Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Patel N, Petraco R, Dall'Armellina E, et al. Zero-flow pressure measured immediately after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction provides the best invasive index for predicting the extent of myocardial infarction at 6 months: an OxAMI study (Oxford Acute Myocardial Infarction). J Am Coll Cardiol Intv 2015;8:1410–21.

2. Kramer MC, van der Wal AC, Koch KT, et al. Presence of older thrombus is an independent predictor of long-term mortality in patients with ST-elevation myocardial infarction treated with thrombus aspiration during primary percutaneous coronary intervention. Circulation 2008;118:1810–6.

3. Spaan JA, Piek JJ, Hoffman JI, Siemes M. Physiological basis of clinically used coronary hemodynamic indices. Circulation 2006;113:446–55.

4. Tamita K, Yamamuro A, Kaji S, Furukawa Y, Yoshikawa J. Impact of elevated coronary wedge pressure on long-term cardiovascular events after primary coronary intervention for acute myocardial infarction (abstr). J Am Coll Cardiol 2012;59 Suppl 1:E36.

5. Bellandi F, Maioli M, Gallopin M, Toso A, Dabizzi RP. Increase of myocardial salvage and left ventricular function recovery with intracoronary abciximab downstream of the coronary occlusion in patients with acute myocardial infarction treated with primary coronary intervention. Cathet Cardiovasc Interv 2004;62:186–92.

REPLY: Is Coronary Wedge Pressure a Technique to Identify High-Risk Patients Who May Benefit From Alternative Treatment in Acute Myocardial Infarction?

Is This The Next Step?

We would like to thank Prof. Iancu and colleagues for their comments about our recent publication (1). They raise 3 important points:

1. Which patient and procedural factors impact on microvascular function (MF) after primary angioplasty (PPCI)? We have not analyzed thrombus size and composition, but we agree that this could provide insights into the mechanisms of MF observed at the completion of PPCI. MF is multifactorial in this situation, reflecting a combination of ischemic injury, prior and procedure-associated distal embolization, and patient factors such as age and diabetes. We have recently addressed the specific effect of coronary stent implantation on MF, and identified that the most important determinants of change in MF are lesion location, thrombus burden, implanted stent volume, and baseline MF (2).
2. Use of coronary wedge pressure (CWP): There are a number of indices of MF available. The specific aim of our study was to compare Doppler and thermodilution-derived indices. We agree that offline analysis is time-consuming, but we do not believe that this finding provides only prognostic information. We have previously shown that final myocardial salvage is related to both end-of-procedure MF and how MF changes over the subsequent day, suggesting that identification of patients with impaired MF at the completion of PPCI could identify an especially high-risk group in which additional interventions maybe most beneficial (3).
3. Assessment of CWP before coronary stenting: CWP provides a simple measure, but in patients with collateral flow especially, it is maybe less reliable than a number of alternative indices. Ultimately, however, an enhanced understanding of the coronary microcirculation at the time of PPCI and the utility of different measures is essential if we are to achieve better outcomes from reperfusion for all of our patients.

Niket Patel, MBBS, BSc
Adrian P. Banning, MBBS, MD
***Rajesh K. Kharbanda, MD, PhD**

*Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Oxford, Oxfordshire OX3 9DU
United Kingdom
E-mail: rajesh.kharbanda@ouh.nhs.uk

http://dx.doi.org/10.1016/j.jcin.2015.10.016

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Patel N, Petraco R, Dall'Armellina E, et al. Zero-flow pressure measured immediately after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction provides the best invasive index for predicting the extent of myocardial infarction at 6 months. J Am Coll Cardiol Intv 2015;8:1410–21.

2. De Maria GL, Cuculi F, Patel N, et al. How does coronary stent implantation impact on the status of the microcirculation during primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction? Eur Heart J 2015 Aug 7 [E-pub ahead of print].

3. Cuculi F, Dall'Armellina E, Manlhiot C, et al. Early change in invasive measures of microvascular function can predict myocardial recovery following PCI for ST-elevation myocardial infarction. Eur Heart J 2014;35:1971–80.

Personalized Antiplatelet Therapy

The Odyssey Continues

We read with great interest the RECLOSE 3 (REsponsiveness to CLOpidogrel and Stent Thrombosis 3) study reported by Valenti et al. (1) in which

the authors investigated the clinical efficacy of prasugrel in clopidogrel nonresponders undergoing percutaneous coronary intervention (PCI) with drug-eluting stents. As stated by the authors, clopidogrel nonresponse or high on-treatment platelet reactivity (HTPR) after a clopidogrel loading dose has been identified as a major risk factor for recurrent ischemic events in acute coronary syndrome patients undergoing PCI. It is associated with an increased risk of cardiovascular (CV) death, myocardial infarction, and stent thrombosis (2). Consistent with the results of this study, a meta-analysis by Aradi et al. (3) suggested that HTPR was associated with a 3.35-fold increase in CV mortality. This issue is very relevant because a large majority of patients undergoing PCI are currently treated with clopidogrel despite its limitations.

However, the RECLOSE 3 trial has methodological limitations that distort its conclusion. First, as stated by the authors, it is a historical cohort comparison with the RECLOSE 2 (REsponsiveness to CLOpidogrel and Stent Thrombosis 2) trial, which represents the "control" group of clopidogrel nonresponders. However, the RECLOSE 2 trial was already an interventional trial in which clopidogrel nonresponders had an increase in their clopidogrel maintenance dose in order to reach a platelet reactivity (PR) <70% on an adenosine diphosphate test. This group of patients therefore cannot represent a valid clopidogrel nonresponders group. Second, the RECLOSE 3 trial population, unlike that of the RECLOSE 2 trial, included stable patients who are at low risk of events and in whom HTPR has limited prognosis implications (4). This could skew the results despite adjustments, and they should have been excluded from the analysis.

Third, in the present study, there are 2 limitations to the antiplatelet therapy protocol proposed. First, no prasugrel loading dose was used. It is well demonstrated that most events related to HTPR are early events, including periprocedural events, and therefore a prasugrel loading dose should have been used to optimize PR inhibition (3). In addition, the duration of dual antiplatelet therapy is not provided. After publication of the DAPT trial, it could be postulated that a difference in the duration of dual antiplatelet therapy between the 2 groups may have contributed to the observed difference in outcome (5).

Another major limitation lies in the fact that bleeding events were not reported. In fact, prasugrel is associated with a significant increase in major bleeding events in ACS patients undergoing PCI, which could offset its potential benefit on ischemic events. Balancing ischemic and bleeding events is critical to improve outcomes in patients undergoing PCI.

Finally, several studies have investigated the potential of PR monitoring in order to improve the outcome in patients with HTPR undergoing PCI. However, although small studies had promising results, large-scale randomized trials failed to show any difference in outcome. An adequately designed and powered trial is still warranted to provide a safe and efficient alternative to clopidogrel in patients with HTPR. Selection of patients and of the intervention to overcome HTPR will be critical in this lasting odyssey.

*Laurent Bonello, MD, PhD
Françoise Dignat-George, PhD
Marc Laine, MD

*MARS Cardio Cardiology Department
Hopital Universitaire Nord
Chemin des Bourrely
13015 Marseille
France
E-mail: laurentbonello@yahoo.fr

http://dx.doi.org/10.1016/j.jcin.2015.10.017

Please note: Dr. Bonello has received honoraria from AstraZeneca and Eli Lilly and research grants from AstraZeneca. The other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Valenti R, Marcucci R, Comito V, et al. Prasugrel in clopidogrel non-responders undergoing percutaneous coronary intervention: the RECLOSE (REsponsiveness to CLOpidogrel and StEnt Thrombosis) 3 study. J Am Coll Cardiol Intv 2015;8:1563–70.

2. Tantry US, Bonello L, Aradi D, et al., Working Group on On-Treatment Platelet Reactivity. Consensus and update on the definition of on-treatment platelet reactivity to adenosine diphosphate associated with ischemia and bleeding. J Am Coll Cardiol 2013;62:2261–3.

3. Aradi D, Komócsi A, Vorobcsuk A, et al. Prognostic significance of high on-clopidogrel platelet reactivity after percutaneous coronary intervention: systematic review and meta-analysis. Am Heart J 2010;160:543–51.

4. Park DW, Ahn JM, Song HG, et al. Differential prognostic impact of high on-treatment platelet reactivity among patients with acute coronary syndromes versus stable coronary artery disease undergoing percutaneous coronary intervention. Am Heart J 2013;165:34–42.

5. Mauri L, Kereiakes DJ, Yeh RW, et al., DAPT Study Investigators. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014;371:2155–66.

REPLY: Personalized Antiplatelet Therapy: The Odyssey Continues

We appreciate the interest of Dr. Bonello and colleagues in our paper on the RECLOSE-3 (REsponsiveness to CLOpidogrel and StEnt Thrombosis 3) study (1). However, all their comments and criticisms