Reply to the Editor:

We thank Dr Li and colleagues for their important comments to our article and appreciate their remarks. In particular, their results in patients during the postoperative period concerning determinants and implications of oxygen consumption (VO_2), a patient group that was not included by us, are essential.¹

In addition, their work presents the important conclusion that also other predictive equations published by LaFarge-Miettinen, Lundell and associates², Wessel and colleagues,³ and Lindahl⁴ do not accurately estimate VO_2 . Of course we should have cited their article.^{1,5}

Our study was especially designed to assess the importance of measured VO_2 in the preoperative diagnostic hemodynamic evaluation during cardiac catheterization. Our results emphasize that both the Krovetz-Goldbloom formula,⁶ which was used so far in our institution, and the most commonly used formula published by LaFarge and Miettinen² are not feasible in all patients to assume VO_2 to calculate cardiac output by using the Fick principle.

In contrast to the studies by Li and associates,^{1,5} VO_2 was measured with the standard commercial metabolic monitor Deltatrac II (Datex-Engström, Helsinki, Finland). This system is an open-air system equipped with a fast differential paramagnetic oxygen sensor to measure a differential signal between inspired and expired gases and a gas dilution system to measure flow.^{7,8} In contrast to the mass spectrometer method used by Li and associates, in our design no special adaptation in ventilated patients was necessary. After exclusion of any relevant air leak, the Deltatrac II device is easy to handle and allows a feasible and reliable method to measure VO_2 .

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Anesthetic preconditioning as the alternative to ischemic preconditioning

To the Editor:

We read with interest the article by Canyon and Dobson¹ presenting a combination of the adenosine A1 agonist 2-chloro-N6-cyclopentyladenosine (CCPA) and lidocaine as a possibly useful alternative to ischemic preconditioning in the clinical setting. As Canyon and Dobson¹ state, "A goal for more than 2 decades has been to develop a pharmacologic mimetic of IPC [ischemic preconditioning] to protect the heart during acute regional ischemia." Canyon and Dobson¹ unfortunately did not mention that volatile anesthetics are potent triggers of preconditioning, especially in the perioperative setting. Volatile anesthetic-induced preconditioning leads to a profound infarct size reduction, as effectively as does ischemic preconditioning,² and follows a dose-response relationship.³ Desflurane, enflurane, halothane, isoflurane, and sevoflurane induce anesthetic preconditioning.^{4,5} Apart from these experimental data, there is clear evidence for preconditioning by volatile anesthetics in human beings. Recent clinical studies indicate that volatile anesthetics confer cardioprotective effects in high-risk patients undergoing coronary surgery.⁶⁻⁸ Sevoflurane-induced preconditioning has

been seen to preserve myocardial function and decrease troponin I levels after cardiopulmonary bypass⁷ and even to reduce the incidence of late adverse cardiac events during the first year after surgery.⁸ Canyon and Dobson¹ emphasized that coadministration of lidocaine and CCPA was able to prevent life-threatening arrhythmias during ischemia and reperfusion. Again, volatile anesthetics show similar qualities: anesthetic preconditioning significantly reduces arrhythmias after ischemic periods.⁹ Stimulation of adenosine A1 receptors, among other membrane receptors, is part of the signal transduction pathway of anesthetic preconditioning.¹⁰ Therefore, it is unlikely that the administration of a selective adenosine A1 agonist in addition to a volatile anesthetic would further enhance cardioprotection. Canyon and Dobson¹ suggest intracoronary administration of CCPA and lidocaine for percutaneous interventions, off-pump and on-pump heart surgery, and perioperative applications. Apart from percutaneous coronary interventions, patients are anesthetized throughout these procedures. An inhalational anesthetic regimen would therefore appear to be the method of choice for patients at risk for perioperative ischemia because it would confer profound cardioprotection without the need for potentially deleterious additional intracoronary medication. Patients undergoing percutaneous coronary interventions might benefit from emulsified volatile anesthetics, administered intravenously at subanesthetic doses, in the near future.¹¹

In conclusion, there is a large body of evidence demonstrating that volatile anesthetics effectively induce cardioprotection, to the benefit of high-risk cardiac patients. Therefore, the need for adjuvant CCPA or lidocaine administered additionally to a patient already being protected by volatile anesthetics is questionable and remains to be proven.

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Reply to the Editor:

My colleagues and I thank Lange and colleagues for pointing out that we omitted mentioning the importance of volatile anesthetics and ischemic preconditioning (IPC) in a number of animal models and possibly human beings. For example, Kersten and coworkers¹ showed that halothane preconditioning in barbiturate-anesthetized dogs led to a profound infarct size reduction ($25.3\% \pm 2.9\%$ to $11.8\% \pm 2.7\%$) and that this reduction

was as effective as IPC ($9.6\% \pm 2.0\%$). We were remiss in not discussing these results and their importance to IPC. Lange and colleagues also stated, "Anesthetic preconditioning significantly reduces arrhythmias after ischemic periods." The antiarrhythmic effect of volatile anesthetics is more problematic. Recently Owczuk and associates² discussed how desflurane can prolong the QTc interval and may result in lethal cardiac arrhythmias. Huneke and coworkers³ also reported that halothane, and to a lesser extent isoflurane and sevoflurane, may lead to ventricular arrhythmias by shortening the refractory period. In addition, volatile anesthetics are known to inhibit a number of voltage-gated potassium ion channels, which could further increase the risk of ventricular tachycardia in predisposed patients.³ It is unfortunate that most animal studies investigating volatile anesthetics and IPC rarely report the incidence and duration of arrhythmias during ischemia-reperfusion. On the other hand, we reported that pretreating the heart with an intravenous solution of the adenosine A1 receptor agonist 2-chloro-N6-cyclopentyladenosine and sodium ion fast-channel modulator lidocaine (AIL) administered 5 minutes before and during 30 minutes of acute regional ischemia in the rat in vivo resulted in no deaths, virtually no severe ventricular arrhythmias and an infarct size equivalent to that seen with IPC.⁴ Finally, Lange and colleagues believe it is unlikely that the administration of a selective A1 agonist plus a volatile anesthetic could further enhance cardioprotection. However, we believe the combination may reduce the amount of each agent needed to exert cardioprotection; that is, the A1 receptor agonist may reduce the effective therapeutic threshold of the volatile anesthetic agent. This concept was recently reported by Chiari and colleagues,⁵ in whose study postconditioning during early reperfusion reduced the concentration of isoflurane necessary to exert cardioprotection. Because the underlying mechanisms of volatile anesthetics and the AIL combination are not fully understood, the synergistic effects of volatile anesthetics and A1 analogs (or AIL) remain to be determined. Moreover, modulating cardiac voltage-gated sodium ion fast channels with local anesthetics has received surprisingly little attention in IPC strategies, despite the resetting of the resting membrane potential toward a

more depolarized state during ischemic injury.³ To quote nineteenth century essayist and politician Benjamin Disraeli, "What we anticipate seldom occurs; what we least expected generally happens."⁵ Importantly, our work has shown that it is the combination of A1 agonist (or adenosine) and lidocaine administration that confers functional, electrical, and metabolic protection during myocardial ischemia-reperfusion.³ It would be of interest to study the effects of volatile anesthetics in the presence of the combination of A1 agonist (or adenosine) and lidocaine during and after acute myocardial ischemia in clinically relevant experimental models.⁶

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Management of pediatric airway obstruction

To the Editor:

We read with interest Vinograd and colleagues' article¹ on the management of airway obstruction in children by using self-expandable metal stents (SEMS). We commend the authors on a thorough and detailed description of the difficulties encountered in treating children with this complex problem.