Latest Clinical Data on Testing for High On-Treatment Platelet Reactivity

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Antiplatelet therapy is the cornerstone of treatment for patients with acute coronary syndromes and in those who are undergoing percutaneous coronary intervention (PCI). Clopidogrel, a second-generation thienopyridine antiplatelet agent, is currently used to prevent vascular complications in atherothrombotic patients, to prevent stent thrombosis in patients undergoing PCI, and in the long-term prevention of cardiovascular and cerebrovascular events. Unfortunately, despite treatment with clopidogrel, some patients continue to have cardiovascular events. This may be due in part to a suboptimal response to the drug, with minimal inhibition of platelet aggregation and/or high on-treatment platelet reactivity. Point-of-care testing of clopidogrel response, together with a reliable diagnostic cutoff, can identify patients with high on-treatment platelet reactivity and optimize their clinical management. This article reviews the impact of poor clopidogrel responsiveness on clinical outcomes, the major clinical studies using VerifyNow P2Y12 Assay® (Accumetrics, San Diego, CA) to assess on-clopidogrel platelet reactivity, and efforts to determine a reliable cutoff.

[Rev Cardiovasc Med. *2011;12(suppl 1):S14-S22 doi:10.3909/ricm12S1S0001*]

Key words: Clopidogrel • Platelet reactivity • VerifyNow

Antiplatelet therapy is the cornerstone of treatment for patients with acute coronary syndromes (ACS) and those who are undergoing percutaneous coronary intervention (PCI). Clopidogrel, a second-generation thienopyridine antiplatelet agent, is currently used worldwide to prevent vascular complications in atherothrombotic patients, to prevent stent thrombosis in patients undergoing PCI, and in the long-term prevention of cardiovascular and cerebrovascular events.

Clopidogrel is an inactive prodrug that requires oxidation by the hepatic cytochrome P-450 (CYP) system to generate an active metabolite able to inhibit platelet aggregation.[1] Unfortunately, despite treatment with clopidogrel, some patients continue to have cardiovascular events. This may be due to a suboptimal response to the drug, with minimal inhibition of platelet aggregation or high on-treatment platelet reactivity. Clopidogrel responsiveness should not be considered in a dichotomous way (resistant vs nonresistant), but as a continuous and mutable parameter. Using light transmission aggregometry, 4% to 30% of patients treated with clopidogrel do not have adequate antiplatelet response (according to the agonist and cutoff chosen).[2,3] Mechanisms responsible for poor response to clopidogrel are not fully elucidated, but poor compliance, under dosing, elevated platelet reactivity (commonly observed in specific clinical scenarios such as ACS, increased body mass index, and diabetes mellitus), and polymorphisms of *CYP2C19* and *ABCB1* are most frequently responsible (Table 1). In recognition of the clinical relapse of the problem, many efforts have been made to use such data in routine clinical practice, enhancing the tailoring of treatment.

Point-of-care testing of clopidogrel response, together with a reliable diagnostic cutoff, can identify patients with high on-treatment platelet reactivity (HTPR) and optimize their clinical management.

Table 1
Major Factors Influencing the Response to Clopidogrel

Major Relevance
Polymorphisms of *CYP2C19*
Polymorphisms of *ABCB1*
Poor compliance
Under-dosing
Elevated platelet basal reactivity
Diabetes mellitus
Acute coronary syndromes
Intermediate Relevance
Reduced *CYP3A* metabolic activity
Polymorphisms of $P2Y_{12}$
Polymorphisms of GP IIIa
Up-regulation of the $P2Y_{12}$ pathway
Up-regulation of P2Y-indipendent pathway (collagen, thromboxane A_2, thrombin)
Drug–drug interaction (atorvastatin or omeprazole)
Insufficient intestinal absorption
High body mass index
Congestive heart failure
Low Relevance
Polymorphisms of GP Ia
Up-regulation of the $P2Y_{12}$ pathway
Increased ADP exposure
Accelerated platelet turnover
Female sex

ADP, adenosine diphosphate; GP, glycoprotein.

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Available Assays to Test for High On-Treatment Platelet Reactivity

Light Transmission Aggregometry

Light transmission aggregometry (LTA) measures the increase in light transmission by crossing a platelet suspension that occurs when platelets aggregate in response to an agonist (generally adenosine diphosphate [ADP]). LTA is currently considered the gold standard, but it presents several limitations. In particular, this method requires a lengthy analysis time, dedicated staff, and an overestimation of the true incidence of the phenomenon of resistance; it also has variation in reproducibility, it is expensive, and it is necessary to manipulate the blood to obtain plasma or its derivatives required for the analysis. Therefore, it lacks reproducibility, which greatly limits its use in both clinical and multicenter clinical trial settings.

Vasodilator-Stimulated Phosphoprotein Phosphorylation Analysis

The vasodilator-stimulated phosphoprotein (VASP) index is an in vitro test that accurately detects biologic clopidogrel response. To assess the clopidogrel effect, blood samples are incubated in vitro with ADP and/or prostaglandin E_1 (PGE_1) before fixation.[4] This test gives a VASP index that corresponds to a ratio of the VASP phosphorylation of activated platelets versus resting platelets. This index, expressed as a mean percentage of platelet reactivity, is inversely correlated with clopidogrel efficiency, and strongly correlates with ADP LTA and a VASP index > 50%, which corresponds to a nearly 90% $P2Y_{12}$ receptor blockage. The principal drawbacks of this assay are that it requires a flow cytometer, skilled personnel, and blood manipulation to obtain plasma or derivates. Moreover, it is time-intensive and is relatively expensive.

Multiplate Analyzer

The Multiplate® analyzer (Dynabyte Informationssysteme GmbH, Munich, Germany) is a simple device based on multiple electrode platelet aggregometry (MEA), which works with the whole blood sample. The MEA implements the principle of impedance aggregometry with no need for blood centrifugation and has the ability to assess platelet function in approximately 10 minutes.[5] However, hand pipetting is still required, even if the process is fully automated. The MEA assessment on the Multiplate analyzer shows it is extremely useful in detecting the effect of clopidogrel treatment, and the results correlate well with LTA.[2] Platelet aggregation is continuously recorded for 5 minutes. Impedance with MEA is then transformed to arbitrary aggregation units (AU) that are plotted against time (AU · min). In contrast to LTA, in which aggregation occurs in a liquid phase, the aggregation in MEA takes place on surfaces. This is similar to in vivo conditions in which platelet aggregation also takes place on surfaces such as ruptured plaques, and at sites of vascular injury. MEA is capable of detecting the amount of platelet inhibition achieved by using different $P2Y_{12}$ antagonists, including clopidogrel, cangrelor, and the active metabolites of clopidogrel and prasugrel in varying doses.[6]

All these assays showed several limitations in their introduction to daily clinical practice. Advantages and drawbacks of all platelet function tests are summarized in Table 2. Currently, the only available test that works with whole blood samples and provides results in only a few minutes is the VerifyNow P2Y12 Assay® (Accumetrics, San Diego, CA).

The VerifyNow P2Y12 Assay

The VerifyNow P2Y12 Assay is a simple test that measures the agglutination of fibrinogen-coated beads by platelets stimulated by an agonist in citrated whole blood. This device measures the degree of inhibition mediated by clopidogrel on the $P2Y_{12}$ platelet receptor. The assay device consists of two whole blood assay channels; the first channel contains the platelet agonist ADP at a concentration equivalent to that observed with 5 µM in studies performed using platelet-rich plasma in an optical aggregometer, fibrinogen-coated polystyrene beads, and the PGE_1 to decrease the nonspecific contribution of $P2Y_{12}$ receptor. The second channel contains the thrombin receptor-activating peptides (protease-activated receptors 1 and 4 [PAR_1 and PAR_4]), which are able to activate all platelet aggregatory pathways. The beads in either channel will agglutinate in whole blood in direct proportion to the number of uninhibited platelets present. The clopidogrel metabolite inhibits aggregation in the ADP-containing channel, but not in the channel containing PAR_1 and PAR_4. In the two channels, aggregation is measured by the increase in light transmittance reported as $P2Y_{12}$ reaction units (PRUs). The thrombin receptor-activating peptide channel has been calibrated in the device so that the inhibition percentage of the $P2Y_{12}$ receptor is calculated by dividing the PRU value of the ADP channel by the PRU value of the thrombin receptor-activating peptide channel and converting this into a percentage.[2] The major advantages to using this point-of-care system is that it is simple and rapid, the results are immediate, dedicated staff is not required, it requires only a small whole blood sample, and it correlates with LTA. Even more important HTPR, this is the point-of-care device for which the most abundant and solid data linking on-clopidogrel platelet reactivity and outcomes have been generated.

Major Clinical Studies Using the VerifyNow P2Y12 Assay to Assess On-Treatment Platelet Reactivity

The identification of a reliable cutoff allows clinicians to distinguish patients with HTPR (ie, clopidogrel poor responders) from those with low on-treatment platelet reactivity (ie, clopidogrel responders). Several studies have been conducted to identify the cutoff with the best specificity and sensitivity.

The identification of a reliable cutoff allows clinicians to distinguish patients with high on-treatment platelet reactivity (ie, clopidogrel poor responders) from those with low on-treatment platelet reactivity (ie, clopidogrel responders).

Table 2
Principal Assays to Evaluate the Response to $P2Y_{12}$ Inhibitors

Assay	Advantages	Drawbacks
LTA	• Gold standard • Many studies	• Overestimates the incidence of resistance • Variable reproducibility • Time consuming • Requires blood manipulation to obtain plasma or derivatives • Expensive • Requires large sample volume
VASP Index	• Correlated with ADP-induced platelet aggregometry • Requires low sample volume • Test $P2Y_{12}$-dependent • High sensitivity	• Requires blood manipulation to obtain plasma or derivatives • Requires a flow cytometer • Requires skilled personnel • Expensive • Time consuming
Multiplate Analyzer[a]	• Good correlation with LTA • Uses whole blood sample • Aggregation occurs on surface (similar to in vivo conditions)	• Time consuming • Requires pipetting
VerifyNow P2Y12 Assay[b]	• Correlates with LTA • Does not require dedicated staff • Uses whole blood sample • Simple and rapid • Requires small sample volume • Fast analysis time	• Aggregation occurs in a liquid phase • Higher cost • Separate assays and cartridges for aspirin, clopidogrel, and GP IIb/IIIa inhibitors

ADP, adenosine diphosphate; GP, glycoprotein; LTA, light transmission aggregometry; VASP, vasodilator-stimulated phosphoprotein.
[a]The Multiplate® analyzer is manufactured by Dynabyte Informationssysteme GmbH (Munich, Germany).
[b]The VerifyNow P2Y12 Assay® is manufactured by Accumetrics (San Diego, CA).

The first clinical study in this direction was led by Price and colleagues.[7] The study was designed to determine if platelet reactivity during clopidogrel therapy, measured with the VerifyNow P2Y12 Assay, is associated with thrombotic events after PCI with a drug-eluting stent (DES). On-treatment platelet reactivity was measured in 380 patients undergoing PCI with DES. Clinical endpoints measured were cardiovascular death, nonfatal myocardial infarction (MI), and stent thrombosis. After discharge at 6 months, there were three cardiovascular deaths (0.8%) and one non–cardiovascular-related death. Nonfatal MI occurred in five patients (1.3%). There were six overall episodes of stent thrombosis (1.6%; of which 3 were subacute and 3 were late). Hence, the combined endpoint of cardiovascular death, nonfatal MI, or stent thrombosis occurred in 10 patients (2.6%). The receiver operating characteristic curve (ROC) analysis showed that post-treatment PRU values were able to distinguish between patients with and without subsequent adverse events. A PRU value ≥ 235 was identified as the cutoff that provides the maximum sum of the sensitivity and specificity to predict postdischarge 6-month outcomes, providing a sensitivity of 78% (95% confidence interval [CI], 46-94), specificity of 68% (95% CI, 67-69), and a negative predictive value of 99% (95% CI, 98-100).[7]

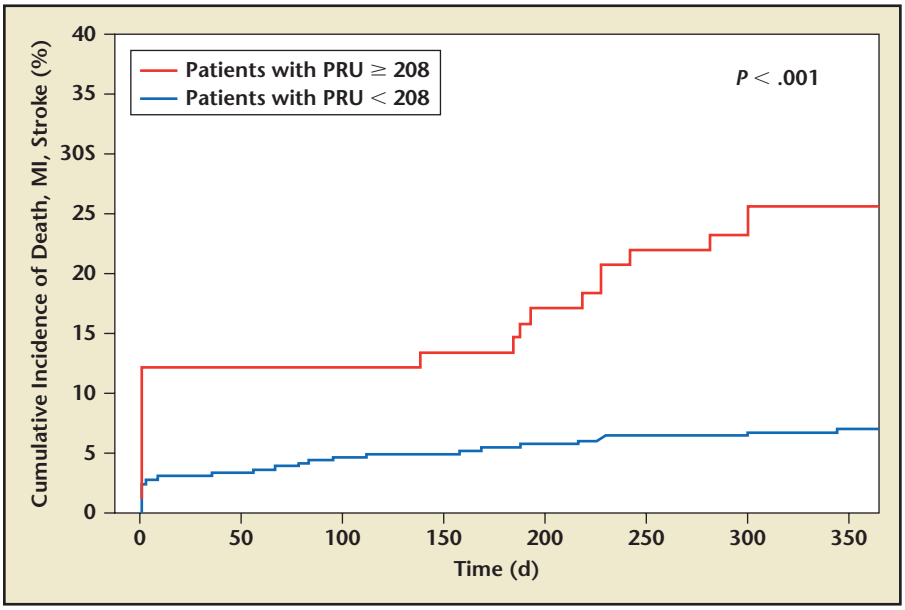
In the Antiplatelet therapy for Reduction of Myocardial Damage during Angioplasty-Platelet Reactivity Predicts Outcome (ARMYDA-PRO) study, Patti and associates[8] enrolled 160 patients receiving clopidogrel before PCI. The aim of the study was to evaluate the correlation of point-of-care measurement of PI with clinical outcomes in patients undergoing PCI. Platelet reactivity was measured by the VerifyNow P2Y12 Assay. Patients with a variety of coronary syndromes, including non–ST-elevation (NSTE) ACS were enrolled. The primary endpoint was 30-day occurrence of major adverse cardiac events (MACE) according to quartile distribution of PRU.

The study showed that mean PRU absolute levels were higher in patients with periprocedural MI (258 ± 53 vs 219 ± 69 in patients without; $P = .030$). In this study the ROC curve analysis showed that PRU levels significantly discriminate between patients with and without 30-day MACE with an area under the curve of 0.69 (95% CI, 0.56-0.81; $P = .016$). A PRU value ≥ 240 was identified as the optimal cutoff point to predict 30-day outcome, with sensitivity of 81% and specificity of 53%.[7]

Marcucci and colleagues[9] used the VerifyNow P2Y12 Assay to determine the on-treatment platelet reactivity in response to ADP in 683 patients with ACS undergoing dual antiplatelet therapy who underwent PCI with bare-metal or DES implantation. The best cutoff in predicting 12-month cardiovascular death or nonfatal MI was identified at PRU ≥ 240, providing a sensitivity of 61%, a specificity of 70%, a negative predictive value of 96%, and a positive predictive value of 12%.[9]

Campo and coworkers[10] studied the long-term outcome after elective PCI in low-risk patients screened for aspirin and/or clopidogrel responsiveness in the Tailoring Treatment With Tirofiban in Patients Showing Resistance to Aspirin and/or Resistance to Clopidogrel (3T/2R) study. The response to aspirin and clopidogrel were measured with VerifyNow P2Y12 Assay. After PCI, death, stroke, and MI were assessed up to 1 year. This study differs from the previous one, principally because of the study population enrolled. In the 3T/2R trial, only stable patients with a very low-risk profile and negative cardiac markers before procedure were enrolled. Unlike other studies, this group identified the optimal cutoff to predict 1-year composite endpoint as percentage of platelet inhibition ≤ 23 and a PRU value ≥ 208 (Figure 1).[10] The results of this study may therefore suggest that (for stable patients) the cutoff for platelet reactivity discriminating patients with cardiovascular events as compared with those without may be slightly lower than that in patients with a recent acute event.[11] The same group has recently provided corroborative data to their previous findings. They enrolled 300 consecutive patients, both stable and with ACS, who were treated with PCI and stent implantation. On-treatment platelet reactivity was measured at baseline (before PCI procedure, but at least 12 hours after 600-mg clopidogrel intake), and at 1 and 6 months thereafter.[12] The main finding was a significant reduction in on-treatment platelet reactivity from index hospitalization to 1 month. Consistently, the percentage of poor responders, based on 235 PRU values, decreased from 35% (at baseline) to 13% at 1 month. This is a key finding because it suggests that one single assessment of platelet reactivity at baseline may lead to an overestimation of the true proportion of individuals with on-treatment platelet reactivity at follow-up. To a lesser extent, this is due to the fact that clopidogrel has a slow onset of action, but more importantly because individual platelet reactivity decreases over time in the first weeks after intervention. This pattern is more pronounced in patients with ACS, but it is still detectable and significant in stable patients as well. Finally, on ROC analysis, the ability of on-treatment platelet reactivity to discriminate outcomes was significantly better when assessed at 1 month as compared with baseline measurement. This may be because baseline PRU values are influenced by several confounding factors, particularly acute atherothrombotic events and inflammation.[12] These factors progressively either reduce their influence or disappear; 1-month platelet function evaluation better described the patient's real response to

Figure 1. *Cumulative incidence of death, MI, and stroke in the 3T/2R population stratified according PRU value (above vs below 208). 3T/2R, Tailoring Treatment With Tirofiban in Patients Showing Resistance to Aspirin and/or Resistance to Clopidogrel; MI, myocardial infarction; PRU, $P2Y_{12}$ reaction unit.*



clopidogrel, allowing better discrimination between patients with chronic and persistent HTPR possibly leading to a higher risk of adverse events.

Campo and associates,[12] for the first time, reported the possibility of using PRU value to predict bleeding risk. In particular, a PRU value of < 85 at 1 month after PCI identifies patients who are highly likely to have a bleeding event in the next 11 months. Hence, a full therapeutic window for $P2Y_{12}$ inhibitors may be possible in the future, so that patients who require this medication can prevent subsequent ischemic events without the risk of bleeding. This concept needs to be validated prospectively by a well-designed and powered clinical study.

Patient Level Meta-Analysis to Establish a Common Cutoff

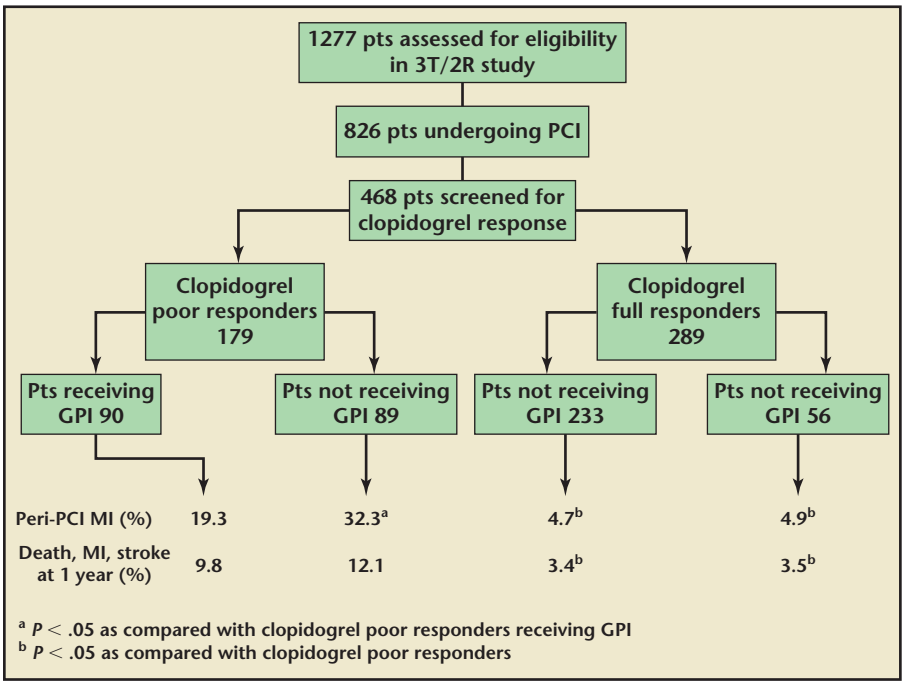
A recent patient-level meta-analysis of six major observational studies was recently conducted, with the goal of identifying a single cutoff point for platelet reactivity that is able to differentiate patients at higher risk for cardiovascular events. A total of 3059 patients were involved, including both stable patients and those with NSTE ACS undergoing PCI. In each study, clopidogrel responsiveness was assessed using the VerifyNow P2Y12 Assay. The primary endpoint of the study was the composite of death, MI, or stent thrombosis from the index PCI. The primary endpoint occurred more frequently in higher quartiles of PRU values: quartile I, 5.8%; quartile II, 6.9%; quartile III, 10.9%; quartile IV, 15.8% ($P < .001$), which was largely consistent across the single components of the primary endpoint. The event rate for the primary endpoint in the highest quartile of PRU values was significantly almost threefold greater as compared with the lowest quartile, 15.8% versus 5.8% (hazard ratio, 2.62; 95% CI, 1.77-3.87; $P < .001$). The ROC curve analysis revealed that a PRU value > 230 assessed at the time of PCI, best predicts death, MI, or stent thrombosis through 1 year ($P < .001$; sensitivity 55%, specificity 65%, positive predictive value 11%, and negative predictive value 95%).[13]

Tailoring Antiplatelet Therapy Based on Actual Platelet Reactivity Assessed Via the VerifyNow P2Y12 Assay

The 3T/2R Study

In the 3T/2R study, Valgimigli and colleagues[11] screened 1277 patients. The final population included 93 aspirin poor responders, 147 clopidogrel poor responders, and 23 dual poor responders, based on the VerifyNow P2Y12 Assay. All patients included in the study underwent elective PCI due to stable coronary disease or low-risk unstable angina (cardiac markers had to be consistently negative). Therefore, per protocol, the risk profile of the included population was low. According to current guidelines, the recommended antiplatelet therapy in these patients is aspirin and clopidogrel. In particular, the use of glycoprotein (GP) IIb/IIIa inhibitors during PCI is not the best choice and there is no evidence of benefit. In the study, patients were randomly assigned to receive tirofiban or placebo in addition to aspirin and clopidogrel. The primary endpoint was the occurrence of periprocedural MI. The primary endpoint was significantly lower in the group of patients receiving tirofiban (20.4% vs 35.1%). The rate of MACE within 30 days in the tirofiban-treated group also was reduced (3.8% vs 10.7%; $P = .031$). This trial showed that triple antiplatelet therapy, including a tailored infusion of tirofiban in patients who responded

Figure 2. *Study population and outcome in the 3T/2R study. 3T/2R, Tailoring Treatment With Tirofiban in Patients Showing Resistance to Aspirin and/or Resistance to Clopidogrel; GPI, glycoprotein inhibitors; MI, myocardial infarction; PCI, percutaneous coronary intervention; Pts, patients.*



poorly to aspirin, clopidogrel, or both, resulted in a > 40% reduction in the incidence of periprocedural MI compared with standard care and resulted in a lower rate of MACE at 30 days without an increased incidence of bleeding.[11] Figure 2 depicts the peri-PCI and the 1-year outcomes of all screened patients.

The rate of periprocedural myocardial infarction was extremely low in aspirin and clopidogrel good responders and, interestingly, it was not affected by the addition of tirofiban, which strongly reinforces the concept that the benefit of adding a third intravenous antiplatelet agent is restricted to patients with high on-treatment platelet reactivity.

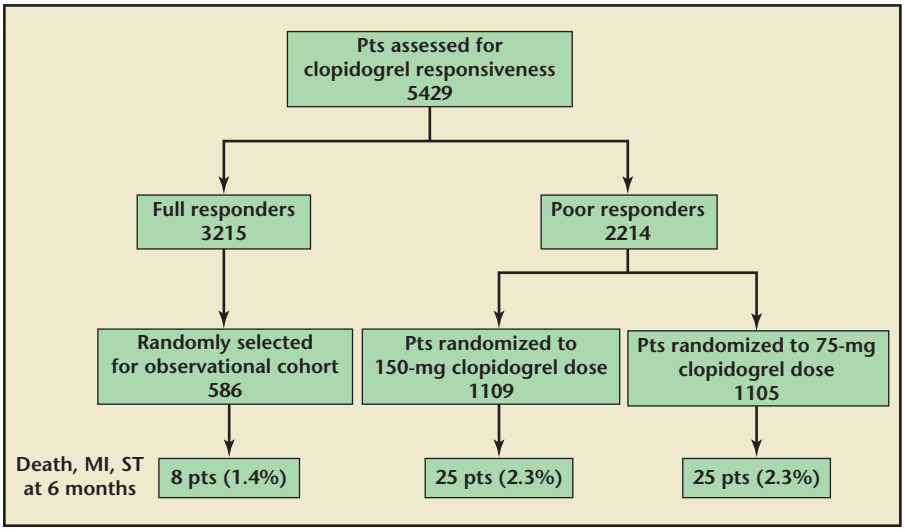
The rate of periprocedural MI was extremely low in aspirin and clopidogrel good responders; interestingly, it was not affected by the addition of tirofiban, which strongly reinforces the concept that the benefit of adding a third intravenous antiplatelet agent is restricted to patients with HTPR. Based on these findings, our group has adopted a systematic policy of assessing on-treatment platelet reactivity in elective PCI candidates and adding a GP IIb/IIIa inhibitor selectively in patients with HTPR, as assessed via the VerifyNow P2Y12 Assay.

Standard Versus High-Dose Clopidogrel Based on Platelet Function Testing After PCI Trial

In the more recent Gauging Responsiveness With a VerifyNow Assay–Impact on Thrombosis and Safety (GRAVITAS) trial, Price and coworkers[14] assessed PR in 5429 people using the VerifyNow P2Y12 Assay. The primary endpoint was the 6-month incidence of death from cardiovascular causes, nonfatal MI, or stent thrombosis. Patients were eligible to be enrolled if they received PCI with 1 or more DES for the treatment of stable and unstable coronary artery disease (including STEMI). Cutoff was a PRU value ≥ 230. In all, 2214 patients (40.8%) had HTPR and were randomly assigned to either high-dose (150 mg/d) or standard-dose (75 mg/d) clopidogrel. At 6 months, the primary endpoint occurred in 25 of 1109 patients (2.3%) receiving high-dose clopidogrel compared with 25 of 1105 patients (2.3%) receiving standard-dose clopidogrel (Figure 3). Severe or moderate bleeding was not increased with the high-dose regimen. Intracranial hemorrhage occurred in none of the patients with HTPR randomly assigned to high-dose clopidogrel, in two patients (0.2%) with HTPR randomly assigned to standard-dose clopidogrel, and in one patient (0.2%) without HTPR treated with standard-dose clopidogrel. This study failed to show any difference in 6-month outcomes in patients treated with high-dose compared with standard-dose clopidogrel. It is interesting to note that HTPR measured 12 to 24 hours after PCI resolved at the 30-day follow-up in 38% of the patients randomly assigned to standard-dose clopidogrel. A possible explanation for this decrease in reactivity in the post-PCI period may be that early HTPR is a manifestation of post-stenting platelet activation in a subset of patients.[15] These results are highly consistent with the findings of Campo and associates,[12] discussed earlier, showing a decrease in platelet reactivity from baseline to 2-month follow-up. The null finding in this study has several potential explanations.

The low event rate of 2.3% in both groups, which is much lower than what was anticipated by the investigators, led to a reduced power of the study to identify statistically significant differences for the composite primary endpoints of death, MI, or stent thrombosis. As stated above, many patients have been labeled as

Figure 3. *Study population and outcome in the Gauging Responsiveness With a VerifyNow Assay-Impact on Thrombosis and Safety (GRAVITAS) study. MI, myocardial infarction; Pts, patients; ST, stent thrombosis.*



having HTPR and subsequently randomized into the study, which has contributed to further reduce the impact of the study.

Finally, the choice to double the dose of clopidogrel may have not been effective in many patients with true HTPR. Several studies showed that a double dose of clopidogrel is not sufficient to overcome clopidogrel poor response.[16,17] It may be speculated that a tailored treatment with prasugrel or ticagrelor, both more effective and powerful than 150 mg of clopidogrel, may have at least partially changed the study results.

The null finding of the GRAVITAS study cannot be considered as good evidence for the lack of benefit in tailoring antiplatelet therapy based on phenotype assessment. A properly powered study in a high-risk patient population using a more contemporary $P2Y_{12}$ oral receptor blocker is warranted. Finally, multiple platelet reactivity assessments before and after customized therapy to ensure that true HTPR patients have been selected and that platelet reactivity is correctly overcome by means of the new customized therapy would be highly desirable in such a study.

Conclusions

There is abundant evidence supporting a role for platelet reactivity testing in clinical practice to risk stratify the cardiovascular outcomes of patients who undergo PCI. Most of the evidence has been generated utilizing the VerifyNow P2Y12 Assay, for which clear and consistent cutoffs for PRU have been identified for ischemic and—more recently—bleeding complications. What still needs to be completely elucidated is whether a different patient population (ie, stable vs unstable presentations) may have a differential platelet reactivity cutoff value able to best predict outcomes. Alternatively, the slight inconsistencies in the cutoffs identified so far may simply reflect a chance finding.

Personalized medicine, in which therapy is based on a selection of multiple agents and dosages after careful phenotype and genotype assessments, appears to be a powerful approach to optimizing patient care. As with all novel strategies for patient care, the safety and efficacy of this approach must continually be tested and evaluated by ongoing clinical studies. ■

Drs. Fileti and Campo report no real or apparent conflicts of interest. Dr. Valgimigli has received honoraria for advisory board, lectures, and research grants from Merck & Co., Iroko Cardio International, Eli Lilly & Co., and Medtronic Inc.; honoraria for advisory board and lectures from The Medicines Company, Eli Lilly & Co., Daiichi Sankyo Inc., St. Jude Medical Inc., and Abbott Vascular; and honoraria for lectures from Cordis Corp., CID, Accumetrics Inc., and Terumo Medical Corp.

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Main Points

- Antiplatelet therapy is the cornerstone of treatment for patients with acute coronary syndromes and in those who are undergoing percutaneous coronary interventions (PCI).
- Point-of-care platelet function testing, together with a reliable diagnostic cutoff, can identify patients with high on-treatment platelet reactivity and optimize their clinical management.
- The use of the VerifyNow P2Y12 Assay has many advantages, including simplicity and rapidity; the results are immediate, dedicated staff is not required, it uses a small whole blood sample, and correlates with light transmission aggregometry.
- Based on the results from the largest meta-analysis a $P2Y_{12}$ reaction unit value > 230, assessed at the time of PCI, best predicts death, myocardial infarction, or stent thrombosis through 1 year.

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