

## Perioperative Cardiovascular Risk Evaluation and Care for Noncardiac Surgery – Part I

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Systematic perioperative cardiovascular risk evaluation for noncardiac surgery is essential. Indeed, patients who undergo this type of surgery are at a substantial risk for cardiac events. Annually, 500,000 to 900,000 patients worldwide will experience a major perioperative cardiac complication, such as death, myocardial infarction (MI) or nonfatal cardiac arrest.<sup>1</sup> The number of patients undergoing a noncardiac surgery is constantly increasing and patients with coronary artery disease (CAD) live longer. They are thus likely to require all types of surgical operations.<sup>1,2</sup>

Another crucial aspect to consider is that of informed consent. The patient has the right to know the degree of risk associated with a type of surgery, even more so when surgery is elective and does not affect vital prognosis. Appropriate risk evaluation also makes it easier for the physician to make certain decisions (such as choice of the operative procedure, intensity of postoperative care, etc).

This issue of *Anesthesiology Rounds* is published in two parts and will attempt to answer the following questions: In a given clinical context, how can one carry out the best possible perioperative risk evaluation? Which patients benefit from a more thorough investigation of their cardiovascular state? When should one consider revascularization? For which patients should  $\beta$ -blockers be prescribed in preparation for surgery? Are there other agents that could reduce the risk? Finally, the issue includes a review of the most recent guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA), which were updated in October 2007.<sup>3</sup>

### EPIDEMIOLOGY OF MAJOR PERIOPERATIVE EVENTS

It is important to know the impact of a major cardiovascular event occurring in a surgical context. Postoperative MI is associated with an intrahospital mortality of 15%-25%. It is also an independent risk factor for cardiovascular mortality, as well as, for the recurrence of nonfatal MI, for up to 6 months following surgery. Postoperative nonfatal cardiac arrest, on the other hand, is associated with an intrahospital mortality of 65%.<sup>1,4</sup>

Approximately 10% of noncardiac surgeries are carried out in an urgent context and they are then associated with an even greater event risk. On average, these adverse events will lengthen hospital stay by 11 days and will thus have a considerable financial impact.<sup>5</sup> A recently published article based on major cohort studies suggests that 3.9% of patients (95% confidence interval [CI], 3.3% - 4.6%) will develop a major perioperative cardiac event (cardiac mortality, nonfatal MI, nonfatal cardiac arrest).<sup>1</sup>

One important cohort study<sup>6</sup> evaluated the outcome of relatively nonselected patients (ie, the selection was not limited to patients who were referred to a perioperative medical consultation service, to those with peripheral vascular disease, or to those at risk of, or with, CAD). A rate of 1.4% of major perioperative cardiac events was observed in this cohort. However, urgent surgeries were excluded, suggesting that this is a conservative estimate of the event rate. The current incidence of major cardiac events remains vague because the majority of studies were carried out over 10 years ago.

Although not very frequent, perioperative MI remains a serious complication. Generally, it occurs in the first three days after surgery, a period during which the patients receive analgesics, morphine derivatives, or are sometimes still intubated in the intensive care unit. As a result, it is rare to observe the traditional signs and symptoms associated with infarction and the caregiver must remain vigilant and search for the presence of this adverse event.<sup>5,7</sup>

The majority of perioperative MIs will be silent and without ST segment elevation, and <5% of MIs or other major events will occur during the perioperative period itself. The electrocardiogram

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(ECG) obtained immediately after surgery allows a reassessment of the patient's risk. The occurrence of new ischemic changes will have an unfavourable impact on the subsequent outcome and these patients will benefit from a closer follow-up. Prolonged perioperative and otherwise unexplained hypotension is another factor that allows the identification of patients who are at a higher postoperative risk of events.<sup>9</sup>

The definition of a perioperative MI will obviously have an impact on its incidence. There are no standardized diagnostic criteria, but troponins and the ECG play a very important role. A typical increase in troponin levels or a typical fall after a raised value, without an alternative explanation (eg, pulmonary embolism) should be looked for, in addition to one of the following factors:<sup>10</sup>

- Signs or symptoms of ischemia (including dyspnea)
- Appearance of new Q waves on the ECG or changes indicative of ischemia
- New (or presumed new) regional wall motion abnormalities on echocardiography or perfusion defects as visualized with nuclear medicine imaging
- The presence of new Q waves on the ECG in a context where troponins were not measured constitutes a reliable diagnostic criterion of perioperative MI.

According to the ACC and the European Society of Cardiology (ESC), MI is defined by an increase in levels of troponins T or I beyond a "value exceeding the 99<sup>th</sup> percentile of a reference control group" at least once during the first 24 hours following the index event.<sup>10,11</sup> Several studies have shown that an elevation in troponins is associated with poor long-term prognosis, even following a vascular surgery.<sup>12,13</sup> It is actually an independent risk factor for mortality, nonfatal acute coronary syndrome, and for angina requiring revascularization after surgery.<sup>12,14</sup> Although the rise in troponins sometimes corresponds to a subclinical myonecrosis (without symptoms), it could potentially have an unfavourable impact on the long-term prognosis.

Nevertheless, the use of troponins as a single indicator of perioperative MI remains controversial. Indeed, some studies have not revealed evidence of an association between postoperative elevations in troponins and an adverse impact on long-term outcomes.<sup>15</sup> This is one of the reasons why the most recent ACC/AHA guidelines do not support routine postoperative dosing of troponins. It is preferable to measure serum levels in the presence of clinical signs or symptoms of cardiovascular dysfunction or when the ECG indicates ischemic changes.<sup>3</sup>

## **PATHOPHYSIOLOGY OF PERIOPERATIVE MYOCARDIAL INFARCTION**

Numerous factors are involved in the susceptibility to perioperative MI. Surgery-related trauma is associated with the occurrence of an inflammatory and hypercoagulable state, which is responsible for a cascade of events that can lead to MI. The activation of multiple mediators of inflammation (eg, tumour necrosis factor  $\alpha$  [TNF $\alpha$ ], interleukin [IL] 1 and 6, and C-reactive protein [CRP]) is involved in the process of preexistent coronary plaque instability and fissure. An increase in platelet reactivity is also observed, as well as increases in Factor VIII concentrations and plasminogen activator inhibitor-1 (PAI-1) levels, together with a reduction in antithrombin levels. This favours the hypercoagulable state and the process of acute coronary thrombosis.<sup>1,16,17</sup>

Despite anesthesia, surgery often results in a global state of stress with release of cortisol and catecholamines.

This leads to increased shearing forces and contributes to coronary plaque fissure or rupture. These stress hormones also increase the oxygen demand of the myocardium and, therefore, predispose the patient to a perioperative MI.<sup>1,18</sup> Nevertheless, certain aspects of the pathophysiology of perioperative MI remain controversial. It is not clear whether the factor that is primarily implicated in the genesis of an MI remains the severity of the coronary stenosis or, rather, the composition of the plaque itself. Angiographic studies have demonstrated that the majority of MIs result from the rupture of a vulnerable plaque, which has a core rich in lipids and macrophages, and is surrounded by a thin fibrous cap. These plaques, more prone to rupture, tend not to narrow the coronary lumen to a significant degree before breaking. Thus, the segment responsible for the MI is seldom the one that has the most significant stenosis, even during the perioperative period.<sup>19</sup>

A substudy of the Coronary Artery Surgery Study (CASS) trial examined the influence of surgical revascularization vs medical treatment, to reduce the risk of postoperative cardiac complications.<sup>20</sup> In a somewhat contradictory manner, this study revealed that the risk of MI was proportional to the severity of the lesions, the most severe plaques being at a much higher risk of occlusion.

Finally, a case study demonstrated that complications following vascular surgery correlate more with the number of lesions >30% than with the severity of the lesions, except for complete occlusions that directly increase the risk of death or MI.<sup>21</sup> The presence of a significant 3-vessel or left main disease would also increase the risk of perioperative complications.

## **CLINICAL RISK EVALUATION**

In general, risk evaluation is based on the use of clinical markers, the functional capacity of the patient, and the specific risks of the surgery<sup>3</sup>.

### *History, functional capacity, and physical examination*

First, the history must look for the elements mentioned in Table 1 while trying to specify the severity and/or the stability of the condition.<sup>3</sup> Unstable angina and "recent" MI are associated with major perioperative risk. A prospective study, published in the beginning of the 1980s, demonstrated that the more recent the occurrence of MI, the more elevated the risk of reinfarction in a surgical context.<sup>22</sup> It is recommended to wait a minimum of 4 to 6 weeks before elective surgery after an MI.<sup>3</sup>

It is also necessary to carry out a targeted physical examination to diagnose the presence of a significant cardiac pathology:<sup>3</sup>

- Blood pressure in both arms
  - Search for arterial hypertension, coarctation of the aorta, chronic dissection...
- Pulsation and murmur in the carotid arteries
  - An abnormality may indicate peripheral artery disease and, therefore, hidden coronary disease.
- Jugular veins
  - Elevated jugular venous pressure and/or a positive hepatojugular reflux indicate increased pressure in the right atrium, most often secondary to a hypervolemic state found in heart failure patients
- Cardiac and pulmonary auscultation
  - Search for aortic and/or mitral murmur, signs of heart failure with S3 or pulmonary rales.
- Palpation of the abdomen

**TABLE 1: History and functional capacity**

- Personal history of coronary artery disease (CAD)
- Angina
- Heart failure
- Valvulopathy (ies)
- Arrhythmia (s)
- Presence of a pacemaker or a defibrillator
- Arterial hypertension
- Peripheral vascular disease
- Revascularization in the 5 years preceding surgery
- Anatomical or functional evaluation in the 2 years preceding the surgery
- Evaluation of effort tolerance (functional capacity)
- Presence of comorbidities (diabetes, chronic obstructive pulmonary disease, history of stroke, renal failure, hematological disorders)
- Pharmacological treatment (prescribed or available over-the-counter)
- Use of drugs or alcohol

– Search for ascites, pulsatile liver in right heart failure, aortic aneurysm.

- Examination of the extremities for edema and vascular integrity

– Abnormal peripheral perfusion if cardiac output is low or there is significant peripheral vascular disease.

– The presence of peripheral edema is not a reliable indicator of chronic heart failure unless it is associated with a rise in jugular venous pressure or with a positive hepatojugular reflux.

*Aortic stenosis or decompensated heart failure are 2 conditions associated with a high risk of perioperative cardiac complications.*

## ELECTROCARDIOGRAM

A preoperative 12-lead ECG is recommended in patients having at least one clinical risk factor (history of CAD, heart failure or cerebral vascular accident, diabetes, renal failure, or peripheral vascular disease) and undergoing a high- or intermediate-risk surgery.<sup>3</sup> It is also reasonable to obtain an ECG for an asymptomatic patient without risk factors, but undergoing vascular surgery. In practice, the majority of patients will have an ECG before surgery, unless it is a minor operation.

There are multiple conditions that can alter the initial ECG (metabolic and electrolytic abnormalities, intracranial pathologies, pulmonary disease, drugs etc). Disorders of conduction such as right bundle branch block or first-degree atrioventricular (AV) block do not justify additional investigations. This is often true in cases of benign asymptomatic ventricular arrhythmias, even in the presence of underlying structural disease. On the other hand, it is necessary to carefully search for the presence of Q waves or for significant ST abnormalities on the ECG because such findings are associated with an increased risk of cardiac adverse events. Left ventricular hypertrophy with an overload strain pattern and left bundle branch block in a patient with established CAD are also associated with a reduction in life expectancy.<sup>3</sup> Based on the context, these findings usually warrant an additional investigation by noninvasive methods.

### Type of surgery planned

An urgent surgery is associated with a rate of cardiac complications 2 to 5 times higher compared with elective surgery.<sup>23</sup> Other factors, such as the experience of the

surgeon or of the institution with the procedure, can also influence risk.<sup>24-26</sup> In general, the rate of cardiovascular death or nonfatal MI is directly related to the type of surgery. The risk of cardiovascular mortality, according to the ACC/AHA, is described in Table 2.

## RISK ASSESSMENT WITH PREDICTION INDICES

Various tools for risk evaluation have been developed by Goldman and Detsky, among others.<sup>27,28</sup> These risk indices are particularly useful for the stratification of patients who are at intermediate risk and they are based on surgical candidates. It should be stressed that the American Society of Anesthesiologists' (ASA) Physical Status class has never been developed with the aim of predicting surgical risk. This tool rests on very qualitative clinical criteria and its interpretation is at the discretion of the clinician. Despite its subjectivity, the performance of this tool in predicting perioperative cardiac risk is relatively good.<sup>29,30</sup>

The Goldman risk index has several limitations. There were few vascular surgery patients in the population studied, thus this score cannot really apply to this subgroup of patients. It is a scale that was developed in the 1970s and does not reflect the surgical and anesthetic techniques used today. Detsky and collaborators have suggested a revision of the Goldman index, where they added angina and pulmonary oedema to the original variables.<sup>28</sup> The main weakness of the Detsky and Goldman index is the lack of power to distinguish significant CAD among patients who are at the bottom of the spectrum of clinical risk.<sup>31</sup>

In order to simplify the prediction of risk, Lee and collaborators studied 4,315 patients undergoing elective, major, noncardiac surgery.<sup>6</sup> They identified 6 independent factors for major cardiac complications:

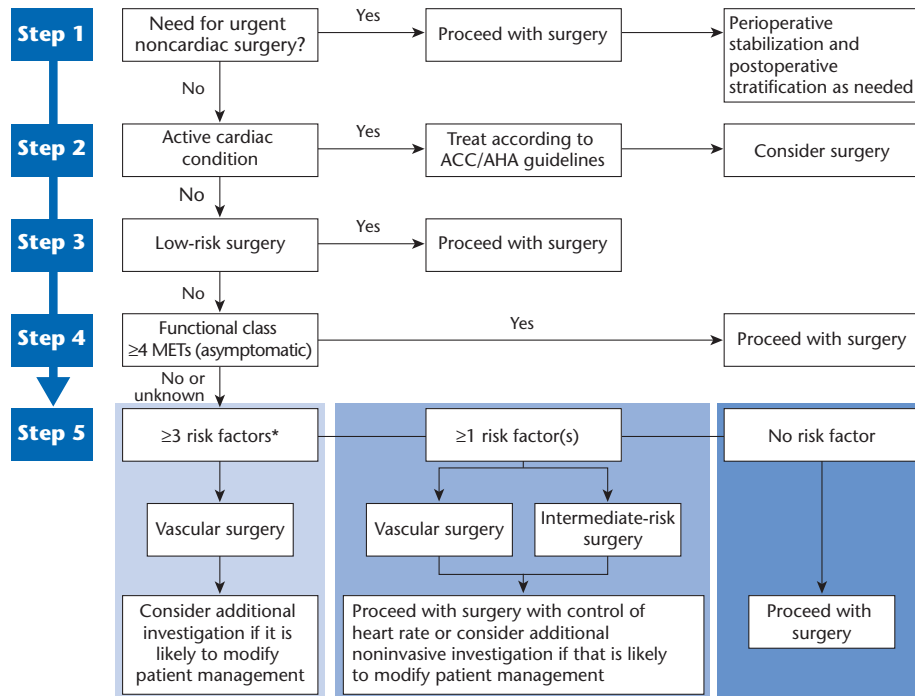
- High-risk surgery (vascular, thoracic, or intra-abdominal)
- History of CAD
- History of heart failure
- History of cerebral vascular disease
- Diabetes treated with insulin
- Creatinine >2 mg/dL (177 µmol/L)

The majority of experts currently agree that Goldman's Cardiac Risk Index revised by Lee has the best predictive value. Moreover, the new ACC/AHA guidelines rest their evaluation of stable patient risk on Lee's index.

**TABLE 2: Risk of cardiovascular mortality<sup>3</sup>**

- >5% for a high-risk procedure
  - Major urgent surgery, particularly in the elderly
  - Aortic surgery or other major vascular surgeries
  - Peripheral vascular surgery
  - Prolonged surgical procedure with substantial bleeding or important volemic changes
- 1-5 % for an intermediate-risk procedure
  - Intrathoracic or intraperitoneal surgery
  - Carotid endarterectomy
  - Surgery of the head and neck
  - Orthopedic surgery
  - Prostate surgery
- <1% for a low-risk procedure
  - Endoscopic procedures
  - Breast surgery
  - Cataract surgery
  - Other "superficial" minor procedures
  - Ambulatory surgery

**FIGURE 1 : Algorithm for the evaluation and management of cardiac risk**



\* Factors: coronary artery disease, heart failure, diabetes, cerebrovascular disease, or renal failure; MET = metabolic equivalents

### RISK EVALUATION ACCORDING TO THE NEW ACC/AHA GUIDELINES (FIGURE 1)

The ACC/AHA guidelines were recently revised.<sup>3</sup> The new version tends to simplify the approach, given that the new studies available cast some doubt on the value of functional stratification and prophylactic revascularization before surgery.<sup>32,33</sup> In general, it is recommended to proceed with an investigation or revascularization only if these are justified independently of the surgical context. Therefore, it is not necessary to proceed with an investigation or revascularization strictly in order to allow the patient to survive his/her surgery.

The first step consists of evaluating the urgency of surgery. Although an urgent surgery is associated with increased risk, current recommendations are to proceed with adequate perioperative monitoring and to stratify the patient after the surgery, if necessary.

The second step consists in evaluating the presence of an active cardiac condition, formerly considered as a major risk factor for complications. These conditions are:

#### Unstable acute coronary syndromes

- Acute MI (<7 days) or recent (>7 days, but ≤30 days)
- Unstable or severe angina

#### Severe or uncompensated heart failure

##### Significant arrhythmias

- High-degree AV block
- Symptomatic ventricular arrhythmias in the presence of an underlying CAD
- Supraventricular arrhythmias with uncontrolled ventricular response (>100 beats per minute at rest)
- Symptomatic bradycardia

#### Severe valvular disease

- Severe aortic stenosis (mean pressure gradient >40 mm Hg, valvular area <1 cm<sup>2</sup>, or symptomatic)
- Symptomatic mitral stenosis (progressive dyspnea or presyncope with effort, heart failure)
- Mitral or aortic insufficiency with criteria of severity

For any patient presenting one of these known, unstable conditions, it is recommended to defer elective surgery and implement suitable treatment according to current guidelines. These must be recognized as essentially precarious cardiac conditions that warrant intensive care and rapid stabilization, whether surgery is planned or not.

Aortic stenosis remains a substantial risk factor for perioperative adverse events. A retrospective cohort study evaluated the outcome of 108 patients with aortic stenosis and valvular area <1 cm<sup>2</sup> who underwent noncardiac surgery.<sup>34</sup> This study confirmed that the rate of death and nonfatal MI was much higher among patients with aortic stenosis compared with the control group (14% vs 2%;  $P<0.001$ ). Moderate (area of 1.0-1.5 cm<sup>2</sup>, gradient 25-40 mm Hg) to severe (area <1 cm<sup>2</sup>, gradient >40 mm Hg) aortic stenosis is also associated with an increased tendency to excessive bleeding during surgery, due to an acquired von Willebrand syndrome. This syndrome is described in 67%-92% of patients with severe aortic stenosis and is mainly accounted for by the mechanical degradation of von Willebrand factor multimers during the turbulent passage of blood through the narrowed valve and by an increase in platelet clearance.<sup>35</sup> In the presence of recognized indications, the aortic valve should be replaced before an elective, noncardiac operation, if the patient is symptomatic.

The third step consists in identifying the risk inherent to the type of surgery. For example, if the patient must undergo low-risk surgery (as mentioned above) and is clinically stable, it is not necessary to conduct any additional evaluations, even in patients at high risk of a cardiac event. The surgery can thus be performed as planned.

The clinical evaluation of the functional capacity of the patient represents the fourth step to be followed. Functional capacity has a very important prognostic value. It is expressed in "metabolic equivalents," (MET) where 1 MET = 3.5 mL O<sub>2</sub>/kg/min and corresponds to the oxygen uptake at rest in the sitting position. The perioperative and long-term risk is increased to a significant degree if the patient is unable to do 4 METs, such as walking up 1 flight of stairs or a few blocks. A patient who is capable of this level of effort daily is at very low risk of perioperative complications, and surgery can be recommended without additional evaluation. Nevertheless, evaluation of the functional capacity can be problematic in the presence of CAD with important claudication or other mobility problems.

When the patient has a low, or impossible to determine, functional capacity or is symptomatic, it is necessary to evaluate the number of risk factors according to Lee's index. This fifth step will determine whether a more thorough evaluation of the cardiovascular status using functional tests is desirable or not. Thus, patients who do not present any of the risk factors according to the index could be operated on without additional investigation. In the presence of one of these factors (history of CAD, history of heart failure, history of stroke, diabetes treated with insulin or renal failure), it is recommended to consider a functional investigation, but only if it is likely to modify the perioperative process. Despite all of the above, the usefulness of a functional test and screening of inducible ischemia remains uncertain.

## FUNCTIONAL EVALUATION

Currently, the use of noninvasive examinations aimed at detecting inducible coronary ischemia, in order to predict the perioperative risk, remains very controversial. It is the initial risk of the patient that will determine the value of a noninvasive test. In general, the negative predictive value (NPV) is excellent (90%-100%) for these tests, but the positive predictive value (PPV) is low (generally 20%-25%).<sup>3</sup> As a result, these tests are more useful to determine a decrease in risk when the test is normal (NPV) than to identify patients at very high risk when the test is positive.<sup>29</sup> They mainly allow the risk estimate to be refined, especially in patients considered to be at "intermediate risk" (without an active cardiac condition, with poor functional class, and with at least one factor on the Lee index).

A treadmill test is usually preferable because it allows the evaluation of tolerance to exercise, an important predictive risk factor. Pharmacological stress testing should be reserved for patients presenting a functional limitation with the conventional stress test. For patients who are unable to exercise significantly, dobutamine echocardiography and dipyridamole

choice to predict operative risk. Dobutamine echocardiography shows a higher specificity and offers the advantage of defining valvular anatomy precisely.<sup>36</sup>

Finally, it should be noted that it is the extent of ischemia, and not only its presence, which seems to be associated with the occurrence of events.<sup>37</sup>

This type of evaluation is for a restricted patient population, since this additional investigation can affect the timing of surgery and lead to a preoperative revascularization decision. A recent study, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE II) could not demonstrate the advantage of detecting inducible ischemia among moderate-risk patients undergoing vascular surgery who are, therefore, considered to be at high risk.<sup>33</sup> In this group of patients treated with  $\beta$ -blockers, the screening of ischemia did not lead to a reduction in perioperative events. However, very few patients underwent a diagnostic coronarography or a revascularization despite having a positive test. In other words, the screening of ischemia, if it does not change clinical management, will not reduce perioperative risk. Therefore, the most recent ACC/AHA guidelines highlight the importance of making this type of evaluation only if a change in the management of the patient is contemplated following the results of the test.

Thus, at present, the process to be followed after a "positive" functional examination remains controversial. Several authors suggest a two-tiered approach, with inducible ischemia being the only important variable. Such an approach would cause an increase in coronary angiograms and coronary artery surgery, often without proven benefit. Some suggest evaluating the results of functional testing according to a concept of "high vs low risk." Since myocardial revascularization will have a favourable impact only in a small proportion of patients, the use of criteria indicating a greater probability of multivessel or left main coronary disease was proposed, in order to improve the PPV of the test and select patients who could receive more benefits from revascularization. Although the extent of ischemia is a marker of perioperative cardiac risk, its correlation with unfavourable coronary anatomy, such as multivessel disease, unstable plaque, or significant left main disease, remains uncertain.<sup>38</sup> In summary, a noninvasive test is *more useful to reduce the initially estimated risk, if it is negative (or normal) than to identify patients at risk if it is positive.*

The second part of this text will address the prevention of cardiac events, the management of antiplatelet treatment, and the administration of a  $\beta$ -blocker, a statin and/or ASA (Aspirin) in the perioperative setting.

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## Upcoming Scientific Meetings

2-7 March 2008

**14<sup>th</sup> World Congress of Anesthesiologists**

Cape Town, South Africa

Contact: Barbara Quantz

Tel: 00-32-26-417-470 Fax: 00-32-26-417-471

Email: WCA2008@optionsglobal.com

Website: <http://www.wca2008.com/default.asp>

9-14 March 2008

**Society of Cardiovascular Anesthesiologists (SCA)**

**13<sup>th</sup> Annual Update on Cardiopulmonary Bypass**

Whistler, British Columbia

Contact: SCA

Tel: 804-282-0084 Fax: 804-282-0090

Email: [sca@societyhq.com](mailto:sca@societyhq.com)

Website: <http://www.scahq.org/sca3/events/2008/cpb/>

13 to 17 June 2008

**64<sup>th</sup> Annual Meeting Canadian Anesthesiologists' Society**

World Trade & Convention Centre & Delta Halifax

Halifax, Nova Scotia

Contact: SCA

Tel: 416-480-0602 ext – 12 Fax: 416-480-0320

Email: [meetings@cas.ca](mailto:meetings@cas.ca)

Website: <http://www.cas.ca>

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