0.001. Patients could have had more than one type of end point.

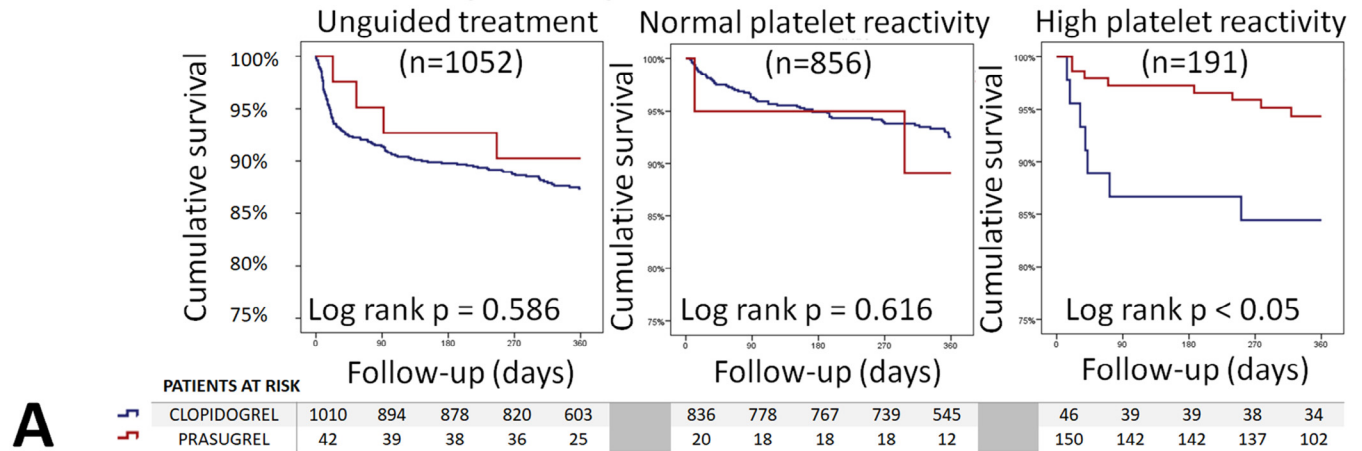
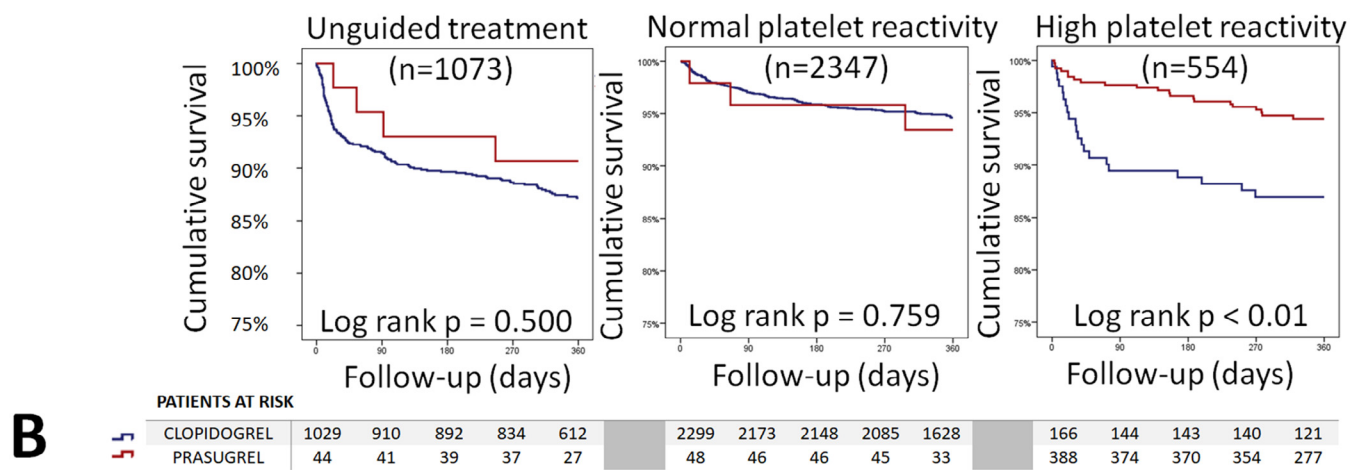
PS matched cohort (n=2104)**Unmatched cohort (n=3974)**

Figure 4. Kaplan-Meier curves depicting the outcome of patients with prasugrel or clopidogrel treatment in the strata of unguided treatment, HPRoC or no HPRoC. (A) Propensity-matched cohort (n = 2,104). (B) Unmatched cohort (n = 3,974).

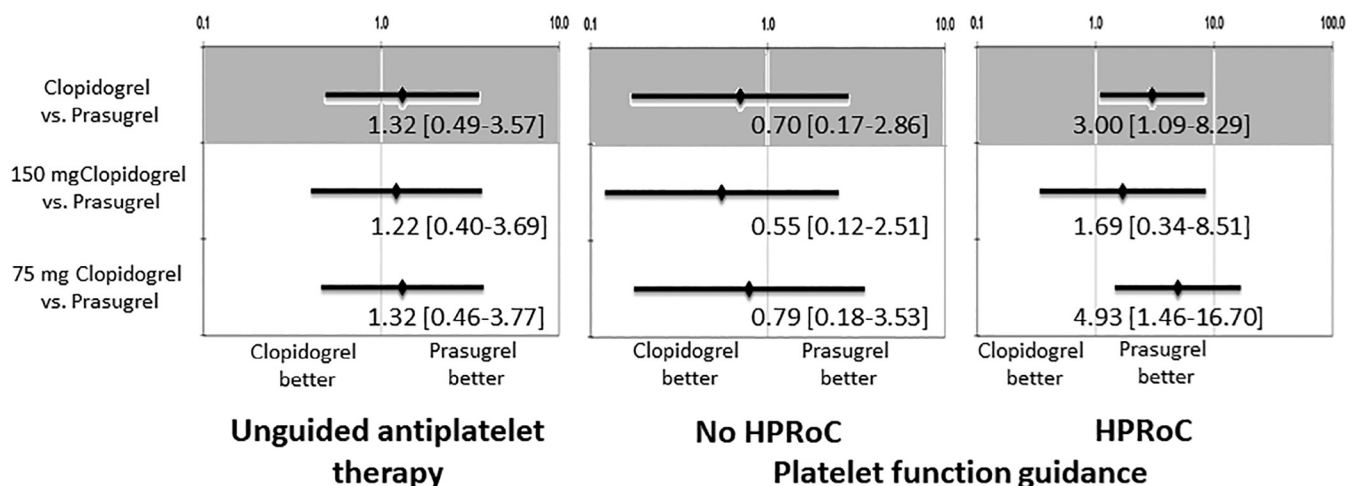


Figure 5. Subgroup analyses within the propensity-matched cohort according to platelet function test results. Forest plots depict HR and 95% CI of 1-year mortality according to the used P2Y₁₂ blocker. P_{interaction} = 0.63.

Table 3

Clinical, procedural, and pharmacological predictors of all-cause death at one year

Variable	Univariate Cox proportional hazard model	p-value	Multivariate Cox proportional hazard model	p-value
	Hazard Ratio [95% Confidence Interval]		Hazard Ratio [95% Confidence Interval]	
History of peripheral artery disease	2.79 [2.01–3.88]	<0.001	2.97 [2.11–4.18]	0.001
Smoker	1.59 [1.17–2.17]	0.003	1.74 [1.27–2.38]	0.001
Age (per 10 yrs increase)	1.56 [1.34–1.82]	<0.001	1.62 [1.38–1.90]	<0.001
Heart rate (per 10/min increase)	1.26 [1.18–1.34]	<0.001	1.25 [1.17–1.33]	<0.001
Systolic blood pressure (per 10 Hgmm increase)	0.85 [0.80–0.90]	<0.001	0.83 [0.78–0.88]	<0.001
Platelet function test guidance	0.57 [0.43–0.77]	<0.001	0.52 [0.39–0.69]	<0.001
Hypertension	1.24 [0.93–1.66]	0.149	1.56 [1.14–2.10]	0.005
Diabetes	1.57 [1.18–2.08]	0.002	1.55 [1.11–2.03]	0.005
Culprit artery: left main coronary	3.01 [1.80–5.02]	<0.001	2.01 [1.18–3.39]	<0.009
Diastolic blood pressure (per 10 mm Hg increase)	0.98 [0.93–1.03]	0.422	0.94 [0.88–1.00]	0.036
Male gender	0.92 [0.67–1.22]	0.545		
Hyperlipidaemia	0.83 [0.39–1.76]	0.626		
Prior myocardial infarction	0.98 [0.72–1.35]	0.910		
Prior of coronary bypass operation	1.09 [0.27–4.39]	0.905		
ST segment elevation myocardial infarction	1.27 [0.96–1.68]	0.102		
Prasugrel treatment	0.65 [0.38–1.11]	0.116		

weight was shown. These, together with the higher-treatment costs, still limit the clinical uptake of newer P2Y₁₂-receptor inhibitors in the routine.^{3,15,16} Tailoring treatments based on biomarkers and genes is an emerging field in multiple areas of medicine. Studies of genetic testing may identify subjects with characteristics that may affect pharmacodynamic effects of clopidogrel, whereas theoretically, PFT could be useful in measuring the achieved platelet inhibition and guide the choice of the P2Y₁₂ inhibitor to reach an optimal range of platelet inhibition.^{17,18} Genetic polymorphisms targeted by the tests may affect clopidogrel absorption, metabolism that has minor or no influence on new-generation P2Y₁₂ blockers' effects. In contrast, PFT is more subject to methodologic difficulties but reflect an actual state of platelet inhibition.^{12,17–19} Importantly, 3 available randomized controlled trials failed to support the use of PFT to adjust treatment in patients undergoing coronary intervention.^{2,20–22} Consequently the 2017 ESC-focused update document on dual antiplatelet therapy in coronary artery disease does not recommend the routine PFT to adjust antiplatelet therapy before or after elective stenting.²

From 2011, Hungarian health insurer reimbursed prasugrel for acute coronary syndrome patients undergoing coronary intervention who had either diabetes or AMI, but only in cases when PFT verified the clopidogrel nonresponder status. The reimbursement is independent from the genetic characteristics. This regulation practically acts as a prasugrel prescribing policy due to the high costs of unreimbursed prasugrel for patients and resulted in a high frequency of PFT screening. Our data are in line with the results of the GRAVITAS trial as we did not detect a significant clinical difference between high-dose and standard-dose clopidogrel in case of HPRoC.²⁰ The ARCTIC study randomized patients to PFT-guided and unguided strategies, similar to our design. However, cases with ST segment elevation—similar to the GRAVITAS trial—were excluded. Importantly, interventions to overcome low responsiveness included complex pharmacologic strategies,

but switching over to prasugrel was rarely used (9%).²¹ In the ANTARCTIC acute coronary patients over 75 years received either 5 mg of prasugrel or PFT-guided therapy including 5 or 10 mg of prasugrel or 75 mg of clopidogrel according to the results of VerifyNow testing. Importantly, the ANTARCTIC study was mostly a step-down trial with 40% of the patients switched back to clopidogrel and only 4% scaled up to 10 mg of prasugrel.²² Similar to ANTARCTIC, the recently published TROPICAL ACS trial also used a PFT-guided de-escalation approach based on the Multiplate (Roche Diagnostics GmbH) assay. In the trial, patients with AMI were randomized to universal prasugrel treatment or PFT-guided early de-escalation from prasugrel to clopidogrel if no HPRoC was detected. The TROPICAL ACS study is the first to support that a PFT-guided strategy is equally safe and effective as the guideline-recommended strategy.²³ Our registry recruited a high-risk, routine AMI cohort with patients including 55% ST-segment elevation and 45% AMI without ST-segment elevation applying 70% switchover rate to prasugrel. In this high-risk registry cohort, we could analyze predictors of mortality, resulting in strong statistical associations.

Although in the trial leading to the approval of prasugrel previous exposure to clopidogrel was an exclusion criterion for study entry, we have increasing amount of data regarding switching between antiplatelets.^{3,13,24} In fact, switching occurs frequently in clinical practice for various reasons. Differences in pharmacology due to binding site, half-life, and speed of onset and offset of action differences may incite drug interactions. Studies have not raised any major concerns associated with the clopidogrel–prasugrel switch but consistently showed a decreased level of residual platelet reactivity.²⁴ The most relevant studies were the SWAP and the TRIPLET trials that included acute cases with results raising no concerns regarding prasugrel administration in clopidogrel-treated patients.^{25,26} The recently published ESC-focused update on dual antiplatelet therapy in coronary artery disease also provides switching algorithms in case of clinical need.²

Our data originate from a nationwide, multicenter screening system using uniform whole-blood impedance aggregometry that strengthens the results; however, there remain important limitations to acknowledge. First, we have no information on how the individual decisions based on patient characteristics and logistics were made. Indeed, patients in whom PFT was performed differed in several features from the unguided patients. Although the exclusion of cases with absolute and relative contraindications to prasugrel and PS matching balanced significant differences observed between the PFT-guided and unguided groups, other, potentially uncontrolled variables may also exist that potentially influenced the choice of treatment. Keeping this limitation in mind, the statistically robust difference ($p < 0.001$) in the propensity-matched cohorts confirms the validity of the results. Second, we collected information regarding the clinical events using a payer's database that may not have been used as standardized definitions for a bleeding event, stent thrombosis, and myocardial infarction as usual in clinical trials. Furthermore, because ticagrelor was not available at the time of the study, it may restrict its generalizability. Third, in our prospective database we lack reliable information regarding the drug-compliance and later changes on medications, and we confined our analyses to intention-to-treat groups based on the discharge summaries of the index events.

Conclusions

Based on the results from an all-comer, high-risk cohort of a nationwide registry of AMI patients, cases with PFT-guided selection of P2Y₁₂-inhibitor therapy had lower mortality in contrast to lack of PFT guidance and clinical decision making. Although the PFT-guided group showed a higher frequency of switchover to prasugrel, allocation to prasugrel versus clopidogrel did not reduce mortality in the overall cohort. In contrast, prasugrel treatment significantly improved survival in patients with HPRoC compared with standard- and high-dose clopidogrel.

Disclosures

Dr. Komócsi reports nonfinancial support from Eli Lilly and Company during the conduct of the study and personal fees from Eli Lilly and Company, Bayer Pharma AG, Pfizer, Krka, d. d., Merck & Co., Inc., and Servier outside of the submitted work.

Dr. Aradi reports personal fees from Roche Diagnostics, DSI/Lilly, AstraZeneca Krka, Bayer, Pfizer, and MSD outside of the submitted work. The other authors report no conflicts of interest.

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