2. Budaj A, Yusuf S, Mehta SR, et al. Benefit of clopidogrel in patients with acute coronary syndromes without ST-segment elevation in various risk groups. Circulation 2002;106:1622–6.
3. Eikelboom JW, Hirsh J, Weitz JI, Johnston M, Yi Q, Yusuf S. Aspirin-resistant thromboxane biosynthesis and the risk of myocardial infarction, stroke, or cardiovascular death in patients at high risk for cardiovascular events. Circulation 2002;105:1650–5.
4. Petricevic M, Biocina B, Milicic D, et al. Bleeding risk assessment using multiple electrode aggregometry in patients following coronary artery bypass surgery. J Thromb Thrombolysis 2013;35:31–40.

Reply

Reply: $P2Y_{12}$-Based Platelet Function Assays Should be Complemented With Cyclooxygenase-Dependent Testing in Framing the Therapeutic Windows for Dual Antiplatelet Therapy

We thank Drs. Gasparovic and Petricevic for their interest in our study (1) and their comments. They strongly suggest that $P2Y_{12}$-based platelet function assays should be complemented with cyclooxygenase-dependent testing in framing the therapeutic windows for dual antiplatelet therapy. We think that this statement is highly speculative and not supported by the available evidence. Indeed, aspirin resistance has been extensively discussed as a real entity by itself and its association with clinical outcomes. First, response to aspirin assessed by cyclooxygenase-dependent testing has probably been overestimated due to a problem of compliance, and a previous study by our group showed that noncompliance was the main explanation for aspirin resistance, being a rare entity in compliant patients (2). For ischemic risk, some studies suggest the potential impact of aspirin resistance on ischemic events (3), but a recent study assessing the benefit of tailored therapy based on platelet testing of aspirin response failed to show any significant benefit (4). Therefore, testing aspirin response for ischemic prognosis and increasing aspirin dose on the basis of the test results is not supported by available evidence. For bleeding risk, as assessed in our study, to our knowledge, no study has ever linked the variability of aspirin response and bleeding complications in patients undergoing percutaneous coronary intervention after acute coronary syndrome. Therefore, the proposal in their letter is not in line with current data available on platelet monitoring. Also, the major risk of assessing aspirin response could be to use a higher dose in some patients, whereas recent evidence clearly showed that a high dose of aspirin does not provide any ischemic benefit, only a constant increase in bleeding and gastrointestinal events (5).

Accordingly, we performed an additional analysis to confirm previous assumptions. In the present study, aspirin response was assessed by arachidonic acid–induced platelet aggregation (AA-Ag). The rate of aspirin resistance was very low, with only 60 patients (4%) with aspirin resistance defined as AA-Ag above the 30% threshold previously proposed. We did not observe any relationship between AA-Ag and the occurrence of bleeding complications in our population, as suggested by Gasparovic et al. This could also be explained by the biological profile of aspirin response in 1,082 patients (70%) of patients with AA-Ag = 0%. Indeed, to identify a predictor of bleeding with platelet monitoring, we need to define *hyperresponse*, which is probably impossible with a drug providing 0% in more than two thirds of the patients with the present test.

We appreciate the suggestions of Drs. Gasparovic and Petricevic; however, this statement is supported neither by available evidence nor by the new analysis provided in this letter. Therefore, it was not an omission, and we believe that does not compromise the robustness of the presented data. Following the proposal to integrate the aspirin effect into bleeding risk assessment, the next step might be to use the new $P2Y_{12}$ blockers as long-term monotherapy without aspirin as currently tested in the GLOBAL LEADERS study (NCT01813435).

*Thomas Cuisset, MD, PhD
Jacques Quilici, MD
Jean-Louis Bonnet, MD
Marie-Christine Alessi, MD, PhD

*Département de Cardiologie
University Hospital La Timone
Rue Saint Pierre
13385 Marseille
France
E-mail: thomas.cuisset@ap-hm.fr

http://dx.doi.org/10.1016/j.jcin.2013.10.011

Please note: Dr. Cuisset has received consultant fees from Daiichi-Sankyo and Eli Lilly; research grants from Daiichi-Sankyo and Eli Lilly; and lecture fees from AstraZeneca, Daiichi-Sankyo, and Eli Lilly. Dr. Alessi has a relationship with Stago and sanofi-aventis. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Cuisset T, Grosdidier C, Loundou AD, et al. Clinical implications of very low on-treatment platelet reactivity in patients treated with thienopyridine: the POBA study (Predictor of Bleedings With Antiplatelet Drugs). J Am Coll Cardiol Intv 2013;6:854–63.
2. Cuisset T, Frere C, Quilici J, et al. Aspirin noncompliance is the major cause of "aspirin resistance" in patients undergoing coronary stenting. Am Heart J 2009;157:889–93.
3. Eikelboom JW, Hirsh J, Weitz JI, Johnston M, Yi Q, Yusuf S. Aspirin-resistant thromboxane biosynthesis and the risk of myocardial infarction, stroke, or cardiovascular death in patients at high risk for cardiovascular events. Circulation 2002;105:1650–5.
4. Collet JP, Cuisset T, Rangé G, et al., ARCTIC Investigators. Bedside monitoring to adjust antiplatelet therapy for coronary stenting. N Engl J Med 2012;367:2100–9.
5. CURRENT-OASIS 7 Investigators, Mehta SR, Bassand JP, Chrolavicius S, et al. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. N Engl J Med 2010;363:930–42.

Looking for the Native Annulus After Transcatheter Aortic Valve Replacement?

I read with great interest the recently published paper by Binder et al. (1) that described the impact of post-implantation SAPIEN XT (Edwards Lifesciences Inc., Irvine, California) geometry and positioning on clinical outcome after transcatheter aortic valve replacement (TAVR).