

some methodologic considerations should also be addressed. Although case-control matching was used to reduce the effect of potential confounders and the calculated propensity scores included preoperative aspirin administration management, the lack of aspirin-specific platelet function testing was a drawback of the study.<sup>1</sup> Multivariate analysis confirmed preoperative aspirin use as an independent predictor of the need for  $\geq 3$  U of packed red blood cells.<sup>1</sup> Evidence has shown that certain patients have an accentuated response to the usual doses of preoperative aspirin that could result in increased perioperative blood loss.<sup>2,3</sup> Recently, our research group found that patients who had received packed red blood cell transfusions had had significantly lower aspirin-sensitive platelet function test values than had the patients not exposed to packed red blood cells ( $P = .002$ ).<sup>3</sup> Therefore, it would seem reasonable to use concomitant platelet function assays sensitive to both clopidogrel and aspirin. An increasing proportion of patients have been exposed preoperatively to dual antiplatelet therapy (aspirin and clopidogrel). Awidi and colleagues<sup>4</sup> found that the combination of aspirin and clopidogrel had greater inhibitory effects on platelet aggregation than either agent alone. Furthermore, evidence has shown that clopidogrel, when administered concomitantly with aspirin, reduces the incidence of aspirin resistance.<sup>5</sup> Therefore, the platelet inhibitory response to aspirin and consequent risk of excessive bleeding and transfusion requirements in cases of pronounced platelet inhibition should not be underestimated. The influence of aspirin and clopidogrel on bleeding should be assessed separately using drug-specific platelet function tests, facilitating an individual therapeutic approach for each antiplatelet agent preoperatively. Prospective studies evaluating the relationship between the drug-specific platelet function

test values and outcomes in this particular population should provide firm cutoff values that will delineate, not only the bleeding tendency, but also the proclivity toward ischemic events for patients with high on-treatment platelet reactivity. For such patients, too early discontinuation could cause platelet hyperactivity, followed by a rebound phenomenon that could finally result in ischemic events while awaiting surgery. Firm cutoffs would allow a possible frame of a “safety window” range for platelet drug-specific reactivity. The lower bound would delineate the bleeding tendency and the upper the proclivity toward ischemic events.

We congratulate the authors on this timely and elegant study. Additional studies using platelet function testing that are sufficiently powered to assess the possible benefits in clinical outcomes are needed to provide the most precise and reliable information about the benefits and risks of point-of-care-guided preoperative administration and discontinuation for each antiplatelet agent, facilitating an individual approach to patients with the aim of reducing both bleeding and adverse ischemic events.

Ivan Burcar, MD<sup>a</sup>

Bojan Biocina, MD, PhD<sup>a</sup>

Josko Bulum, MD, PhD<sup>b</sup>

Mate Petricevic, MD, PhD<sup>a</sup>

<sup>a</sup>Department of Cardiac Surgery

University of Zagreb School of

Medicine

University Hospital Center Zagreb

Zagreb, Croatia

<sup>b</sup>Department of Cardiovascular

Diseases

University of Zagreb School of

Medicine

University Hospital Center Zagreb

Zagreb, Croatia

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## Reply to the Editor:

We thank Dr Burcar and colleagues for their interest in our article,<sup>1</sup> which gives us the opportunity to address some aspects of our study design. We also thank the Editor for the possibility to reply.

First, it is necessary to keep in mind that our study included only patients who underwent coronary artery bypass grafting for acute coronary syndrome (group A = 100 patients, group B = 100 patients). According to the guidelines, aspirin was not discontinued before surgery whenever assumed.<sup>2</sup> We are aware that this strategy could be a potential confounder for postoperative bleeding analysis; however, a comparative analysis of chest tube drainage with respect to preoperative aspirin exposure was similar in aspirin users and nonusers. In the specific design of our study, this result tends to rule out the misleading impact of aspirin on postoperative bleeding as a potential confounder among groups. Nevertheless, and not surprisingly, within each group, aspirin users showed a tendency to require the transfusion of 3 or more units of packed red blood cells after surgery. Therefore, as a general rule, preoperative aspirin resulted in increased perioperative blood loss.

In regard to the use of concomitant dual antiplatelet therapy, we analyzed the effects of clopidogrel in addition to aspirin in our randomized study, prevention of Coronary artery bypass occlusion After off-pump procedures (CRYSSA).<sup>3</sup> Our results indicated that (1) the antiplatelet effect of aspirin is independent of additional clopidogrel administration; (2) the antiplatelet effect of aspirin is independent of clopidogrel resistance; (3) the antiplatelet effect of clopidogrel is independent of aspirin resistance; (4) aspirin and clopidogrel have an additive effect that extends the efficacy of treatment to a larger number of patients; and (5) aspirin in combination with clopidogrel in patients responsive to both drugs displays a synergistic inhibitory effect that potentiates the antithrombotic efficacy of clopidogrel. As a consequence, because of the wide individual variability of clopidogrel or aspirin response, we are in agreement with Petricevic and colleagues,<sup>4</sup> who suggested the use of platelet function assay devices for the preoperative quantification of platelet function in patients taking aspirin or clopidogrel. We also believe that a relatively cheap and easy to use point-of-care platelet function test could facilitate the individual approach to patients for each antiplatelet agent. This policy would reduce the risk of adverse ischemic events while awaiting surgery and of perioperative bleeding.

Vito Mannacio, MD<sup>a</sup>

Pascal Meier, MD<sup>b,c</sup>

Anita Antignano, MD<sup>d</sup>

Luigi Di Tommaso, MD<sup>a</sup>

Vincenzo De Amicis, MD<sup>a</sup>

Carlo Vosa, MD<sup>a</sup>

<sup>a</sup>Department of Cardiac Surgery  
University of Naples Federico II

Naples, Italy

<sup>b</sup>Divisions of Cardiology and Cardiac  
Surgery

Yale Medical School

New Haven, Conn

<sup>c</sup>Cardiology  
University College London Hospital  
London, United Kingdom

<sup>d</sup>Department of Cardiology  
Azienda Ospedaliera  
Santobono-Pausillipon  
Naples, Italy

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## PREVENTING PLEURAL MESOTHELIOMA IN PATIENTS WITH RECOGNIZABLE ASBESTOS-RELATED PLEURAL PLAQUES

### To the Editor:

I note the careful “analysis of surgical morbidity and mortality” in the treatment of malignant pleural mesothelioma, published in the July 2014 issue of the *Journal*.<sup>1</sup>

This again lists the postoperative complications in what is eventually a lethal disease.

A very large group of individuals exists, those treated with pleurodesis as young adults for complications of spontaneous pneumothorax, who have reportedly never developed malignant pleural mesothelioma.

Many of these individuals have undoubtedly been exposed to asbestos either before or after pleurodesis.

Consideration must surely be given to the value of pleurodesis in preventing pleural mesothelioma in those with evidence of simple asbestos-related pleural change.

Vincent Acton, MBBS (Syd),

FRANZCR

Radiologist

Private Practice

Sydney, New South Wales, Australia

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## Reply to the Editor:

Mechanical and chemical pleurodesis has been used to treat pneumothorax and malignant pleural effusion. Although good long-term survival after talc pleurodesis as the primary treatment of some patients with pleural effusion associated with mesothelioma has been reported, we are unaware of any link between pleurodesis and the prevention of this disease.<sup>1</sup> In the past, talc preparations contained asbestos and were thought to cause mesothelioma; however, for decades, medical talc preparations have been asbestos free, and the protective antitumor properties of talc have been suggested in the basic science data. For example, talc has been shown to induce apoptosis in human mesothelioma cells<sup>2</sup> and to promote an angiostatic environment in the pleural space.<sup>3</sup> Although using pleurodesis to prevent pleural mesothelioma in individuals with simple asbestos-related pleural change is an interesting idea, we believe that more preclinical