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Prevention and Prediction of Postsurgical Pain: Comment

To the Editor:

Although we applaud the Heart Surgery and Persistent Postsurgical Pain (Heart PPPAIN) study by Anwar *et al.*[1] for highlighting and addressing the complex and challenging condition of chronic pain after sternotomy, we would like to clarify some details before adopting their protocol into clinical use. The authors well recognize the

fact that chronic postsurgical pain is associated with preoperative anxiety and catastrophization as well as with the intensity of perioperative pain management.[1,2] Yet, missing intraoperative data let us wonder whether these issues were considered.

Although ketamine has an established role in the management of chronic pain, and as an opioid-sparing agent in acute pain, the debate about its optimal use in terms of dose, duration, and timing still continues. The dose used here was small, which was perhaps reflected in the outcome in the combined group. Possibly to minimize sedation, the authors deliberately chose this strategy. The drug also has cardiovascular and at times negative inotropic effects that may be undesirable in this population. Equally, the efficacy of pregabalin as preventive analgesia in coronary artery bypass graft surgery is to date unclear. However, lower, less-effective doses can cause postoperative sedation and hypotension, whereas higher and effective doses necessitate more perioperative vasopressors. This may impact graft survival and lead to postoperative acute renal failure.[3,4] Ultimately, sedation may be prolonged, especially when pregabalin is continued postoperatively. In this regard, we would welcome data on intraoperative vitals and inotrope requirements, and in general on whether there was any impact on intraoperative hemodynamics and immediately thereafter.

Finally, we would observe that noradrenaline, the most common vasopressor used, may modulate pain and alter its pain perception.[5] Its use may have differed significantly between patients, just as there were wide variations in the use of fentanyl. Comments from the authors on this would be welcome.

We again commend the team on making such a significant impact on a serious clinical problem, through the use of simple and familiar drugs. We hope to incorporate their regimen into our practice.

Competing Interests

The authors declare no competing interests.

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Prevention and Prediction of Postsurgical Pain: Reply

In Reply:

We are grateful for the comments and ideas suggested in response to our clinical trial of perioperative analgesia for cardiac surgery.[1]

Acknowledgment is given for the role of anxiety and catastrophization in predicting persistent postsurgical pain, but with some suggestion that intraoperative data may somehow shed further light on this. Our trial corroborates the literature in terms of the link with the former but, without any biologic plausibility for the latter, we saw no reason to collect these data for a pain trial of this nature.

The role of catecholamines in synaptic processing is well established, and the uptake of noradrenaline as well as adrenaline at the synaptic cleft does influence efficiency of nociceptive transmission in preclinical and clinical settings. It is important, however, to separate this from the peripheral infusion of a drug which does not readily cross the blood–brain barrier.[2]

The comment on our work also alludes to the potential effect of pregabalin on vasopressor requirements, graft survival, and renal failure, citing the work of Joshi and

Jagadeesh.[3] However, this report in fact clearly states that "[n]o overt cardiovascular effects are known," and no specific reference to these phenomena is to be found within the article. Further confirmation is suggested from the review by Mishriky *et al.*,[4] but this systematic review and meta-analysis also fails to describe an effect of pregabalin on organ perfusion or function.

Competing Interests

The author declares no competing interests.

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Physiologic Effects of Pulmonary Artery Occlusion: Comment

To the Editor:

Langer *et al.* demonstrated that a regional pulmonary vascular occlusion is associated with a diversion of ventilation from nonperfused to perfused lung areas.[1] This compensation, due to hypocapnic bronchoconstriction, in combination with pneumo-constriction, limits the increase in dead-space ventilation, improves ventilation-perfusion matching, and thus may decrease the work of breathing during spontaneous ventilation. Wheezing occurs with acute pulmonary embolism in patients both with and without previous cardiopulmonary disease.[2] Wheezing due to bronchoconstriction thus may be just be a marker or consequence and not the cause of respiratory dysfunction. Since the bronchoconstriction may have beneficial effects, do the authors recommend not treating the wheezing associated with pulmonary embolus, particularly in patients with no previous cardiopulmonary disease, where the wheezing is likely to be caused solely by the hypocapnic bronchoconstriction reflex?

Competing Interests

The author declares no competing interests.

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Physiologic Effects of Pulmonary Artery Occlusion: Reply

In Reply:

We thank Dr. Roth for the interest in our experimental study, in which we described the changes in blood flow