CORRESPONDENCE

Letters to the Editor

Cardioprotection by Volatile Anesthetics in Noncardiac Surgery? No, Not Yet At Least

In the recently published article by Fleisher et al. (1), the authors advise using volatile anesthetics as cardioprotective agents in patients at risk for myocardial ischemia undergoing noncardiac surgery. These drugs have indeed shown marked cardioprotective properties in cardiac surgery, reducing post-operative mortality and myocardial infarction rate when compared with total intravenous anesthesia (2).

No study to date has allowed these interesting results to be translated in noncardiac surgery settings. A recent meta-analysis including more than 80 randomized controlled studies in which volatile anesthetics were compared with total intravenous anesthesia in noncardiac surgery highlighted the complete lack of published randomized clinical trials reporting data regarding postoperative mortality or cardiac complications after noncardiac surgery (3), which indicates that cardioprotection by halogenated anesthetics in noncardiac surgery is a new and interesting subject that deserves further study.

Because the authors of the guidelines suggest a class of evidence IIa, level B ("some conflicting evidence from single randomized trial or non-randomized studies"), we would appreciate knowing which article(s) provided the evidence to state that "it can be beneficial to use volatile anesthetics during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia."

*Giovanni Landoni, MD
Oliviero Fochi, MD
Alberto Zangrillo, MD

*Department of Cardiothoracic Anesthesia and Intensive Care
Istituto Scientifico San Raffaele, Milano, Italia
Via Olgettina 60
Milan 20132
Italy
E-mail: landoni.giovanni@hsr.it


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Reply

There is intense interest in the actions of volatile anesthetics agents to pre- and post-condition myocardium against injury after myocardial ischemia and reperfusion. Anesthetic pre-conditioning was first demonstrated in animal models in 1997 (1,2) and in patients undergoing coronary artery bypass graft surgery in 1999 (3). The American College of Cardiology/American Heart Association 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery (4) summarize the findings of 15 randomized clinical trials in patients undergoing coronary artery bypass graft surgery demonstrating that volatile anesthetic agents decrease troponin release and enhance left ventricular function compared with several intravenous anesthetics. Studies designed to evaluate the efficacy of anesthetic pre- or post-conditioning against myocardial injury have been conducted in patients undergoing cardiac surgery because the timing and duration of the myocardial ischemic stimulus is relatively well defined. In addition, the majority of these investigations controlled for important variables that could influence anesthetic cardioprotection, such as by discontinuing sulfonylurea hypoglycemic agents that block anesthetic pre- and post-conditioning. The data indicate that volatile anesthetic agents are protective against myocardial ischemia/reperfusion injury and can likely be generalized to patients with coronary artery disease undergoing noncardiac surgery. To date, there have been no published studies specifically designed to assess the efficacy of anesthetic pre- or post-conditioning against myocardial injury in patients undergoing noncardiac surgery. Also, volatile anesthetics produce important negative inotropic effects, and the risks and benefits of these drugs in hemodynamically unstable patients are unclear. There is a great need for further investigation in this area. The conduct of adequately powered and well-controlled studies of anesthetic cardioprotection in noncardiac surgical patients will be challenging. Meta-analyses of heterogeneous clinical trials using volatile or intravenous anesthetics in patients who are at low or intermediate risk for developing myocardial ischemia due to the nature of the surgical procedure, the burden of disease, or both may not be adequate to elucidate the risks versus benefits of specific anesthetic agents to produce cardioprotection. Per the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Methodology, unpublished data cannot be used to formulate guideline recommendations. Thus, the weight of the evidence suggests that volatile anesthetics are protective against myocardial ischemia/reperfusion injury, and in the absence of data to indicate
that these commonly used anesthetics increase risk in hemodynamically stable patients, their use is recommended.

*Judy R. Kersten, MD, FACC
Lee A. Fleisher, MD, FACC
*Medical College of Wisconsin
8701 West Watertown Plank Road
Milwaukee, Wisconsin 53226-3548
E-mail: jkersten@mcw.edu


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Biomarker Sensitivity and Specificity Require Pre-Test Probability of Disease Diagnosis to Be Collated

Additional Points on the Interpretation of Pro–B-Type Natriuretic Peptide Triage of Dyspnea in the Copenhagen Heart Study

The Copenhagen City Heart study (1) provides important insight into community assessment of breathlessness. The report could be taken to support pro–B-type natriuretic peptide (proBNP) triage of all breathless patients in this setting. We feel this is a simplistic analysis of the potential contribution of biomarker technology and that a number of additional points should be considered.

The relationship of BNP measures to cardiac impairment has been confirmed, and their utility tested in a variety of settings (1,2). However, the sampling frame of most surveys (2,3) is of little relevance to the general practitioner. Importantly in the Copenhagen study, 48% of their breathless patients had neither cardiac nor pulmonary abnormality. In fact, the major causes of dyspnea in a population-based study were obesity, depression, and older age (4). Thus, even before addressing the performance of proBNP analysis, the authors must surely also address the relative diagnostic void that is presented for almost half of the patients in their study.

Secondly, the incremental value of proBNP testing is not clearly put in the context of clinical history, physical examination and simple bedside tests such as a 12-lead electrocardiogram and a chest roentgenogram. Although these may individually have low sensitivity and specificity and are operator specific (5,6), they contribute to pre-test diagnostic probability, which, in turn, affects the performance of any biomarker and the post-test probability of the presence of cardiac dysfunction (7). By excluding the contribution of the physician, the ability of the test to function cost-effectively could alternatively be compromised or enhanced.

Thus, a dyspneic patient with a high proBNP level could undergo echocardiography, even in the absence of abnormalities on examination and bedside investigations. Surely in such patients resources would be better employed establishing a noncardiac cause for dyspnea.

Thirdly, although the authors accounted for age and gender, they need to interpret point measurement of proBNP levels with great care due to their large intraindividual and interindividual variability (33.3% and 36.5%, respectively, in normal individuals [8]). Both symptomatic and asymptomatic patients with stable systolic heart failure present with wide ranges of plasma BNP, with up to 21% of symptomatic patients having BNP levels below what would be considered "diagnostic"(9).

Finally, the concept that pulmonary disease can be defined by spirometry alone is not acceptable. This limited technique does not rule out the presence of significant parenchymal lung disease. Moreover, proBNP levels can be elevated in lung conditions resulting in right heart strain and pulmonary hypertension (10,11).

The authors are to be congratulated on their effort in challenging the use of biomarker technology for the community assessment of breathlessness. However, its commercial exploitation needs to be based on its cost-effectiveness and applicability to realistic clinical practice. It needs to be interpolated in the light of clinical assessment, particularly given the large percentage of true negative results for either cardiac or pulmonary abnormalities.

*Robert J. MacFadyen, BSc, MD, PhD, FRCP
M. Jennyfer Ng Kam Chuen, MBBS, MRCP
*University Department of Medicine
City Hospital
Dudley Road
Birmingham B18 7QH
United Kingdom
E-mail: Robert.macfadyen@swbh.nhs.uk

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