

Only major neurologic complications that are rare in clinical practice were evaluated. It would have been interesting to assess the risk of minor neurologic complications that are often underdiagnosed, especially in elderly patients.

When venous air embolism occurs, the authors suggest placing the patient in a left lateral recumbent position. Animal studies have found no benefit from the left lateral position in improving hemodynamic performance,^{6,7} and human data are lacking. Conversely, in the case of a major event, such as cerebral gas embolism, the authors did not mention hyperbaric oxygen therapy. This therapy has potential benefits in the case of arterial gas embolism^{8,9} and has to be mentioned in the therapeutic arsenal.

Finally, we are clearly faced with a paradox. Venous air embolism is frequently found during laparoscopic procedures,^{1,10} PFO exists in 25 to 30% of patients, and mechanical ventilation increases right atrial pressure favoring right-to-left flow through a foramen ovale, especially if there is positive end-expiratory pressure.¹¹ However, systemic complications as a result of paradoxical embolism, especially cerebral complications, are rare. An explanation often evoked is the high solubility of carbon dioxide in blood. However, a gas embolism is rapidly transformed into a nongas embolism because of the adhesion of platelets to the bubble.¹² Moreover, if bubbles are detected in the heart, they can be in the brain, only a few seconds later through a PFO.

To conclude, it is perhaps time to call for a large study allowing the evaluation of the frequency of cerebral complications of gas embolism during laparoscopic surgery, especially minor ones, and to open a database of major complications, which are possibly underestimated today and most of them not being published. After all, we want to ask a question: should we contraindicate laparoscopic surgery in patients with a known PFO and prefer total abdominal surgery?

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In Reply:

We appreciate the comments and questions from Drs. Dubar and Fischler regarding our article.¹

We agree that the detection of a patent foramen ovale (PFO) would have been enhanced if we had used the methods that they had recommended. Because the incidence of PFO in Koreans has been well known,^{2,3} our focus was not the incidence of PFO in this study.

We also tried to find bubbles in the left heart, especially PFO cases and any neurologic complications after surgery, but we did not find any. However, if we had conducted postoperative cognitive function test, such as the Mini Mental State Examination,⁴ minor neurologic complications might have been found.

Although animal studies found no benefit from the left-lateral decubitus (Durant's) position in improving hemodynamic performance, it can allow gas bubbles to rise into the apex of the right atrium. So, it may be helpful for trapping and aspirating bubbles entrained in the right atrium.

As one of the specialists in diving medicine, the corresponding author (K.J.K.) totally agrees with them that hyperbaric oxygen therapy has potential benefits for arterial air embolism and cerebral air embolism.

The major reason why systemic complications resulting from paradoxical embolism with carbon dioxide are rare may be because of the high solubility of carbon dioxide in blood (0.60 ml CO₂/ml blood).⁵ Air embolism can be rapidly transformed into a nonair embolism because of the adhesion of platelets to the bubble, as they had pointed out. However, endothelial cells are important because they can be damaged by bubbles that are small enough to pass through the blood circulation without obstructing the blood flow.

In contrast to laparotomy, laparoscopic surgery has several benefits such as improved and more rapid recovery, re-

duced postoperative fatigue, heightened feeling of well-being, and better maintenance of homeostasis.⁶⁻⁸ Moreover, clinically significant carbon dioxide embolism is rare (0.001%) during laparoscopic procedures^{9,10} unlike PFO whose incidence is relatively high. Therefore, we believe that PFO cannot be a ground for eliminating laparoscopic surgery from possible surgical treatments.

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Anesthetic Effects and Lipid Resuscitation Protocols

To the Editor:

Hicks *et al.*¹ studied the effect of lipid emulsion, epinephrine, and vasopressin on survival rate after bupivacaine-induced cardiac arrest in a porcine model. The results of the authors demonstrated a completely different and unexpected outcome when compared with previous studies that used rodent and canine models. Although species difference may partially

explain the different outcomes, one must acknowledge that the anesthetics used in these studies were also markedly different. It is possible to study conscious animals in a canine model because dogs are easily trained. This closely mimics the human clinical scenario when bupivacaine is inadvertently injected intravenously during an attempted regional anesthetic with minimal sedation. Conversely, swine are more difficult to handle without heavy sedation or general anesthesia. Governmental regulations may sometimes disallow animal experimentation in the conscious state. Hicks *et al.* used ketamine, xylazine, and α -chloralose to induce general anesthesia. These drugs are known to work well in large animals such as swine. In a similar porcine study, Mayr *et al.*² used azaperone, atropine, ketamine, and piritramid followed by isoflurane after intubation. These anesthetic regimens produce hemodynamic and cardiac electrophysiologic effects, which may explain the failure of lipid rescue protocols in these studies.

Azaperone is a butyrophenone that, like droperidol, may have detrimental electrophysiologic effects at the high doses used in animals.² Azaperone also blocks α -adrenergic receptors, producing hypotension, impaired thermoregulation,^{3,4} and probably causing the extreme hypotension in the absence of epinephrine in the study of Mayr *et al.*² Hicks *et al.*¹ used α -chloralose, an anesthetic that was historically used as a rodenticide.⁵ α -Chloralose decreases cardiac conduction velocity in the cardiac muscle and atrioventricular node, prolongs the QTc interval, delays atrioventricular conduction, increases the ventricular refractory period, and exacerbates atrioventricular block caused by verapamil.⁶ Drugs that decrease cardiac conduction velocity will enhance bupivacaine arrhythmias,⁷ and α -chloralose has also been shown to be proarrhythmic toward the ischemic porcine heart.⁸ One can speculate that even if lipid rescue could partially reverse the effects of lipophilic drugs such as bupivacaine, one would not expect this for hydrophilic drugs such as α -chloralose. Through multiple hemodynamic and electrophysiologic effects, the anesthetics, as used in these porcine studies of bupivacaine-induced cardiac arrest, may have contributed to the failure of lipid rescue. For animal studies to optimally contribute to our understanding of resuscitation from inadvertent bupivacaine toxicity, studies should incorporate anesthetic and sedative techniques as that used in humans.

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