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FOCUS ON ACUTE CORONARY SYNDROMES

Observational Study of Platelet Reactivity in Patients Presenting With ST-Segment Elevation Myocardial Infarction Due to Coronary Stent Thrombosis Undergoing Primary Percutaneous Coronary Intervention

Results From the European PREvention of Stent Thrombosis by an Interdisciplinary Global European Effort Registry

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ABSTRACT

OBJECTIVES High platelet reactivity (HPR) was studied in patients presenting with ST-segment elevation myocardial infarction (STEMI) due to stent thrombosis (ST) undergoing immediate percutaneous coronary intervention (PCI).

BACKGROUND HPR on $P2Y_{12}$ inhibitors (HPR-ADP) is frequently observed in stable patients who have experienced ST. The HPR rates in patients presenting with ST for immediate PCI are unknown.

METHODS Consecutive patients presenting with definite ST were included in a multicenter ST registry. Platelet reactivity was measured before immediate PCI with the VerifyNow $P2Y_{12}$ or Aspirin assay.

RESULTS Platelet reactivity was measured in 129 ST patients presenting with STEMI undergoing immediate PCI. HPR-ADP was observed in 76% of the patients, and HPR on aspirin (HPR-AA) was observed in 13% of the patients. HPR rates were similar in patients who were on maintenance $P2Y_{12}$ inhibitor or aspirin since stent placement versus those without these medications. In addition, HPR-ADP was similar in patients loaded with a $P2Y_{12}$ inhibitor shortly before immediate PCI versus those who were not. In contrast, HPR-AA trended to be lower in patients loaded with aspirin as compared with those not loaded.

CONCLUSIONS Approximately 3 out of 4 ST patients with STEMI undergoing immediate PCI had HPR-ADP, and 13% had HPR-AA. Whether patients were on maintenance antiplatelet therapy while developing ST or loaded with $P2Y_{12}$ inhibitors shortly before undergoing immediate PCI had no influence on the HPR rates. This raises concerns that the majority of patients with ST have suboptimal platelet inhibition undergoing immediate PCI. (J Am Coll Cardiol Intv 2017;10:2548–56)

Prior studies have shown that patients with high platelet reactivity (HPR) on treatment with the $P2Y_{12}$ inhibitor clopidogrel after percutaneous coronary intervention (PCI) are at higher risk of death, myocardial infarction, and coronary stent thrombosis (ST) during follow-up (1). ST is a rare but severe complication of PCI. In a stable phase after ST, HPR on clopidogrel treatment has been reported in many patients (2,3); however, nothing is known about the platelet reactivity and HPR rates in patients presenting with ST undergoing immediate PCI.

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It can be hypothesized that the HPR rates in ST patients presenting with ST-segment elevation myocardial infarction (STEMI) might be similar as in patients with spontaneous STEMI, as around 80% of ST patients present with a myocardial infarction (4,5). In patients presenting with STEMI, it is known that 63% to 93% have HPR measured at the time of immediate PCI after loading with $P2Y_{12}$ inhibitors (clopidogrel, prasugrel, or ticagrelor) (6–9), and HPR after intravenously administration of aspirin in patients presenting with STEMI was observed in 6% of the patients (10). A clear difference however is that part of the ST patients are on antiplatelet therapy (APT) while developing ST, whereas spontaneous STEMI patients are not. We wonder therefore how maintenance APT while developing ST and loading with APT shortly before immediate PCI influence platelet reactivity and HPR rates in ST patients presenting with STEMI.

Therefore, the goal of this observational platelet function study of the PRESTIGE (PREvention of late Stent Thrombosis by an Interdisciplinary Global European effort) registry was to characterize platelet reactivity and HPR rates in ST patients presenting with STEMI undergoing immediate PCI. Platelet reactivity was also assessed 1 to 3 days after ST.

ABBREVIATIONS AND ACRONYMS

ADP = adenosine diphosphate

APT = antiplatelet therapy

ARU = aspirin reaction unit

HPR = high platelet reactivity

HPR-AA = high platelet reactivity on aspirin

HPR-ADP = high platelet reactivity on $P2Y_{12}$ inhibitors

PCI = percutaneous coronary intervention

ST = stent thrombosis

STEMI = ST-segment elevation myocardial infarction

METHODS

PATIENT POPULATION AND STUDY DESIGN. The PRESTIGE consortium was formed to investigate multiple aspects of ST including the degree of platelet inhibition measured with standard platelet function tests at several time points (11). The PRESTIGE

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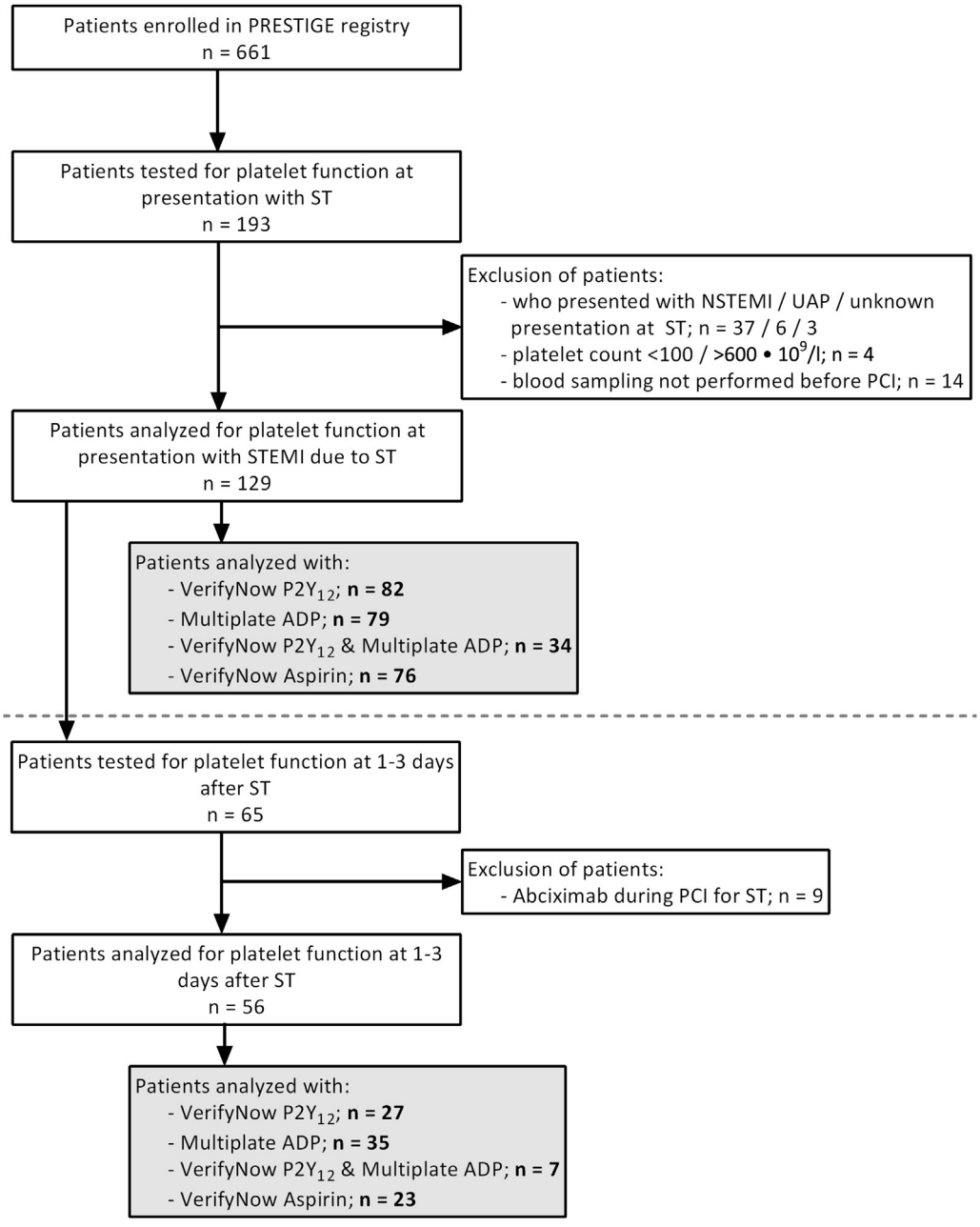
FIGURE 1 Flowchart of Patient Inclusion



Flowchart of patient inclusion displays the number of patients analyzed for platelet reactivity and with which platelet function test at presentation with ST, and 1 to 3 days after ST. ADP = adenosine diphosphate; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PRESTIGE = PREvention of late Stent Thrombosis by an Interdisciplinary Global European effort; ST = stent thrombosis; STEMI = ST-segment elevation myocardial infarction; UAP = unstable angina pectoris.

registry clinical work package registered consecutive study eligible patients presenting with definite ST. The timing of ST was defined as early ST, including acute (<24 h after stent implantation) and subacute ST (1 to 30 days), late ST (>30 to 365 days), and very late ST (>1 year) (12). Patients were prospectively included in the registry using a centralized telephone registration system. Data were collected according to a standardized protocol and were entered in a central electronic database (Open Clinica, Leuven

Coordinating Centre, Leuven, Belgium). Patient management and choice of APT were at the discretion of the treating physician. All patients provided written informed consent. The study was approved by the local ethical committees in each of the recruiting centers and was conducted according to the principles of the Declaration of Helsinki. Funding for the PRESTIGE registry was provided by the European Commission under the Seventh Framework Program (grant agreement no. 260309). The participating European centers are listed in the Online Appendix.

BLOOD SAMPLING AND PLATELET FUNCTION TESTS. Consecutive patients underwent platelet function testing in the centers equipped with the appropriate facilities. Blood samples were collected via the arterial sheet on presentation with ST in the catheterization laboratory immediately before the start of the PCI procedure after loading with APT, and at 1 to 3 days after ST via the antecubital vein. Blood samples were collected into 3.2% sodium citrate Vacuette tubes (Greiner Bio-one, Frickenhausen, Germany) for testing with the VerifyNow (Accriva Diagnostics, San Diego, California), and into hirudin blood tubes (Roche Diagnostics, Rotkreuz, Switzerland) for testing with the Multiplate analyzer (Roche Diagnostics). Both tests were performed according to manufacturer's instructions.

Platelet reactivity was measured using the assays available in each center; the VerifyNow $P2Y_{12}$, VerifyNow Aspirin, or Multiplate adenosine diphosphate (ADP) assay. HPR-ADP was defined as >208 $P2Y_{12}$ reaction units by the VerifyNow $P2Y_{12}$, and as >46 units (1 unit = 10 AU/min) by the Multiplate ADP assay. HPR on aspirin (HPR-AA) was defined as >550 aspirin reaction units (ARU) by the VerifyNow Aspirin assay. Platelet function test results that fell below these cutoff values were considered as indicative of no HPR. Patients with platelet counts of $<100 \times 10^9$/l or $>600 \times 10^9$/l were excluded from the analysis.

STATISTICAL ANALYSIS. Analyses were performed using IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, New York). Categorical data are expressed as frequencies (%) and continuous data as mean ± SD. Baseline characteristics are presented for patients with acute, subacute, late, or very late ST. Differences in platelet reactivity and HPR rates were analyzed using Fisher exact test for categorical data or Mann-Whitney *U* test for continuous data. Differences in platelet reactivity between assessment of the platelet inhibition at presentation with ST for immediate PCI and at 1 to 3 days after ST were analyzed using the Wilcoxon signed-rank test. All tests were 2-tailed and a p value <0.05 was considered statistically significant.

TABLE 1 Baseline Characteristics at the Time of Index PCI

	Acute ST (n = 10)	Subacute ST (n = 37)	Late ST (n = 10)	Very Late ST (n = 72)
Age, yrs	64 ± 10	68 ± 11	64 ± 11	57 ± 12
Sex (male)	6 (60.0)	30 (81.1)	8 (80.0)	60 (80.6)
Body mass index, kg/m^2	27.4 ± 5.5	27.7 ± 6.7	28.6 ± 10.1	27.6 ± 4.3
Cardiovascular risk factors				
Active smoker	3 (30.0)	6 (18.2)	2 (20.0)	26 (37.1)
Diabetes	4 (40.0)	13 (35.1)	4 (40.0)	10 (13.9)
Hypertension	3 (33.3)	22 (59.5)	5 (50.0)	33 (47.1)
Hypercholesterolemia	9 (90.0)	36 (97.3)	10 (100)	66 (93.0)
Prior myocardial infarction	1 (11.1)	5 (13.9)	2 (20.0)	25 (36.2)
Prior CABG	0 (0)	2 (5.4)	1 (10.0)	3 (4.2)
History of atrium fibrillation	0 (0)	6 (16.7)	0 (0)	3 (4.3)
Renal failure*	0 (0)	0 (0)	0 (0)	2 (2.8)
Malignancy	0 (0)	2 (5.6)	0 (0)	1 (1.4)
Peripheral artery diseases	1 (10)	4 (10.8)	2 (20.0)	2 (2.8)
Stroke	0 (0)	3 (8.1)	0 (0)	5 (6.9)
Thrombo-embolic events	0 (0)	3 (8.1)	1 (10.0)	6 (8.5)
Heart failure (LVEF < 30%)	0 (0)	2 (5.6)	0 (0)	2 (2.9)
Presentation for index PCI				
SAP	1 (11.1)	12 (33.3)	1 (10.0)	15 (21.4)
UAP	0 (0.0)	3 (8.3)	2 (20.0)	18 (25.7)
NSTEMI	0 (0.0)	9 (25.0)	1 (10.0)	15 (21.4)
STEMI	8 (88.9)	12 (33.3)	6 (60.0)	22 (31.4)
Target vessel for index PCI				
RCA	8 (80.0)	10 (27.8)	6 (66.7)	25 (37.9)
LAD	2 (20.0)	20 (55.6)	3 (33.3)	34 (51.5)
Cx	0 (0)	5 (13.9)	0 (0)	7 (10.6)
Left main	0 (0)	1 (2.8)	0 (0)	0 (0)
Stent type at index PCI				
BMS	3 (30.0)	12 (32.4)	2 (20.0)	23 (35.9)
DES	7 (70.0)	24 (64.9)	8 (80.0)	41 (64.1)
BRS	0 (0)	1 (2.7)	0 (0)	0 (0)

Values are n (%) or mean ± SD. *eGFR<30 ml/min/1.73m^2.

BMS = bare-metal stent(s); BRS = bioresorbable vascular scaffold; CABG = coronary artery bypass grafting; Cx = circumflex artery; DES = drug-eluting stent(s); eGFR = estimated glomerular filtration rate; LAD = left anterior descending coronary artery; LVEF = left ventricular ejection fraction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; SAP = stable angina pectoris; ST = stent thrombosis; STEMI = ST-segment elevation myocardial infarction; UAP = unstable angina pectoris.

RESULTS

STUDY POPULATION. In total, 661 patients with definite ST were enrolled in the PRESTIGE registry. Platelet function testing was performed in a total of 193 patients presenting with ST. Of these, 147 patients presented with STEMI. Eighteen patients were excluded from the analysis because of abnormal platelet counts or because blood sampling was not performed before PCI. Platelet reactivity was therefore measured in 129 patients, and in 65 of these patients the measurements were repeated at 1 to 3 days after ST. Of the latter, platelet function data were excluded from the analysis in 9 patients because of administration of the glycoprotein IIb or IIIa receptor antagonist abciximab during immediate PCI (Figure 1).

TABLE 2 Baseline Characteristics at the Time of Presentation With ST for Immediate PCI

	Acute ST (n = 10)	Subacute ST (n = 37)	Late ST (n = 10)	Very Late ST (n = 72)
Age, yrs	64 ± 10	68 ± 11	64 ± 11	63 ± 12
Body mass index, kg/m^2	28.1 ± 5.2	28.0 ± 6.6	27.9 ± 8.3	27.2 ± 4.3
Active smoker	3 (30.0)	5 (14.3)	2 (20.0)	14 (19.7)
Being on maintenance APT				
Aspirin	5 (50.0)	32 (86.5)	9 (90.0)	63 (84.5)
Clopidogrel	3 (30.0)	22 (59.5)	3 (30.0)	5 (6.9)
Prasugrel	1 (10.0)	2 (5.4)	3 (30.0)	1 (1.4)
Ticagrelor	0 (0)	6 (16.2)	1 (10.0)	0 (0)
Loaded with APT				
Aspirin	7 (70.0)	14 (38.9)	6 (60.0)	60 (84.5)
Clopidogrel	4 (40.0)	7 (19.4)	4 (40.0)	28 (38.9)
Prasugrel	0 (0)	12 (33.3)	2 (20.0)	26 (36.1)
Ticagrelor	2 (20.0)	4 (11.1)	2 (20.0)	13 (18.1)
Hemoglobin (mmol/L)	8.7 ± 1.2	8.0 ± 1.0	8.2 ± 0.6	8.6 ± 1.1
Platelets (10^9/L)	233 ± 26	335 ± 111	290 ± 72	232 ± 54

Values are n (%) or mean ± SD.
APT = antiplatelet therapy; other abbreviations as in Table 1.

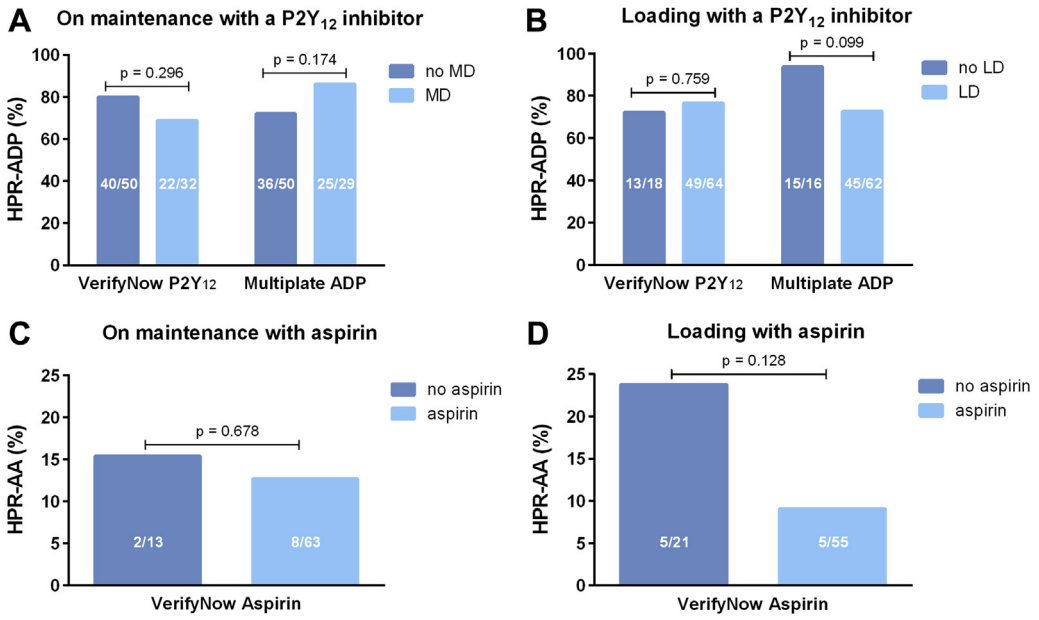
Of the unselected 129 patients with platelet function testing at presentation with ST, 10 patients presented with acute ST, 37 with subacute ST, 10 with late ST, and 72 with very late ST. Baseline characteristics at the time of index PCI (PCI of stent placement) are shown in Table 1. At presentation, 40% of the patients with acute, 81% with subacute, 70% with late, and 8% with very late ST were on maintenance therapy with a $P2Y_{12}$ inhibitor while developing ST. Sixty percent of the patients with acute, 65% with subacute, 90% with late, and 97% with very late ST were loaded with a $P2Y_{12}$ inhibitor shortly before immediate PCI (Table 2).

Baseline characteristics of ST patients presenting with STEMI with and without platelet function testing were comparable, except that patients with platelet function testing received a loading dose of clopidogrel at presentation for immediate PCI more often than patients without platelet function testing (33.6 vs. 24.7%; p = 0.050) (Online Tables 1 **and** 2), which is probably due to the observational character of the study.

At presentation, HPR-ADP was observed in 62 of 82 (75.6%) patients and in 61 of 79 (77.2%) patients measured with VerifyNow $P2Y_{12}$ and Multiplate ADP, respectively. HPR-AA was observed in 10 of 76 (13.2%) patients measured with VerifyNow Aspirin.

HPR IN PATIENTS ON MAINTENANCE APT AT PRESENTATION WITH ST. At presentation with ST for immediate PCI, 32 of 82 patients and 29 of 79 patients measured with VerifyNow $P2Y_{12}$ and Multiplate ADP, respectively, were on maintenance therapy with a

FIGURE 2 High Platelet Reactivity Rates in Patients on Maintenance or Loaded With APT at Presentation With ST for Immediate PCI



High platelet reactivity rates are displayed for on maintenance or loaded with $P2Y_{12}$ inhibitors or not, measured with VerifyNow $P2Y_{12}$ or Multiplate ADP **(A, B)**, and for on maintenance or loaded with aspirin measured with VerifyNow Aspirin **(C, D)**. APT = antiplatelet therapy; HPR = high on-treatment platelet reactivity; HPR-AA = high platelet reactivity on aspirin; HPR-ADP = high platelet reactivity on $P2Y_{12}$ inhibitors; LD = loading dose; MD = maintenance dose.

$P2Y_{12}$ inhibitor, and 63 of 76 patients were on maintenance aspirin. HPR-ADP rates were no different in patients who were on maintenance therapy with a $P2Y_{12}$ inhibitor while developing ST than in those without this therapy (Figure 2A). The number of patients was too low to differentiate between maintenance therapies with the different $P2Y_{12}$ inhibitors. HPR-AA was also similar in patients who were on aspirin at presentation with ST compared with those who were not (Figure 2C). The majority of the patients who were not on maintenance therapy with a $P2Y_{12}$ inhibitor presented with very late ST (80%).

HPR IN PATIENTS LOADED WITH APT AT PRESENTATION WITH ST. At presentation with ST for immediate PCI, 64 of 82 patients and 62 of 79 patients measured with VerifyNow $P2Y_{12}$ and Multiplate ADP, respectively, were loaded with a $P2Y_{12}$ inhibitor shortly before immediate PCI and blood sampling, and 55 of 76 patients were loaded with aspirin. The HPR-ADP rates were similar in patients loaded with a $P2Y_{12}$ inhibitor shortly before undergoing immediate PCI for ST versus to those not loaded (Figure 2B). No differences in HPR-ADP rates were observed in patients loaded with the different $P2Y_{12}$ inhibitors. The HPR-AA rate was nonsignificantly lower in patients loaded with aspirin (Figure 2D). The actual platelet reactivity levels of patients loaded with aspirin were lower than in those who were not (loaded vs. not loaded: 442 ± 66 ARU vs. 498 ± 108 ARU; p = 0.006).

The mean time between loading of APT and blood sampling was 94 ± 123 min (n = 65) when loaded with a $P2Y_{12}$ inhibitor, and 128 ± 146 min (n = 48) when loaded with aspirin. The loading time when loaded with $P2Y_{12}$ inhibitors was significantly shorter in patients with HPR-ADP than in patients without HPR-ADP (Table 3).

HPR IN PATIENTS 1 TO 3 DAYS AFTER ST. Platelet reactivity was measured in 56 patients at a mean of 1.3 ± 0.7 days after ST. In the subset of patients measured at both time points HPR-ADP decreased from 66.7% to 7.4% when measured with VerifyNow $P2Y_{12}$ (n = 27), and from 77.1% to 8.6% when measured with Multiplate ADP (n = 35). HPR-AA decreased from 26.1% to 8.7% (n = 23). Changes in platelet reactivity for patients treated with clopidogrel (38%), prasugrel (41%), or ticagrelor (20%), and aspirin (98%) at 1 to 3 days after ST are presented in Figure 3.

TABLE 3 Time Between Loading With Antiplatelet Therapy and Blood Sampling

Platelet Function Assay	HPR	No HPR	p Value
VerifyNow $P2Y_{12}$	55 ± 48 (n = 30)	127 ± 173 (n = 14)	0.059
Multiplate ADP	89 ± 120 (n = 33)	200 ± 209 (n = 8)	0.026
VerifyNow Aspirin	110 ± 45 (n = 4)	108 ± 134 (n = 35)	0.31

Time is given in minutes, and displayed as mean ± SD.
HPR = high platelet reactivity.

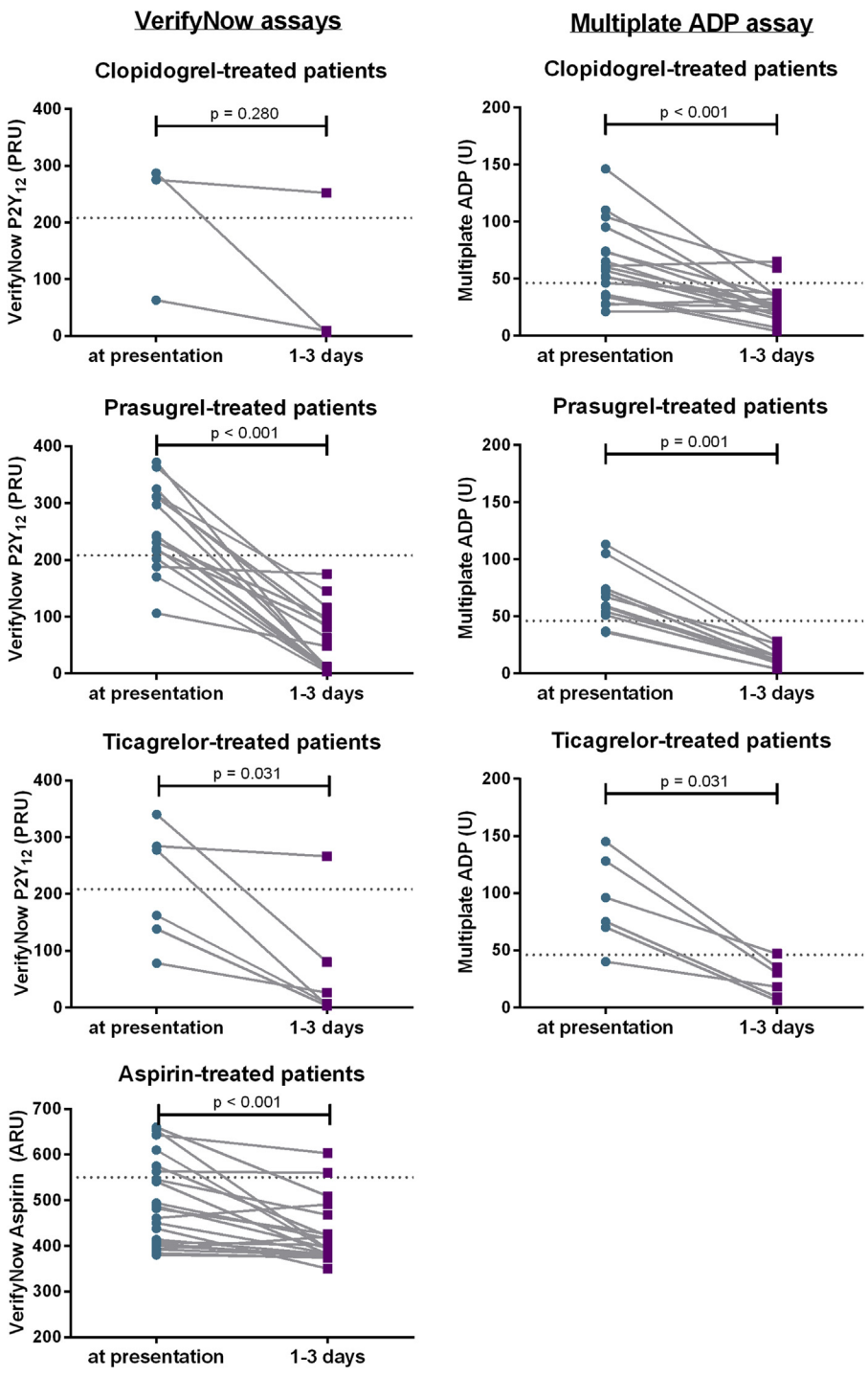
DISCUSSION

The PRESTIGE consortium recruited a large and unique registry of patients with definite ST enabling for the first time assessment of platelet reactivity in ST patients presenting with STEMI undergoing immediate PCI. These patients were also assessed for platelet reactivity 1 to 3 days after ST. The main findings of this registry are the following: 1) HPR-ADP was observed in 76% and HPR-AA in 13% of the patients undergoing immediate PCI for ST; 2) maintenance APT at presentation with ST did not influence the HPR-ADP and HPR-AA rates; 3) similarly, loading with a $P2Y_{12}$ inhibitor at presentation with ST did not influence the HPR-ADP rates; however, loading with aspirin did decrease platelet reactivity; and 4) HPR-ADP and HPR-AA rates were markedly lower 1 to 3 days after ST.

Thus HPR-ADP was observed in ~76% of the ST patients undergoing immediate PCI, which is comparable to the 63% to 93% HPR-ADP rate in patients presenting with spontaneous STEMI (6–9), who are the closest comparison to ST patients presenting with STEMI. Also, the ranges of HPR-ADP rate in ST patients with or without maintenance APT (69% to 86%) or loaded or not with APT (73% to 94%) are comparable with the HPR rate in patients presenting with spontaneous STEMI, although patients presenting with spontaneous STEMI are less often on maintenance APT than patients presenting with ST. The HPR-AA rate of 13% in this registry is somewhat higher than the HPR-AA rate of 6% (measured with light transmission aggregometry) observed in patients presenting with STEMI and intravenous administration of aspirin (10). This difference might be explained by the fact that not all patients in our registry were loaded with intravenous aspirin.

An interesting finding of our registry is that HPR-ADP rates at presentation with ST for immediate PCI were no different in patients with or without maintenance therapy with a $P2Y_{12}$ inhibitor, suggesting that the antiplatelet effects of this maintenance therapy are, to a large extent, overcome by the occurrence of ST. Possible mechanisms may be an increased level of immature platelets or increased platelet turnover immediately before ST occurs, as has previously been suggested for patients presenting with spontaneous STEMI where an increased level of reticulated platelets and higher platelet turnover were associated with an insufficient response to APT (13–17). The included ST patients for these analyses presented with STEMI, which lends support for these presumed mechanisms. Likewise, maintenance

FIGURE 3 Platelet Reactivity at Presentation With ST for Immediate PCI and 1 to 3 Days After ST



Subset of patients treated with antiplatelet therapy at 1 to 3 days after ST who had platelet reactivity also measured at presentation with ST for immediate PCI. Platelet reactivity was measured with VerifyNow $P2Y_{12}$ or Multiplate ADP assays for clopidogrel-, prasugrel-, or ticagrelor-treated patients, and with VerifyNow Aspirin for aspirin-treated patients. **Horizontal lines** display the cutoff value for HPR of the used platelet function assay. ARU = aspirin reaction units; PRU = $P2Y_{12}$ reactions units; U = units; other abbreviations as in Figure 1.

therapy with aspirin did not lower the HPR-AA rate in patients presenting with ST.

Loading with aspirin did lower platelet reactivity in patients presenting with ST, and the HPR-AA rate seemed lower. In daily practice, aspirin is administrated intravenously in STEMI patients and can directly inhibit circulating platelets, including released reticulated platelets. The intravenous administration of aspirin might explain the low HPR-AA rates in patients presenting with ST compared with the high HPR-ADP rates. $P2Y_{12}$ inhibitors are orally administrated, also in acute settings, which results in a delayed onset of action of these drugs due to the slower rate of gastrointestinal uptake and to hemodynamic changes during STEMI (18,19). This may be exacerbated by the use of morphine, which lowers gastrointestinal uptake and is associated with higher platelet reactivity compared with patients without morphine administration (20,21). In addition, clopidogrel and prasugrel need conversion to the active metabolite before platelet reactivity can be inhibited. These mechanisms probably largely explain the absence of differences in HPR-ADP rates in patients who did or did not receive a loading dose. However, because platelet response to $P2Y_{12}$ inhibitors is a time-dependent phenomenon, and the timing of loading with $P2Y_{12}$ inhibitors was not standardized in this registry, this observation should be interpreted with caution. An effect of this time-dependent phenomenon was observed in ST patients, where patients with a longer time interval between loading with a $P2Y_{12}$ inhibitor and measurement were less likely to exhibit HPR-ADP.

HPR on clopidogrel in a stable phase is often seen in patients with a history of ST (2,3). HPR rates on maintenance APT could therefore have contributed to developing ST in this registry. However, the HPR rates we observed are too high to account as sole cause for ST (HPR-ADP at presentation vs. at 1 to 3 days follow-up: ~70% vs. ~8%). Thus we observed that platelet reactivity is not adequately inhibited in patients on maintenance APT and we consider it of great importance that these patients should receive a loading dose of APT. HPR rates fell in the majority of the patients 1 to 3 days after ST, suggesting that loading might have contributed to the observed decrease in platelet reactivity. Also, the use of a direct-acting, strong, intravenous $P2Y_{12}$ inhibitor such as cangrelor, or glycoprotein IIb or IIIa antagonists might be beneficial (21-23), as these patients might be at risk for complications during or shortly after PCI (22-24).

STUDY LIMITATIONS. First, although the overall size of this registry of platelet function data is the largest at present, subgroup analysis was hindered by fragmentation into small numbers. This might explain the difference in HPR-AA rate at presentation with ST (13.2%) versus that in a subset of patients at presentation with ST who were also tested at 1 to 3 days (26.1%). Second, data on the time between loading of APT and blood sampling for platelet function testing were only available for one-half of the patients and were therefore less reliable to correlate to platelet reactivity levels. This might explain the absence of a difference in loading time between patients with or without HPR-AA whereas a difference was observed for patients loaded with $P2Y_{12}$ inhibitors. Third, the majority of recruiting centers used either the VerifyNow or the Multiplate ADP assay. While testing the same measure, these assays do not always provide the same level of sensitivity or specificity to detect HPR. Data for both platelet function tests were therefore presented separately. However, the concordance of HPR or no HPR between the VerifyNow $P2Y_{12}$ and Multiplate ADP assays was high (85%) in the 34 patients measured with both assays at the time of presentation with ST. Fourth, data were not available on the administrated route (intravenously or orally) for aspirin. Fifth, platelet function testing was described but not mandated in the PRESTIGE registry protocol, and platelet function testing was not feasible at all participating centers. Therefore, not every patient included in this registry was tested for platelet reactivity at presentation with ST, or at 1 to 3 days after ST. Nevertheless, even in the remaining small group of patients 1 to 3 days after ST, platelet reactivity levels 1 to 3 days after ST were clearly lower.

CONCLUSIONS

HPR-ADP was observed in a high proportion (approximately 76%) and HPR-AA in the minority (13%) of the ST patients presenting with STEMI undergoing immediate PCI. Whether patients were on maintenance APT whilst developing ST or loaded with $P2Y_{12}$ inhibitors shortly before undergoing immediate PCI had no influence on the HPR rates. This raises concerns that the majority of patients with ST have suboptimal platelet inhibition undergoing immediate PCI.

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PERSPECTIVES

WHAT IS KNOWN? It is known that approximately 80% of the patients presenting with spontaneous STEMI have HPR at presentation for immediate PCI. A difference with ST patients presenting with STEMI is that part of these patients are on maintenance APT since stent placement.

WHAT IS NEW? This study investigated for the first time the platelet reactivity in ST patients presenting with STEMI for immediate PCI, and showed that HPR rates were comparable in patients on maintenance APT or not, and similar in patients loaded with $P2Y_{12}$ inhibitors or not.

WHAT IS NEXT? Follow-up of patients treated with additional direct-acting, intravenous platelet inhibitor treatment during PCI could reveal whether this strategy will reduce the risk for (recurrent) thrombotic events.

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KEY WORDS aspirin, platelet aggregation, platelet function tests, $P2Y_{12}$ receptor antagonists, stent thrombosis

APPENDIX For an expanded Methods section, please see the online version of this paper.