

provided no clinical advantage whatsoever—is certainly clinically important. Based on our large, well-powered trial, we thus conclude that ultrasound guidance alone is generally sufficient for accurately positioning femoral nerve catheters.

### Competing Interests

The authors declare no competing interests.

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## Another Role of Limb Remote Ischemic Preconditioning in Patients with Lung Cancer

To the Editor:

Li *et al.*<sup>1</sup> have demonstrated that limb remote ischemic preconditioning (RIPC) attenuates lung injury after lung resection in patients without severe pulmonary disease under propofol–remifentanyl anesthesia. The authors concluded that lung reexpansion from the one-lung ventilation provoked severe oxidative injuries, which was shown by increased serum levels of an oxidative product malondialdehyde,<sup>2</sup> and that RIPC reduced the oxidative stress, resulting in improvement of pulmonary function after the lung resection.<sup>1</sup> However, I would like to suggest another role of RIPC in the decreased oxidative stress in the study. When I looked at figure 3C of the article, patients receiving RIPC showed a higher serum malondialdehyde level from the time point 2, which was before resuming two-lung ventilation, and the level did not further increase 30 min after reexpansion (the time point 3).<sup>1</sup> These results indicate that the mechanism other than reperfusion should have caused oxidative stress, resulting in increased levels of malondialdehyde. It is interesting to note that patients with lung cancer have a higher production of reactive oxygen species than that in the normal population and that manipulated lung tissue is a source of reactive oxygen species.<sup>3–5</sup> In the study by Li *et al.*,<sup>1</sup> the postoperative morbidity rate for acute lung injury and adult respiratory distress syndrome was too high (8.2 to 17.5%) compared with that reported in previous studies (2.45%),<sup>6</sup> indicating that their study population contained severe lung cancer patients, who were exposed to increased oxidative stress. Therefore, it is likely that RIPC can reduce oxidative stress induced by advanced lung cancer during the operation. I would await additional data regarding this issue from their further studies.

### Competing Interests

The author declares no competing interests.

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#### In Reply:

We thank Dr. Kinoshita for his interest regarding our work.<sup>1</sup> One-lung ventilation (OLV) is widely used in thoracic surgery. In our study, the increase in serum level of an oxidative product malondialdehyde was started 60 min after OLV and did not further increase 30 min after reexpansion. However, patients receiving limb remote ischemic preconditioning showed the lower serum malondialdehyde level during this period. We entirely agree with Dr. Kinoshita's conclusion that it might be the mechanism other than reperfusion should have caused oxidative stress resulting in increased levels of malondialdehyde.

Oxidative stress is the result of an imbalance between radical-generating and radical-scavenging systems, and the total antioxidant status of the human body counteracts oxidative stress. Multiple clinical observations showed that severe oxidative stress was caused by oxygen free radicals induced during the process of OLV and reoxygenation, and the degree of the amount of generated oxygen free radicals was associated with the duration of OLV, especially for patients with lung cancer.<sup>2,3</sup> Cheng *et al.*<sup>4</sup> stated that resuming two-lung ventilation induced a massive superoxide production, but there was no significant decrease in the total antioxidant status, and they thought that severe oxidative injuries after OLV should be considered in patients without adequate antioxidant capacity, such as those with cancer and trauma. Some present data also suggest that with advancing stages of lung cancer, the levels of oxidative stress increased, whereas levels of antioxidant molecules decreased.<sup>5,6</sup> In our study, most of the patients were in advanced stages of lung cancer: stage IV (13.9%), stage III (78.7%), and stage II (7.4%), and none were found in stage I of lung cancer at the time of diagnosis. Thus, any possible perioperative parameter may remarkably affect the level of free radicals. For instance, surgical trauma is associated with the release of inflammatory cytokines and consequently neutrophil chemoattraction, which are the

source of large amounts of oxidants. During the operation, the scavenging systems are unable to confront the oxidant outburst of trauma itself, and oxidative stress is developed. In addition, lung parenchyma manipulation strongly contributes to the generation of free radicals because no reperfusion/reexpansion took place.

We also agree with Dr. Kinoshita's concern that the overall incidence of postoperative acute lung injury in our study was too high compared with that reported in previous studies. It is really because we had enrolled severe lung cancer patients in our study.

As we stated in the original article, since we, for the first time, investigated whether limb remote ischemic preconditioning would reduce the lung injury in patients undergoing elective pulmonary resection, there is a lot of confusion for us. We fully agree with Dr. Kinoshita's suggestion to further evaluate in more detail the role of limb remote ischemic preconditioning on oxidative stress induced by advanced lung cancer during pulmonary resection.

In conclusion, we thank Dr. Kinoshita for bringing forward some interesting and significant questions which will help us improve our future research work.

#### Competing Interests

The authors declare no competing interests.

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