

the patient. Our study results are positive, but as you have mentioned, we need larger prospective studies for more clinical use.

Demet Menekşe Gerede
Department of Cardiology, Faculty of Medicine, Ankara University;
Ankara-Turkey

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Address for Correspondence: Dr. Demet Menekşe Gerede
Ankara Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı
Cebeci Kalp Merkezi, 06590, Cebeci, Ankara-Türkiye
Phone: +90 312 595 62 86 Fax: +90 312 636 22 89
E-mail: drmeneksegerede@yahoo.com

Prognostic value of high on-treatment platelet reactivity

To the Editor,

We have read the article by Tekkesin et al. (1) entitled "The first six-month clinical outcomes and risk factors associated with high on-treatment platelet reactivity of clopidogrel in patients undergoing coronary interventions" published in *Anatol J Cardiol* 2016; 16: 967-73 with great interest. A meta-analysis of 17 studies consisting of 20839 patients indicated that clopidogrel-treated patients with high on-treatment platelet reactivity (HTPR) had a 2.7-fold higher risk for stent thrombosis (ST) and a 1.5-fold higher risk for mortality following percutaneous coronary intervention (PCI) (2). Lack of association of ST and mortality with HTPR in the present study could be linked to the following reasons. Firstly, study population was heterogeneous in stent type and generation. Implantations of bare-metal stents (BMS) and drug-eluting stents (DES) were mentioned without further detail. However, even the second generation DES (everolimus and zotarolimus eluting stents) have lower ST rates than first generation DES (3). Sub-group analysis of HTPR and control groups were not depicted in the study. We think that it could affect the ST and mortality rates. Moreover, platelet function testing after PCI is also of importance in influencing formation of HTPR and control groups. Even though, light transmission aggregometry is historically gold standard, VerifyNow P2Y12 assay and Multiplate analyzer are generally used in studies on HTPR and ischemic events for their advantage of ease of performing. Determination of cut-off level is crucial for the study results. We think that cut-off level should be based on the expert position paper of European Society of Cardiology (4). Additionally, the study by Ko et al. (5) indicated that

HTPR measured by VerifyNow assay was able to discriminate patients who were at a higher risk for myocardial infarction and major adverse cardiac events after PCI better than Multiplate analyzer. This could be also a contributing factor for no differences observed in cardiovascular mortality and ST.

Ali Doğan, Serkan Kahraman¹, Emrah Özdemir, Nuri Kurtoğlu
Department of Cardiology, Faculty of Medicine, İstanbul Yeni Yüzyıl
University, Gaziosmanpaşa Hospital; İstanbul-Turkey
¹Department of Cardiology, Silivri State Hospital; İstanbul-Turkey

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Address for Correspondence: Dr. Ali Doğan
Gaziosmanpaşa Hastanesi, İstanbul Yeni Yüzyıl Üniversitesi
Tıp Fakültesi Kardiyoloji Bölümü
Gaziosmanpaşa, İstanbul-Türkiye
E-mail: drdali@hotmail.com

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at www.anatoljcardiol.com
DOI:10.14744/AnatolJCardiol.2017.7665



Author's Reply

To the Editor,

We would like to thank you for your comments on our article (1) entitled "The first six-month clinical outcomes and risk factors associated with high on-treatment platelet reactivity of clopidogrel in patients undergoing coronary interventions" published in *Anatol J Cardiol* 2016; 16: 967-73, about high on-treatment platelet reactivity of clopidogrel (HTPR), clinical outcomes, and associated risk factors and for the opportunity to discuss the clinical outcomes further.

It was discussed that in a meta-analysis of 17 studies consisting of 20839 patients treated with clopidogrel showed a 2.7-fold higher risk for stent thrombosis (ST) and a 1.5-fold higher risk for mortality following percutaneous coronary intervention (PCI) in HTPR patients (2). However, we found no statistically significant difference between the study and control groups in terms of ST (2.9% vs. 2.6%, $p=0.82$) and cardiovascular mortality (2.9% vs. 4%, $p=0.34$) in the first 6-month follow up (1). First of all, in the abovementioned meta-analysis, non-Western patients were excluded from the study because of different pharmacodynamic response to P2Y12-inhibitors across races. In addition, there is no long-term outcome follow-up (just the first month follow up data were available) in 6 of the 17 studies comprising 4694 of 20839 patients. Despite these methodological differences there may be some confounding variables altering our study results as previously mentioned in the limitations section:

One of the major reasons for ST and stent malapposition could not be evaluated in our study because there was no feasibility of IVUS or OCT when the stent deployed. Another issue about ST is that this entity could be affected by the type and size of stent. In our study, as we specified in limitation section, we do not have data enclosing stent size and type (BMS or DES). We accept that not covering stent type and size could have played a role in evaluation of results.

The prevalence of HTPR varies from study to study. There are many reasons for this disharmony: race, dietary habits, concomitant drug use, time from clopidogrel ingestion to study platelet functions, technique used, and cut-off levels for platelet reactivity. In our study, platelet functions were studied only once (24 hours after clopidogrel ingestion) and Multiplate analyzer was used. Platelet function assessment more than once, as performed in GRAVITAS (3) trial, could predict more accurate outcomes regarding mortality and ST. Another issue concerning platelet function is cut-off levels of assays. In the GRAVITAS (3) trial, when HTPR cut-off level is chosen as 230 PRU (Verify Now), <230 PRU was not associated with a lower risk of the primary end-point at 60 days [hazard ratio (HR), 0.62; 95% confidence interval (CI), 0.25–1.51; $p=0.30$] and at 6 months after PCI (HR, 0.71; 95% CI, 0.41–1.23; $p=0.22$). However, when the cut-off level is chosen as 208 PRU, <230 PRU showed a lower risk of the primary end-point at 60 days (HR, 0.18; 95% CI, 0.04–0.79; $p=0.02$) and at 6 months (HR, 0.43; 95% CI, 0.23–0.82; $p=0.01$). In our study, Multiplate analyzer was used and HTPR was defined with a cut-off level of 200 and the area under the aggregation curve as described by the manufacturer. According to a previously conducted study with Multiplate analyzer (4), an ADP test value >468 AU seems to be the optimal cut-off level to separate patients with high risk of stent thrombosis. Our study was conducted to evaluate not only ST but also find the prevalence of HTPR and associated risk factors, and a cut-off level of 200 was more reasonable than 468. However, there could be a more precise conclusion about ST and mortality if we have chosen 468 as the cut-off level.

Adnan Kaya
Department of Cardiology, Faculty of Medicine, Düzce University;
Düzce-Turkey

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Address for Correspondence: Dr. Adnan Kaya
Düzce Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı
81100, Konuralp, Düzce-Türkiye
E-mail: adnankaya@gmail.com

Fractional flow reserve guided stenting of a myocardial bridge

To the Editor,

Myocardial bridging (MB) is a common congenital coronary anomaly. The treatment is debated in symptomatic forms. Percutaneous coronary intervention (PCI) could be a possible solution; however, in these cases the major adverse cardiac event rate is high (1).

A 52-year-old man presented with chest pain provoked by emotional stress. Laboratory tests and transthoracic echocardiography were normal. Treadmill test was indicated according to Bruce protocol that demonstrated silent ischemia at 125 Watts workload. Beta blocker was uptitrated (bisoprolol 2.5–10 mg daily).

Despite the oral medical therapy, the patient remained symptomatic. Coronary angiography showed MB in the mid left anterior descending artery (LAD) with lumen compression (minimal lumen diameter: 0.26 mm, reference vessel diameter: 2.6 mm, and lesion length: 25.4 mm) but without any atherosclerotic lesions. A fractional flow reserve (FFR) measurement proved significant myocardial ischemia ($Pd/Pa=0.69$). After FFR measurement, the lesion was stented with a 3.0×38 mm paclitaxel eluting stent (Promus Premier, Boston Sci, US) at 14 atm. Control angiography