Non-cardiac surgery and volatile agents – Back to the future

Guest editorial to the article: Cardioprotective Effect of Sevoflurane in Patients with Coronary Artery Disease Undergoing Vascular Surgery.

In this issue of the *Saudi Journal of Anaesthesia*, Bassuoni *et al*.[1] suggest that the cardioprotective properties of sevoflurane might have clinically relevant implications in non-cardiac surgery. In a relatively large randomized controlled trial comparing patients with coronary artery disease undergoing peripheral vascular surgery to receive total intravenous anesthesia (propofol) or an anesthesia plan including a volatile agent (sevoflurane), Bassuoni *et al*.[1] found reduced cardiac troponin release in the overall population and in the subgroup of patients experiencing perioperative ischemia.

These results are extremely important and document for the first time that the powerful cardioprotective properties of volatile agents that have been studied *in vitro* and in animal studies for many years could apply to the vast majority of patients undergoing surgery.

So far, they represent the only evidence-based medicine to support the statement of the American College of Cardiology/American Heart Association (ACC/AHA) guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery that, in 2007, already suggested the use of volatile anesthetics during non-cardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk of myocardial ischemia.

The reduced cardiac troponin release documented in this study should not be taken as a surrogate endpoint since this cardiac biomarker has proven to be strongly associated to clinically relevant outcomes: the higher the cardiac troponin release, the poorer the outcome (irrespective of the setting and of the cause of troponin release).

Access this article online	
Quick Response Code:	Website: www.saudija.org
	DOI: 10.4103/1658-354X.97020

Were Bassuoni *et al*.[1] the first ones to conduct a randomized controlled trial to compare volatile agents versus total intravenous anesthesia in non-cardiac surgery? Of course not. Till 2007, there were at least 79 randomized controlled trials published in peer-reviewed journals, which included 6219 patients receiving total intravenous anesthesia or volatile agents (sevoflurane or desflurane). Unfortunately, none of these studies reported adverse cardiac events or cardiac biomarker release.[2] After 2007, there was only one randomized controlled study addressing the cardioprotective properties of volatile agents in non-cardiac anesthesia[3] and, probably due to the small sample size and to the low risk profile of the included patients, it found no beneficial cardioprotective effects of volatile agents.

Volatile agents might reduce perioperative mortality in low-risk patients undergoing coronary artery bypass grafting,[4] but their effect has not yet been confirmed in high-risk patients undergoing other cardiac surgery operations[5] or stenting procedures, and their effect should be further studied in large randomized controlled trials.

What will happen after the study of Bassuoni *et al*.[1] Should we start using volatile agents in all non-cardiac operations worldwide? Should we include them in guidelines and recommendations? With more than 200 million major non-cardiac surgery procedures performed yearly and approximately 4 million patients experiencing perioperative adverse cardiovascular events or mortality,[6] we are facing a major public health problem and still do not have a magic bullet to help us in reducing this burden. Volatile agents are cheap, not more expensive than total intravenous agents, out of patent, and easy to use. Even if the number needed to treat or prevent one major complication will be 10.000, we can still prevent thousands of adverse events each year.

The answer is no. What we should do is to go on and study them further.[7] Single-center trials have small sample size, limited external validity (e.g., maybe the authors have expertise with volatile agents and are still on the learning curve with the use of intravenous agents), tend to have implausible effect size, may have unequal allocation of resources (e.g., maybe the most skilled team took care of the volatile agents group), and suffer from lack of blinding, although inevitable, which could cause conscious

or unconscious biases. Furthermore, clinically relevant outcomes (mortality) sometimes go in opposite directions of intermediate outcomes.[8]

Unfortunately, bureaucracy prevents us to conduct large randomized trials on simple topics like this one. To compare two standard anesthesia plans such as those proposed by Bassuoni *et al*.,[1] we only would need a web-based randomization and a network of colleagues willing to perform a phone call (alive or dead) to their patients 30 days after the surgical operations. One hundred and thousand patients could be randomized in a few months worldwide, and the entire scientific community and millions of patients would benefit from the results of the study for years. But we are living in a world of bureaucracy and the international policy makers are not even aware that this bureaucracy is indirectly killing thousands of patients per year.

We should therefore go back to the study of Bassuoni *et al*.,[1] thank them for this original and important finding, and wait for some donor to spend millions of dollars to support a large randomized trial to pay the bureaucracy and to confirm or not the extremely promising findings of this pilot study.

Landoni G., Cabrini L.

Department of Anesthesia and Intensive Care,
San Raffaele Hospital,
Via Olgettina 60, Milano 20132, Italy.
E-mail: landoni.giovanni@hsr.it

REFERENCES

1. Bassuoni AS, Amr YM. Cardioprotective effect of sevoflurane in patients with coronary artery disease undergoing vascular surgery. Saudi J Anaesth 2012;6:125-30.
2. Landoni G, Fochi O, Bignami E, Calabrò MG, D'Arpa MC, Moizo E, *et al*. Cardiac protection by volatile anesthetics in non-cardiac surgery? A meta-analysis of randomized controlled studies on clinically relevant endpoints. HSR Proc Intensive Care Cardiovasc Anesth 2009:4;34-43.
3. Zangrillo A, Testa V, Aldrovandi V, Tuoro A, Casiraghi G, Cavenago F, *et al*. Volatile agents for cardiac protection in non-cardiac surgery: A randomized controlled study. J Cardiothorac Vasc Anesth 2011;25:902-7.
4. Landoni G, Augoustides JG, Guarracino F, Santini F, Ponschab M, Pasero D, *et al*. Mortality reduction in cardiac anesthesia and intensive care: Results of the first International Consensus Conference. Acta Anaesthesiol Scand 2011;55:259-66.
5. Bignami E, Landoni G, Gerli C, Testa V, Mizzi A, Fano G, *et al*. Sevoflurane vs. propofol in patients with coronary disease undergoing mitral surgery: A randomised study. Acta Anesthesiologica Scand 2011;56:482-90.
6. Devereaux PJ, Chan M, Eikelboom J. Major vascular complications in patients undergoing noncardiac surgery: The magnitude of the problem, risk prediction, surveillance, and prevention. In: Yusuf S, Cairns JA, Camm AJ, Fallen EL, Gersh BJ, editors. Evidence based Cardiology. 3rd ed. London, England: BMJ Books; 2009.
7. Bellomo R, Warrillow SJ, Reade MC. Why we should be wary of single-center trials. Crit Care Med 2009;37:3114-9.
8. Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, *et al*. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): A randomised controlled trial. Lancet 2008;371:1839-47.

How to cite this article: Landoni G, Cabrini L. Non-cardiac surgery and volatile agents - Back to the future. Saudi J Anaesth 2012;6:107-8.