High Versus Standard Clopidogrel Maintenance Dose After Percutaneous Coronary Intervention and Effects on Platelet Inhibition, Endothelial Function, and Inflammation

Results of the ARMYDA-150 mg (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty) Randomized Study

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Objectives

This study was done to compare effects of high versus standard clopidogrel maintenance doses on platelet inhibition, inflammation, and endothelial function in patients undergoing percutaneous coronary intervention.

Background

Previous data suggested that clopidogrel has various biological actions in addition to antiplatelet effects.

Methods

Fifty patients were randomly assigned 1 month after intervention (T-0) to receive standard (75 mg/day; n = 25) or high (150 mg/day; n = 25) clopidogrel maintenance dose for 30 days (until T-1); at this time-point, cross-over was performed, and the assigned clopidogrel maintenance regimen was switched and continued for a further 30 days (until T-2). Platelet reactivity (expressed as P2Y12 reaction units by the point-of-care VerifyNow assay [Accumetrics, San Diego, California]), endothelial function (evaluated by flow-mediated vasodilation), and highsensitivity C-reactive protein levels were measured at T-0, T-1, and T-2.

Results

Patients in the 150-mg/day arm had higher platelet inhibition (50 ± 20% vs. 31 ± 20% in the 75-mg/day group; p = 0.0001), better flow-mediated vasodilation (16.9 ± 12.6% vs. 7.9 ± 7.5%; p = 0.0001), and lower high-sensitivity C-reactive protein levels (3.6 ± 3.0 mg/l vs. 7.0 ± 8.6 mg/l; p = 0.016). Higher clopidogrel dose was associated with decreased proportion of patients with P2Y12 reaction units ≥240 (12% vs. 32%; p = 0.001), flow-mediated vasodilation <7% (16% vs. 58%; p = 0.0003), and high-sensitivity C-reactive protein levels >3 mg/l (46% vs. 64%; p = 0.07).

Conclusions

For patients undergoing percutaneous coronary intervention, the 150-mg/day clopidogrel maintenance dose is associated with stronger platelet inhibition, improvement of endothelial function, and reduction of inflammation, compared with the currently recommended 75-mg/day regimen; those effects might have a role in the clinical benefit observed with clopidogrel and may provide the rationale for using the higher maintenance regimen in selected patients. (J Am Coll Cardiol 2011;57:771–8) © 2011 by the American College of Cardiology Foundation

A growing number of patients with coronary artery disease receive chronic therapy with clopidogrel; as recommended, patients with acute coronary syndromes (ACS) treated both medically or with percutaneous coronary intervention (PCI) receive 1 year of treatment with clopidogrel in addition to aspirin (1,2); moreover, dual antiplatelet therapy is usually performed for 1 month after bare-metal stent implantation and is extended for at least 12 months after drug-eluting stent implantation to prevent stent thrombosis (3).

Adequacy of platelet inhibition with chronic clopidogrel therapy is a contemporary issue in patients undergoing PCI, as interindividual variability in response to the drug has been reported (4), and a low response may predispose to future cardiac events (5–9). Indeed, in patients receiving the 75 mg/day clopidogrel maintenance dose, a further platelet inhibition is achieved at short-term by giving an additive 600-mg loading dose (10) and chronically by increasing the...
daily dose to 150 mg (11); retrospective data indicated that patients receiving the 600 mg clopidogrel loading plus 150 mg maintenance regimen after PCI may have a lower incidence of cardiac events at 2 months (12).

Previous studies suggest that clopidogrel has anti-inflammatory effects (13,14) and improves endothelial function (15), but no randomized study has addressed the issue of whether a higher clopidogrel maintenance dose exerts, in addition to stronger platelet inhibition, a more intense anti-inflammatory effect and is associated with improved endothelial function versus the standard regimen. Thus, this randomized, prospective study was designed to compare the effectiveness of 75 mg/day versus 150 mg/day clopidogrel maintenance doses on platelet function inhibition, inflammation, and endothelium-dependent vasodilation in patients undergoing PCI.

**Methods**

**Study population and design.** The ARMYDA-150 (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty) study is a prospective, randomized, single-center study with cross-over, performed on 50 consecutive patients receiving PCI and stent implantation for stable angina or non-ST-segment elevation ACS. Exclusion criteria were as follows: primary intervention for ST-segment elevation myocardial infarction; platelet count <70 × 10^9/L; active bleeding or bleeding diathesis; gastrointestinal bleeding <6 months; cerebrovascular accident <3 months; history of malignancy; concomitant need for oral anticoagulant therapy; and severe liver disease or chronic renal failure (serum creatinine >2 mg/dl). Active smokers were also excluded by protocol.

All patients received 600-mg clopidogrel load before PCI (16) and continued, after the procedure, the standard 75 mg/day clopidogrel maintenance dose for 1 month; at this study point (T-0), patients were randomly allocated to receive standard (1 75-mg tablet; n = 25) or high (150 mg, 2 75-mg tablets; n = 25) clopidogrel daily maintenance dose for 30 days (until T-1, i.e., 2 months after PCI) (Fig. 1). At this point, a cross-over was performed, and patients randomly allocated to the 75 mg daily dose were switched to the 150-mg daily dose and vice versa for an additional 30 days (until 3 months after the procedure, T-2). All patients were maintained on aspirin (100 mg/day). To avoid potential interference of concomitant drugs with antiplatelet effect of clopidogrel, during the study period, all patients received an hydrophilic statin (pravastatin) (17) and were

**Figure 1** The ARMYDA-150 Study Design

[Diagram showing study design with flow of patients through different dosing regimens.]
free of proton-pump inhibitors (18). (For patients with indication for gastric protection, ranitidine was used.) Patients who underwent PCI for ACS or received drug-eluting stents continued standard clopidogrel (75 mg/day) for 1 year after study completion.

To assign patients to standard or high clopidogrel maintenance dose, a computer-based randomization system was obtained by a statistician not involved in the study; randomization assignment for each patient was kept in a sealed envelope, which was opened by a trial investigator at the study point T-0.

By protocol, at each time point (T-0, T-1, and T-2) all patients underwent measurement of residual platelet reactivity, noninvasive evaluation of endothelial function, and testing for high-sensitivity C-reactive protein (hsCRP) level detection; investigators performing all those measurements were not aware of the randomization assignment.

Platelet reactivity detection. Platelet reactivity was evaluated by the VerifyNow P2Y12 assay (Accumetrics, San Diego, California), which is a point-of-care assay specifically measuring direct inhibition of clopidogrel on the platelet P2Y12 receptor. Technical details of the assay were previously described (19). The VerifyNow reports 2 measures for each assay: 1) P2Y12 reaction units (PRU), which reflect the extent of adenosine diphosphate-mediated aggregation specific to the P2Y12 receptor and are based on the amount of platelet aggregation in the adenosine diphosphate channel (the lower the PRU value, the greater the amount of platelet aggregation in the thrombin receptor-activating peptide). Previous studies (5,20,21) identified, in patients receiving clopidogrel, a PRU value $\geq 240$ as the optimal cut-off point to predict 30-day outcome after PCI; in particular, patients with impaired clopidogrel response, namely, with PRU above this threshold, had a 6-fold higher risk of adverse cardiac events (5).

Measurement of brachial artery reactivity and hsCRP levels. Noninvasive evaluation of endothelial function was performed by ultrasound detection of brachial artery diameter variations during hyperemia. All vasoactive agents were discontinued at least 48 h before this measurement. Since circadian variations of peripheral vascular tone occur (22), assessment of brachial artery vasomotion was done between 9:00 AM and 9:30 AM in a quiet, temperature-controlled room (22°C to 24°C). Ultrasound evaluation was obtained on the dominant forearm with the patient supine. Patients were kept fasting and at rest for 5 min before, and beverages containing alcohol or caffeine were prohibited within the preceding 12 h. Two-dimensional brachial artery imaging and measurements were performed in all patients by the same operator, with a 7.5 MHz linear array transducer connected to a Hewlett Packard ultrasound machine (Sonos 5500, Andover, Massachusetts); straight segments of the artery, 8 to 10 mm in length, were identified above the antecubital fossa, perpendicular to the ultrasound beam and along its long axis. Flow-mediated dilation (FMD) due to shear-induced endothelial nitric oxide release was evaluated after occlusion of the forearm circulation: 1) a longitudinal image was selected to calculate brachial artery diameter (first baseline value); 2) a blood pressure cuff was inflated on the upper arm to 50 mm Hg above the systolic pressure for 5 min and then deflated; and 3) after 1 min, a second longitudinal scan was obtained, and brachial artery diameter was measured (post-occlusion value). The FMD was expressed as percent diameter variation (absolute diameter changes were also recorded). After 15 min of rest, a new detection of brachial artery diameter was done (second baseline value) and repeated 3 min after administration of 0.5 mg sublingual nitroglycerin (post-nitrates value). Endothelium-independent dilation (nitroglycerin-mediated dilation [NMD]), due to direct effect of nitroglycerin-derived nitric oxide, was then obtained and expressed as percent diameter variation. All brachial artery diameters were measured from near-to-far blood-wall interface (intima-media interfaces); measurements were performed at end-diastole in the cardiac cycle (onset of the R-wave), by electrocardiogram gating during image acquisition. Five cardiac cycles were analyzed and averaged for each scan. In a previous prospective study (23) performed by our study group on patients undergoing PCI with bare-metal stent implantation, an impaired endothelial function, identified by FMD $<7\%$, was associated with a 4.5-fold increased risk of in-stent restenosis during follow-up, whereas FMD $\geq 7\%$ had a negative predictive value of 96% for excluding restenosis.

The hsCRP was assayed by the KRYPTOR-ultrasensitive immunofluorescent assay (BRAHMS, Hennigsdorf/Berlin, Germany), with a detection limit of 0.06 mg/l; 90% of normal values for CRP is $<3$ mg/l, and consistent with previous recommendations from the Centers for Disease Control and Prevention, this cut-off point for CRP was used to differentiate patients at higher versus lower inflammatory status (24).

End points. Clinical follow-up was obtained in all patients at study points T-0, T-1, and T-2 by office visit. Incidence of adverse cardiovascular events, including stent thrombosis and bleeding complications were recorded, as well as of drug-related side effects. Each patient gave written informed consent to the study. Study end points were comparisons in the 2 arms (75 mg/day vs. 150 mg/day clopidogrel maintenance dose) of the following parameters: Platelet reactivity: 1) absolute PRU values; 2) percent inhibition in PRU values from estimated baseline; and 3) percentage of patients with absolute PRU values $\geq 240$. Brachial artery reactivity: 1) percent FMD values; 2) incidence of patients with FMD $<7\%$; and 3) percent NMD values. Inflammation: 1) absolute hsCRP values; and 2) hsCRP variations across study time points.
Statistics. In the ARMYDA-PRO (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty–Platelet Reactivity Predicts Outcome) study (5), the incidence of clopidogrel low-responders, defined by patients with PRU values ≥240, was 30%; if we expect a similar percentage of low-responders in the 75-mg/day arm and hypothesize a relative reduction of low-responders with the 150 mg regimen similar to that reported in a recent randomized study with the vasodilator-stimulated phosphoprotein assay (74%) (25), considering the cross-over design, a sample size of 48 patients would provide a >80% power to detect a difference in low-responders with an alpha (p value) of 0.05.

For the comparison of clinical and procedural features (Table 1) between the 2 arms, the t test was used for normally distributed continuous values (as detected by Kolmogorov-Smirnoff test) and the Mann-Whitney U test for not normally distributed variables, whereas proportions were compared by the Fisher exact test when the expected frequency was <5; otherwise, the chi-square test was applied. Comparisons between the 75- and 150-mg doses for PRU values, FMD, NMD, and hsCRP levels were performed using the Wilcoxon matched-pairs test for continuous variables and the McNemar test for proportions (in particular, for the comparison of patients with PRU ≥240, FMD <7%, and hsCRP >3 mg/l). Possible interactions between 75- and 150-mg daily doses and the 2 arms of the study (75 mg first vs. 150 mg first) were excluded by 2-way analysis of variance. Correlations were determined by the Spearman’s rank test. Results are indicated as mean ± SD. All p values <0.05 (2-tailed) were considered significant. Analysis was done with SPSS 12.0 software (SPSS Inc., Chicago, Illinois).

Results

The main characteristics of the study group are shown in Table 1, and were similar in patients randomized initially to high versus standard clopidogrel dose. During the study period, no patient had adverse cardiovascular events (death, myocardial infarction, stent thrombosis, repeat revascularization, stroke) or bleeding complications; 1 patient in the 150-mg arm reported diarrhea as a side effect, but it occurred at the end of the treatment period, which was nevertheless completed. No patient was lost during study follow-up.

Platelet reactivity. Absolute PRU values at the end of the study drug assignment period were significantly lower with the 150 mg dose (141 ± 73 vs. 198 ± 71 with 75 mg; p = 0.004) (Table 2), and percent inhibition in PRU values from estimated baseline was higher (50 ± 20% vs. 31 ± 20%; p < 0.0001); percentage of patients with absolute PRU values ≥240 was also lower in the high-dose group (12% vs. 32%, p = 0.001; 95% confidence interval of this difference was between −12% and −42%) (Figs. 2 and 3).

Brachial artery reactivity. After 1 month of high clopidogrel maintenance dose FMD was improved (16.9 ± 12.6% vs. 7.9 ± 7.5% in the standard dose arm; p = 0.0001) (Table 2), and incidence of impaired brachial artery reactivity (FMD <7%) was lower (16% vs. 58%, p = 0.0003; 95% confidence interval of this difference: −20% to −60%) (Figs. 2 and 3). The NMD was also higher in patients of the 150 mg group (18.2 ± 17.3% vs. 12.0 ± 10.4%; p = 0.07).

The FMD at 1 month after PCI (T0) was 18.9 ± 23.5% in patients receiving bare-metal stents versus 11.0 ± 10.2% in patients treated with drug-eluting stents (p = 0.25).

hsCRP levels. The hsCRP levels were lower in patients receiving the 150-mg/day regimen (3.6 ± 3.0 mg/l vs. 7.0 ± 0.25 mg/l; p = 0.00001; 95% confidence interval of this difference: −6 mg/l to −0.5 mg/l).

Table 1 Main Features in the 2 Arms

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>150 Followed by 75 mg/day (n = 25)</th>
<th>75 Followed by 150 mg/day (n = 25)</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Age, yrs</td>
<td>60.8 ± 7.3</td>
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<td>Male</td>
<td>21 (84)</td>
<td>21 (84)</td>
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<td>Diabetes mellitus</td>
<td>11 (44)</td>
<td>9 (36)</td>
<td>0.77</td>
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<tr>
<td>Hypertension</td>
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<td>22 (88)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>21 (84)</td>
<td>21 (84)</td>
<td>1.00</td>
</tr>
<tr>
<td>Body mass index</td>
<td>30.3 ± 4.6</td>
<td>28.8 ± 4.2</td>
<td>0.23</td>
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<tr>
<td>Previous myocardial infarction</td>
<td>12 (48)</td>
<td>8 (32)</td>
<td>0.39</td>
</tr>
<tr>
<td>Previous coronary intervention</td>
<td>12 (48)</td>
<td>13 (52)</td>
<td>1.00</td>
</tr>
<tr>
<td>Unstable angina/NSTEMI</td>
<td>10 (40)</td>
<td>8 (32)</td>
<td>0.77</td>
</tr>
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<td>Left ventricular ejection fraction, %</td>
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<td>55.5 ± 5.6</td>
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<td>Serum creatinine, mg/dl</td>
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<td>0.9 ± 0.29</td>
<td>0.32</td>
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<tr>
<td>Multivessel coronary disease</td>
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<td>12 (48)</td>
<td>0.77</td>
</tr>
<tr>
<td>Multivessel intervention</td>
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<td>6 (24)</td>
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<tr>
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<td>25 (100)</td>
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</tr>
<tr>
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<td>25 (100)</td>
<td>—</td>
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<tr>
<td>Proton pump inhibitors</td>
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</table>

Values are given as mean ± SD or n (%).

DES = drug-eluting stent(s); NSTEMI = non-ST-segment elevation myocardial infarction.
8.6 mg/l in the 75-mg arm; \( p = 0.016 \) (Table 2) and hsCRP values from baseline were significantly attenuated \((-3.3 \pm 7.0 \text{ mg/l} \text{ vs. } -0.2 \pm 5.1 \text{ mg/l}; \ p = 0.007)\). Percentage of patients with hsCRP levels \( >3 \text{ mg/l} \) tended to be lower among those treated with the high clopidogrel dose (46% vs. 64% in the standard dose arm, \( p = 0.07 \); 95% confidence interval: 0% to \(-29\%\)) (Figs. 2 and 3).

**Variations of PRU, hsCRP, FMD, and NMD at different time points during the study period.** From study points T-0 to T-1 (Fig. 4), platelet reactivity, hsCRP, and NMD values remained essentially unchanged in the 75 mg arm \( (p \geq 0.16) \), whereas FMD values slightly decreased \( (p = 0.08) \); conversely, in patients initially allocated to the high maintenance regimen, a significant decrease of PRU values \( (p = 0.0001) \) and hsCRP levels \( (p = 0.028) \) was demonstrated, as well as improvement of endothelial function \( (p = 0.05) \).

From study points T-1 to T-2, switching from standard to high maintenance dose was associated with significant reduction of platelet reactivity \( (p = 0.0001) \), attenuation of hsCRP levels \( (p = 0.004) \), FMD increase \( (p = 0.048) \), and a trend toward improved NMD \( (p = 0.10) \); switching from the 150 mg to the 75 mg regimen resulted in significant PRU elevation \( (p = 0.002) \) and FMD worsening \( (p = 0.001) \), whereas hsCRP tended to increase \( (p = 0.12) \) and NMD to decrease \( (p = 0.09) \).

Both hsCRP and FMD values were weakly correlated to PRU values \( (r = 0.21, p = 0.043 \text{ and } r = 0.18, p = 0.06, \text{ respectively}) \).

**Discussion**

The prospective, randomized ARMYDA-150 study demonstrates that, compared with the standard 75-mg daily dose, use of 150-mg/day clopidogrel maintenance regimen is associated with a higher degree of platelet inhibition and reduction of low-responders, as well as with significant improvement of endothelial function and enhanced anti-inflammatory effects. The standard 75-mg/day clopidogrel maintenance dose has been derived from pharmacodynamic studies, as it provides on average a degree of platelet inhibition equivalent to that obtained with a 500-mg daily dose of ticlopidine (26), but it may nevertheless be inadequate in some patients undergoing PCI (8). Antiplatelet effects of clopidogrel may be improved by doubling the chronic dose from 75 to 150 mg/day; aggregometry studies demonstrated that the higher maintenance regimen provides stronger platelet inhibition and reduces incidence of low-responders \( (11,25,27–30) \). Such protocols were performed on specific subgroups of patients, such as patients with diabetes mellitus (29) or patients receiving PCI for an acute myocardial infarction (27); moreover, in those studies, serial pre- and post-treatment platelet function evaluations were not systematically done \( (11,28,30) \) and different loading regimens of clopidogrel were used \( (25) \). The ARMYDA-150 study was performed on a consecutive series of unselected patients who had received the same clopidogrel loading regimen \( (600 \text{ mg}) \) at the time of PCI and were randomly allocated to the 2 clopidogrel doses 30 days after intervention; of note, our protocol excluded concomitant factors or therapies potentially interfering with antiplatelet response to clopidogrel (cigarette smoking, lipophilic statins, proton-pump inhibitors). Both antiplatelet and pleiotropic effects of the 2 maintenance doses were systematically evaluated before and after time periods of 1 month, and the cross-over allowed to have an internal control within the study population. Results of the point-of-care platelet function assay demonstrated in the 150-mg/day clopidogrel arm a significantly higher platelet inhibition from estimated baseline \( (50\% \text{ vs. } 31\% \text{ in the 75-mg group}) \), as well as a 20% absolute reduction of low-responders using a clinically-driven threshold of platelet reactivity \( (\text{PRU} \geq 240) \).

Experimental studies in the isolated pig heart showed that clopidogrel administration is associated with an increase in endothelium-dependent coronary vasodilation, and it is able to cause nitric oxide release from cultured endothelial cells \( (31) \); moreover, a randomized study \( (15) \) of patients with stable coronary artery disease has investigated acute effects of different
clopidogrel loading doses on endothelial function, showing that a 600-mg regimen causes a higher and faster (H110212h) improvement of flow-mediated brachial artery dilation than the 300-mg regimen does; this effect paralleled the antiplatelet effect of the drug, but was not accompanied by changes in platelet oxidative stress and nitric oxide bioavailability. To date, no study evaluated in a randomized protocol the chronic effects of different clopidogrel maintenance doses on endothelial function. The ARMYDA-150 study demonstrated a dose-dependent effect of clopidogrel on brachial artery reactivity: the 150-mg/day regimen was associated with significant improvement in FMD and a 42% absolute reduction of impaired brachial artery reactivity (FMD <7%) compared with the 75-mg daily dose. Our results might have an impact on practice patterns in light of recent data showing that endothelial dysfunction after PCI is associated with a higher risk of in-stent restenosis in patients undergoing bare-metal stent implantation (23), and may theoretically predispose to stent thrombosis after drug-eluting stent implantation. Further studies are needed to evaluate whether improvement of endothelial function by high-dose clopidogrel is linked to drug-induced inhibition of platelet activation, with decreased release by platelets of vasoactive mediators that may contribute to endothelial dysfunction, or whether it is due to a direct interaction with endothelial P2Y12 receptors (32). Indeed, in our study, brachial artery vasodilation properties independent of endothelial nitric oxide production were also improved with the higher regimen.

Anti-inflammatory effects of clopidogrel have been previously described in the setting of PCI, with attenuation of post-procedural raise of CRP levels (13); clopidogrel withdrawal was followed by significant increase of CRP levels in diabetic patients with coronary artery disease (14), whereas a single randomized study on patients with stable angina failed to demonstrate a significant reduction of CRP values in patients chronically receiving 75 mg/day clopidogrel (33). Moreover, in the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) trial (34) a 75 mg daily maintenance dose did not affect markers of inflammation. Recently, 150 mg/day clopidogrel after primary PCI was associated, compared with the standard 75 mg/day regimen, with a more rapid decline of CRP levels after the infarction (27).

The ARMYDA-150 study indicates that the higher clopidogrel maintenance regimen significantly attenuates hsCRP levels after PCI and is associated with 18% absolute reduction of persistently elevated (>3 mg/l) hsCRP levels. These results should be evaluated in light of previous data indicating that elevated CRP levels increase the risk of future cardiac events after PCI, and reduction of such levels may favorably impact prognosis (35). Whether the anti-inflammatory benefit of high-dose clopidogrel reflects a direct anti-inflammatory effect or whether it is a consequence of the higher platelet inhibition...
should be investigated in specific, ad hoc studies. Of note, in our study, both CRP levels and FMD values were weakly correlated to residual platelet reactivity on clopidogrel.

The protocol of the ARMYDA-150 study allowed us to consistently demonstrate significantly higher platelet inhibition, better FMD, and CRP reduction after changing from the 75- to the 150-mg clopidogrel dose, and, conversely, increase of platelet reactivity, impairment of endothelial function, and enhancement of inflammatory status after switching back from a 150- to a 75-mg maintenance regimen. At the beginning of the study, those parameters were similar in the 2 arms (Fig. 4), whereas at T1 (when 1 arm had received the high dose for 1 month), they were different. At T2, there were no significant differences in those parameters between the 2 arms; thus, it is possible that the beneficial effects of the 150-mg dose do not wane completely after 1 month; in particular, FMD and CRP levels did not come back to baseline values after 1 month on 75 mg clopidogrel. However, the main results of the study regarding the comparison between 75- and 150-mg daily dose derive from a paired analysis of all individual data.

Those results may contribute to further illustrate mechanisms of clinical benefit recently observed with the 150-mg versus the 75-mg clopidogrel maintenance regimen in PCI patients; in particular, in the CURRENT-OASIS 7 (Clopidogrel and Aspirin Optimal Dose Usage to Reduce Recurrent Events–Seventh Organization to Assess Strategies in Ischemic Syndromes) trial (36), high clopidogrel doses (600-mg loading plus 150 mg/day for 7 days), compared with 300-mg load followed by 75-mg/day regimen, significantly reduced 30-day incidence of stent thrombosis and myocardial infarction in the subgroup of patients with ACS undergoing PCI.

Conclusions

Our study was not powered or intended to evaluate incidence of clinical events (death, myocardial infarction, stent thrombosis, repeat revascularization) or bleeding complications in the 2 arms. However, ARMYDA-150 indicates that a high clopidogrel maintenance dose, in addition to a stronger antiplatelet effect, is associated with significant “pleiotropic” effects, which may potentially translate into a significant clinical benefit for patients undergoing PCI.

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