Major themes for 2014 in cardiothoracic and vascular anaesthesia and intensive care

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ABSTRACT

There has been significant progress throughout 2014 in cardiothoracic and vascular anaesthesia and intensive care. There has been a revolution in the clinical approach to acute and chronic adult aortic diseases. Contemporary management of adult aortic disease is based on etiology, clinical presentation, extent, and integrated intervention with medical, endovascular and/or surgical measures. Further European guidelines have explored in depth the cardiovascular management in non-cardiac surgery with a thematic focus to reduce perioperative mortality from the leading offender, namely myocardial ischemia. Integrated guidelines address the management of myocardial revascularization including the percutaneous and surgical options. Despite 50 years since the first coronary artery bypass grafting procedure and impressive advances in interventional cardiology, surgical revascularization remains a gold standard for many patients with coronary artery disease. These advances in 2014 will likely further improve perioperative outcomes for our patients.

Keywords: *aorta, guidelines, European Society of Cardiology, European Society of Anaesthesiology, European Association of Cardiothoracic Surgery, myocardial ischemia, non-cardiac surgery, myocardial revascularization, coronary artery bypass grafting, percutaneous coronary intervention, troponin, statins, beta-blockers, aspirin, clonidine, intra-aortic balloon pump, fenoldopam, volatile anesthetics.*

INTRODUCTION

This article is the sixth in an annual series that has reviewed major themes in perioperative cardiothoracic and vascular care (1). The first major theme for 2014 is the revolution in the clinical approach to aortic diseases. The second major theme is integrated cardiovascular assessment and management for non-cardiac surgery.

The third major theme is the balanced approach to myocardial revascularization for advanced coronary artery disease. The past year has witnessed significant progress in these 3 clinical domains that will likely improve important clinical outcomes in perioperative cardiovascular practice.

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The Revolution in the Management of Aortic Disease: the Specialty of 'Aortology'

The 2014 aortic guideline from the European Society of Cardiology (ESC) is groundbreaking because it considers the entire aorta from its origin at the aortic valve to its termination at the iliac bifurcation as compared to previous guidelines that have considered either isolated diseases or specific aortic segments (2-4). This comprehensive guideline reviews the acute and chronic aortic diseases affecting the thoracic and abdominal aorta in adults in an organized fashion (2). While a detailed review of this guideline with 62 pages and 560 references is beyond the scope of this article, an overview of its highlights is presented here.

After an introductory section, the aspects of the normal and ageing aorta are reviewed. Aortic assessment is then discussed from the following perspectives: clinical examination; laboratory testing; and imaging (chest X-ray; echocardiography; abdominal ultrasound; intravascular ultrasound; computed tomography; magnetic resonance imaging; and, aortography) (2).

While transthoracic and transesophageal echocardiography have central roles in the aortic imaging, contemporary management of aortic diseases depends on integrated multimodality imaging beyond echocardiography (2-5). The detail of aortic imaging has recently generated its own multidisciplinary guideline that is focused on the thoracic aorta with 64 pages and 426 references (5).

Furthermore, within specialized procedures such as transcatheter aortic valve replacement, there has also been an imaging revolution that has integrated multiplanar and multimodality imaging to facilitate precise transcatheter interventions within the aortic root (6, 7). This imaging revolution is unfolding not only for specific diseases and procedures but also throughout the thoracic and abdominal aorta to include three-dimensional and transcatheter imaging capabilities (5-8).

The therapeutic options for aortic diseases are then outlined in section 5 with the following major categories: medical management; endovascular therapy; and, surgical intervention (2). In the section about endovascular therapy, there is a detailed discussion of the classification of endoleaks after endovascular aortic repair since they are an important management consideration (9). Furthermore, the role of deliberate hypotension for precise graft deployment is also highlighted (10).

In the section about surgical intervention, the principles of repair are reviewed according to aortic segment as follows: aortic root and ascending aorta; aortic arch; descending aorta; thoraco-abdominal aorta; and, abdominal aorta (2, 11, 12).

The acute thoracic aortic syndromes are then discussed in section 6 as a spectrum including classic dissection, intramural hematoma and penetrating ulcer (2). In acute aortic dissection, the outcome importance of clinical presentation is highlighted both in type A and type B categories (2, 13, 14). The central role of transesophageal echocardiography in the perioperative management of acute thoracic aortic syndromes is emphasized in this guideline (15). The management of aneurysms are then reviewed in section 7 according to extent of aortic involvement (2). The importance of organ preservation is highlighted, including strategies for spinal cord protection in descending thoracic and thoraco-abdominal aortic interventions (12, 16, 17).

The genetic aortopathies are systematically reviewed in section 8, including chromosomal syndromes, bicuspid aortic valve, and coarctation (2, 18, 19). The ESC aortic guideline is concluded with short sections on atherosclerotic lesions, aortitis, tumors, follow-up for chronic aortic diseases, and

gaps in evidence (2). This 2014 guideline is a high-quality management guide to adult aortic disease from the aortic valve to the abdominal aortic bifurcation. It emphasizes the emergence of aortology as a subspecialty but also explains the central role of the cardiovascular anesthesiologist in the perioperative management of aortic disease.

Cardiovascular Assessment and Management in Non-Cardiac Surgery

The 2014 guideline from the ESC and the European Society of Anaesthesiology (ESA) about perioperative cardiovascular approaches for non-cardiac surgery extensively discusses these aspects in a systematic document with 49 pages, 10 sections and 276 references (20). It coincided with the similar 2014 guideline from the American College of Cardiology (ACC) and American Heart Association (AHA) on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery (21).

Although in-depth discussion about these important guidelines is beyond the scope of this highlights article, a commentary on myocardial ischemia in this setting is important since it dominates these guidelines due to its leading contribution to perioperative mortality in across Europe (20-22). Although the classic definition of myocardial ischemia (MI) typically includes symptoms and signs, perioperative MI often remains difficult to diagnose since it frequently presents asymptomatically (23, 24). The lack of better diagnostic methods to detect perioperative MI represents an important gap in evidence.

A recent analysis (N=15,065) from the large international prospective **V**ascular Events **I**n Noncardiac **S**urgery Pat**I**ents C**O**hort Evaluatio**N** (VISION) study tackled this evidence gap through the development of diagnostic criteria for MI after non-cardiac surgery (MINS) (25). The important observation from the VISION clinical registry was that a peak perioperative troponin T level ≥0.03 ng/mL was the best indicator of MINS (25). Note that this diagnostic formulation of MINS does not require classic features of ambulatory MI such as clinical symptoms, signs and electrocardiographic features (20-25). In the VISION registry less than 50% patients with MINS fulfilled the universal definition of myocardial infarction (25).

Furthermore, according to this new definition, MINS had an incidence of 8.0% and explained 34% of all deaths in adults in the first 30 days after non-cardiac surgery (25). The VISION registry and the 2014 ESC/ESA guideline have both emphasized that MINS is common and important (20, 21, 25). Given that about 8 million adults suffer MINS worldwide each year, MINS likely accounts for over 2 million deaths annually (26-28).

The perioperative outcome burden from MINS have been highlighted by recent large trials in Europe and Asia (27, 28).

A large single center analysis from China (N = 117,856: 2003-2011) demonstrated that MINS had an overall incidence of 5.2 per 10,000, although it significantly increased with advanced age (28). The mortality risk in the setting of MINS increased more than 100 fold (36.1% vs 0.32%: $P < 0.001$) (28). Furthermore, MINS in this large study presented most often within 72 hours after surgery without chest pain and with non-ST segment changes on the electrocardiogram (28).

The 2014 ESC/ESA guideline addresses the cardiovascular approach to non-cardiac surgery in the following sections: introduction with a preamble; preoperative evaluation; risk-reduction strategies; specific diseases; perioperative monitoring; anaesthesia; gaps in evidence; and as summary with an appendix section (20). In the setting of signs and symptoms suggestive of perioperative

myocardial ischemia, the ESA/ESC guideline strongly recommends the analysis of an electrocardiogram and the measurement of troponins (20). The measurement of troponins in patients at high risk for MINS has been identified as a possibility in the ESC/ESA guideline (Class IIb Recommendation; Level of Evidence B). The guideline also identified as a major gap in current evidence the lack of interventional studies that take into account the perioperative risk stratification from biomarkers such as high-sensitivity troponin. As a result, troponin determinations in high-risk patient cohorts has not been recommended as a routine due to the absence of a defined management strategy with known risks and benefits (20).

Furthermore, as the guideline highlights, further trials are also required to define the role of brain natriuretic peptide as a risk-stratifying biomarker in perioperative management of patients at high-risk for MINS (20). Perioperative surveillance with biomarkers has facilitated the discovery of a gap in perioperative care, namely the detection and management of MINS (20). Although a troponin-based definition has refined the identification of MINS in at risk patients, the ESC/ESA guideline also discusses in detail possible interventions to minimize this serious complication.

The pharmacological approach to cardiovascular risk-reduction in the perioperative period is reviewed extensively in section 4 of the ESC/ESA guideline, including beta-blockers, statins, angiotensin blockers, alpha-2 agonists, and antiplatelet agents (20). The recommendations for perioperative beta-blockade in the ESC/ESA guideline are based on an extensive discussion of the current evidence to address the scientific misconduct in the work by Dr Poldermans (20, 29, 30). The first strong recommendation in the new guideline is that beta-blockers should be continued in patients undergoing surgery who have been on these agents chronically (Class I recommendation; Level of Evidence B) (20). The second strong recommendation is that beta-blockade should not be commenced in the perioperative period without titration or in low-risk patients (Class III recommendation; Level of Evidence B) (2). The roles of this group of pharmacologic agents both in cardiac and non-cardiac surgery continues to be vigorously explored in the literature (31, 32).

The 2014 ESC/ESA guideline also reviewed the role of perioperative statin therapy (20). Expert opinion strongly recommended perioperative continuation of statins, in particular statins with a long half-life or an extended-release formulation (Class I Recommendation; Level of Evidence C) (20, 33).

The guideline also favored consideration of preoperative initiation of statin therapy in vascular surgical patients at least 2 weeks before surgery (Class IIa recommendation; Level of Evidence B) (20, 33). In the setting of angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers, the guideline has recommended continuation or initiation at least a week before surgery in stable patients with heart failure or left ventricular systolic dysfunction (Class IIa Recommendation; Level of Evidence C) (29). In the setting of hypertensive patients, the guideline has also recommended that transient discontinuation of these agents be considered (20, 34).

The ESC/ESA guideline has also strongly recommended against alpha-2 agonists for prevention of myocardial events in patients undergoing noncardiac surgery (20). The global randomized **P**eri**O**perative **IS**chemic **E**valuation-2 (POISE-2) trial evaluated the effects of clonidine (0.2 mg/day) in patients with or at risk for atherosclerotic disease who underwent non-cardiac surgery (N = 10,010: 135 centers in 23 countries) (35, 36). In this high-quality trial, low-dose clonidine was

initiated just prior to surgery and continued for 72 hours. The primary trial endpoint was defined as a composite of death or nonfatal myocardial infarction at 30 days.

In summary, clonidine did not reduce this primary outcome (hazard ratio 1.08; 95% confidence interval 0.93-1.26; P = 0.29) (36). Furthermore, clonidine exposure significantly increased the risks of clinically important hypotension (hazard ratio 1.32; 95% confidence interval 1.24-1.40; P < 0.001) and nonfatal cardiac arrest (hazard ratio 3.20; 95% confidence interval 1.17-8.73; P = 0.02) (36). Further trials of this caliber are required to inform perioperative management of the high-risk cardiovascular patient for non-cardiac surgery (20, 35, 36).

The POISE-2 investigators have also investigated the effects of aspirin in adult non-cardiac surgery (37). Patients at risk for vascular events were stratified according to previous aspirin exposure. The initiation stratum (N = 5628), consisting of patients who were not previously on aspirin who were subsequently randomized to aspirin or placebo just prior to surgery and thereafter for the first 30 days (37).

The continuation stratum (N = 4382), consisting of patients already on aspirin, were also randomized to aspirin or placebo on the day of surgery for 7 days, after which patients were managed on their usual aspirin regimen. It is important to note that patients with recent coronary stents were excluded, defined as 6 weeks or less after bare metal coronary stent or within 12 months after a drug-eluting coronary stent (37).

The defined primary trial outcome was a composite of death or nonfatal myocardial infarction at 30 days. Aspirin exposure did not decrease the incidence of the defined primary outcome (hazard ratio 0.99; 95% confidence interval 0.86-1.15; P = 0.92) (37). Furthermore, aspirin exposure significantly increased the risk of major bleeding (hazard ratio 1.23; 95% confidence interval 1.01-1.49; P = 0.04) (37). These adverse outcomes from the POISE-2 trial explain the strong recommendation in the 2014 ESC/ESA guideline against routine aspirin therapy in adult non-cardiac surgery. Rather, the decision for perioperative aspirin therapy should be individualized to optimize the risks and benefits (20).

In the setting of recent percutaneous coronary intervention, the 2014 ESC/ESA guideline recommends the continuation of dual antiplatelet therapy for the first 4 weeks after bare metal stent implantation and for the first (3-12) months after drug-eluting stent implantation, given the higher risk of perioperative stent thrombosis in this patient population (38, 39). In patients who have undergone coronary stenting, management of perioperative antiplatelet therapy should be based on a perioperative consensus with consideration of the risks of bleeding versus the risks of stent thrombosis (20, 38-40).

An analysis from a large non-cardiac surgery registry (N = 41,989: 2000-2010) suggests that 3 factors independently predict for major adverse cardiovascular events: emergency hospital admission (odds ratio 4.77; 95% confidence interval 4.07-5.59); myocardial infarction within preceding 6 months (odds ratio 2.63; 95% confidence interval 2.32-2.98); and, a revised cardiac risk index score > 2 (odds ratio 2.13; 95% confidence interval 1.85-2.44) (41). In this perioperative registry, MINS appeared to be independent of coronary stent type or timing of surgery beyond 6 months after stent implantation (41).

These findings challenge the current guideline emphasis on stent type and timing of surgery (42, 43). Although further trials are still required, it is likely that advances in stent design will further reduce the risk of perioperative stent thrombosis (43, 44).

In cardiac surgery, the debate continues about the optimal perioperative manage-

ment of platelet blockers (45, 46). Recent evidence from meta-analysis suggests that, although continuation of platelet blockade increases bleeding, it has no adverse effects on major clinical outcomes and is associated with a low risk for mediastinal exploration (45). Furthermore, aspirin therapy may reduce acute kidney injury and mortality after cardiac surgery in patients with chronic kidney disease (46). The risks and benefits of this perioperative platelet blockers have to be individualized both in cardiac and noncardiac surgery.

Myocardial Revascularization - European Perspectives

The ESC and the European Association of Cardiothoracic Surgery (EACTS) published in 2014 an extensive collaborative guideline about myocardial revascularization consisting of 100 pages and 964 references (47). The following commentary will highlight selected perioperative aspects.

Coronary artery bypass grafting (CABG) was first performed in 1964 and so has its 50th anniversary in 2014 - it has accordingly been selected as a highlight for 2014 (47, 48). The first percutaneous coronary intervention (PCI) was performed in 1977 (49). Since then, these two procedures for myocardial revascularization have undergone multiple advances and have also been subjected to multiple randomized trials and comparisons. The 2014 ESC/EACTS guideline represents a collaborative effort between cardiologists and cardiac surgeons to develop a balanced evidence-based approach to myocardial revascularization that is patient-focused (47).

The role of the intra-aortic balloon pump (IABP) in myocardial revascularization continues to be debated, despite its safety and efficacy profile (47, 50, 51). Although recent trials have challenged the outcome value of IABP in CABG, an updated meta-analysis of randomized controlled trials (N = 625: 8 trials) has demonstrated benefit for preoperative IABP in adult CABG (52). In this meta-analysis, preoperative IABP reduced perioperative mortality in adult CABG (3.5 % versus 11.0 %; risk ratio 0.38; 95 % confidence interval 0.20-0.73; P = 0.04) (52). This survival benefit persisted when analysis was confined to trials with low bias, trials reporting outcomes at 30 days and in patients undergoing on-pump CABG (52). Despite this outcome benefit, the 2014 ESC/EACTS guidelines do not recommend IABP insertion as a routine in patients with cardiogenic shock (Class III Recommendation; Level A Evidence) (47).

The ESC/EACTS guidelines for myocardial revascularization strongly endorse the role of CABG in patients with chronic renal disease (47). In this high-risk population, fenoldopam has been highlighted as a possible perioperative intervention to reduce mortality based on democracy-based medical consensus and recent meta-analyses (53-55). A recent multicenter randomized placebo-controlled trial throughout Italy (N = 667: 19 medical centers) evaluated the effect of fenoldopam on acute kidney injury after cardiac surgery, including CABG (45 % of study sample) (56). The intervention with fenoldopam was with continuous infusion of the drug at a starting dose of 0.1 mcg/kg/min (range 0.025-0.3 mcg/kg/min) (56). The primary trial end point was the rate of renal replacement therapy. After interim analysis, the trial was terminated for futility, given the lack of outcome effect with respect to the primary end point (20 % versus 18 % in the placebo group: P = 0.47) and the significant risk of hypotension associated with exposure to fenoldopam (25 % versus 15 %: P = 0.001) (56). Despite the promising trends in meta-analysis, fenoldopam does not appear to be nephroprotective after cardiac surgery with cardiopulmonary bypass, including CABG (56).

Although the ESC/EACTS guidelines discuss selected procedural aspects of CABG in detail, there is no commentary on anesthetic technique (47). The debate about outcome effects of volatile versus intravenous anesthesia is ongoing in adult cardiac surgery, including CABG (57-60).
Further adequately powered trials are indicated both in cardiac and non-cardiac surgery to delineate whether anesthetic choice for general anesthesia affects major perioperative outcomes such as mortality and renal failure.

CONCLUSION

The past year has seen significant strides forward in our specialty. Acute and chronic adult aortic diseases have experienced major progress in perioperative management with respect to imaging and integrated intervention including endovascular and/or surgical measures. Cardiovascular management in non-cardiac surgery has advanced the focus to reduce perioperative mortality from myocardial ischemia.
Myocardial revascularization includes both percutaneous and surgical options. Despite 50 years since the first coronary artery bypass grafting procedure, this surgical option is still a major therapy for many patients. These 2014 advances will likely further improve perioperative outcomes for our patients.

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