The Future of Cardiothoracic Anesthesia

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- Cardiovascular anesthesia
- Reperfusion
- Stem cell therapy
- Genomics
- Future

“It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change.”  
—Charles Darwin

“The line it is drawn The curse it is cast The slow one now will later be fast as the present now will later be past The order is rapidly fadin’ and the first one now will later be last for the times they are a-changin’.”  
—Bob Dylan

These quotes hint that the future of any specialty lies in adaptation to change. Cardiothoracic anesthesiologists will certainly experience, and preferably effect, change in the health care system in the coming years. The specialty will simultaneously be presented with continuing changes in scientific knowledge, patient comorbidity burden, and novel surgical procedures that will challenge these practitioners to operate within an ever-expanding team of perioperative clinicians. The practice of cardiothoracic anesthesia will continue to evolve in parallel with those changes in technology, patient selection, and advanced procedures, and will also be affected by changes in standards of training, certification, and health care policy. Cardiovascular anesthesiologists already recognize that they have an important role in caring for the increasingly complex patients who will present in the future; it is one of the things that is most appealing about the specialty. It is the evolving complexity of perioperative management that will emphasize the importance of the practitioner’s development of effective communication and systems-based practice and of maintaining their place at the table where health care policy decisions are made.

TRANSLATION OF BASIC SCIENCE RESEARCH

The most fundamental predictor of the future success of cardiovascular anesthesia as a specialty lies in adaptation of the results of basic science research in

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a way that will benefit patients and change daily practice. These practitioners are fortunate to have, within the subspecialty and in their cardiovascular medicine and surgical colleagues, a remarkable group of scientists who are asking the right questions and performing groundbreaking research that will continue to advance the practice.

**Preconditioning and Intermittent Reperfusion**

A large number of surgical procedures involve temporary interruption of blood supply to vital organs, causing ischemia and potential tissue damage. Virtually all cardiac and thoracic surgeries, particularly those involving cardiopulmonary bypass, deep hypothermic circulatory arrest, or organ transplantation, involve ischemia and reperfusion of the heart and lungs. Methods of protection during these periods of ischemia and reperfusion are of great interest and have been the focus of decades of research. Cardiac protection began with the invention of cardiopulmonary bypass, the application of hypothermia, and the performance of antegrade and retrograde cardioplegia. Despite these measures, global and focal cardiac injury, the resulting functional impairment, and ischemic injury to other vital organs, continue to be major concerns for cardiovascular anesthesiologists.

In 1986, the first evidence was reported of a novel concept in protection: that of conditioning for prolonged cardiac ischemia through prior application of shorter cycles of ischemia. This initial study of ischemic preconditioning involved intermittent left anterior descending coronary artery occlusion followed by a longer episode of ischemia (40 minutes) in dogs. Infarction size was markedly reduced when compared with a control group that experienced only a single long episode of ischemia. Direct translation of the method to the clinical arena within cardiac surgery has been challenging. Studies of intermittent cross-clamping of the aorta before prolonged cross-clamping have shown a reduction in arrhythmias, inotropic support, and intensive care unit (ICU) length of stay after coronary artery bypass grafting (CABG). However, significant concern remains with the broad application of a technique that requires repeated clamping and unclamping of the aorta in a patient population known to be at risk for cerebral embolization with cross-clamp application. The search for methods of conditioning that can be more easily applied, such as preconditioning using anesthetics, normobaric or hyperbaric hyperoxia, hypoxia, helium, or low-dose carbon monoxide, has gained momentum in recent years. Lastly, investigators have suggested that reperfusion injury might be attenuated by intermittent or slow reperfusion, particularly of transplanted organs.

Perhaps the most intriguing of all these methods is the possibility of remote ischemic conditioning, wherein intermittent ischemia of a limb confers protection from ischemia for vital organs. The technique has been applied in a variety of settings, including after subarachnoid hemorrhage, before abdominal aortic aneurysm repair, and even in athletic training. Pilot studies initially indicated that this treatment had some benefit in adult patients undergoing CABG, but subsequent trials showed mixed results. Explanations for the inconsistency vary, but in all, results suggest that subsets of the patient population and certain surgical procedures may exist for which remote conditioning would be of benefit. Two large, multicenter, randomized controlled studies are currently underway to help resolve these issues (Effect of Remote Ischemic Preconditioning on Clinical Outcomes in Patients Undergoing Coronary Artery Bypass Graft Surgery, to be completed in 2013; and Remote Ischemic Preconditioning for Heart Surgery, to be completed in 2014). As of October 19, 2012, 29 additional studies for perioperative cardiac surgery match the search term “Cardiac Remote Preconditioning” in the ClinicalTrials.gov database.
In pediatric cardiac surgery, however, the results are far more promising, with an initial study indicating that children treated with remote conditioning required less inotropic support and experienced less myocardial injury.\(^8\) Direct ischemic postconditioning (intermittent release and reapplication of the aortic cross-clamp at the time of reperfusion) has also shown benefit in the pediatric cardiac surgical population in several studies.\(^9\,10\) This pediatric population, in contrast to an adult population with known cardiovascular disease, may have an improved risk/benefit profile with regard to repeated cross-clamping of the aorta, making this postconditioning treatment a viable option. In general, the pediatric population also benefits from a markedly lower burden of coexisting diseases, such as diabetes\(^11\) and hypertension,\(^12\) which may influence the magnitude of effect of conditioning stimuli. In all, these results suggest that preconditioning or postconditioning may be clinically applied to subsets of patients in the near future, pending results of ongoing trials.

**Stem Cell Therapy**

A second therapy that may be nearing implementation in cardiac surgical patients is stem cell therapy. The common result of myriad cardiac diseases is local or global fibrosis of myocardial tissue and a reduction in contractility, resulting in impaired function and cardiac output. The delivery of stem cells within myocardial tissue could, in theory, prevent remodeling and fibrosis caused by injury and maintain cardiac function. The exact mechanism for improvement is not yet clear, but evidence shows that increased cell differentiation, myocardial angiogenesis, and a direct paracrine effect on the extracellular matrix may all play a role.\(^13\) The therapy has been applied in humans after myocardial infarction, and a meta-analysis indicates that there were small but statistically significant improvements in ventricular volumes, infarct size, and left ventricular ejection fraction.\(^14\) Additional trials have shown reductions in mortality and readmission for heart failure,\(^15\) but others have also shown an initial benefit that disappeared after 6 months.\(^16\)

It has been suggested that persistence of effect is highly dependent on cell type and isolation technique,\(^17\) along with the method of delivery of the cells in question. A significant body of work has been generated investigating the ideal type of stem cell, each with advantages and disadvantages primarily involving ease of differentiation and separation of cell types, proliferation and survival of cells, and side effects of implantation.\(^13\) The most striking side effect noted to date has been teratoma formation at the site of injection with undifferentiated embryonic stem cells in mice,\(^18\) an issue that is avoided through implantation of differentiated cells. Delivery methods, perhaps of particular interest to the cardiovascular anesthesiologist, include percutaneous (intravascular, intracoronary, transvenous injection into coronary veins, or transendocardial delivery) or surgical (transepicardial cell or tissue-engineered) options, each meant to balance the risk and benefit of precise delivery with increasing invasiveness for each given patient.\(^17\)

**Perioperative Genomics**

The field of perioperative genomics, particularly for patients undergoing cardiac surgery and cardiopulmonary bypass, has been an area of considerable growth in the past decade. Research in the area primarily aims to identify and associate single nucleotide polymorphisms (SNPs) or sets of nearby SNPs (haplotypes) with various relevant outcomes. Identification is initially made through simultaneous evaluation of numerous SNPs within chromosomes and mitochondrial DNA (or even the entire genome) of individuals known to have had or not had the outcome of interest, and identifying SNPs or haplotypes that are found primarily in one group but not the other.
The concept is also often applied to elements downstream of the DNA: to the RNA, proteins (proteomics), or metabolic products of a cell (metabolomics). A positive association between a SNP, altered protein (structure or function), or metabolite and a disease or outcome can then be used as a hypothesis for more careful investigation of that element’s value as a predictor of risk, disease progression, response to therapy, or even as a therapeutic target.

Associations discovered using genome-wide analysis that are relevant to cardiac surgery and anesthesia include SNPs or haplotypes that relate to atrial fibrillation,19 metabolism of and response to warfarin,20 likelihood of restenosis after percutaneous coronary intervention,21 and propensity to develop thoracic aortic aneurysms (TAAs) and dissections.22 Five SNPs have been found to be associated with left ventricular size and aortic root diameter.23

Further evaluation of the data from genome-wide association studies (GWAS) analyses will be an ongoing task. One variant identified through GWAS as being associated with coronary artery disease and myocardial infarction has been confirmed as being independently associated with perioperative myocardial injury and mortality after CABG, and was shown to improve the prognostic value of the European System for Cardiac Operative Risk Evaluation (euroSCORE).24 A commercial test is available for the genetic variants associated with atrial fibrillation, and is expected to be of use in risk profiling for selected patients.19 The SNP associated with TAAs happened to be located within a gene (FBN1) that, when mutated, is well-known to cause Marfan syndrome, confirming that a genome-wide analysis can bring into focus mutations in genes with considerable clinical significance.22

With the recent and ongoing dramatic reduction in the cost of genetic analysis, whole GWAS for SNPs and haplotypes are becoming more common (Figs. 1 and 2). An enormous amount of hypothesis-generating data has been and will continue to be produced by these analyses. Academic cardiac anesthesiologists are increasingly involved in research implementing genomics, proteomics, and metabolomics to ask...
questions that were, until now, unanswerable using traditional laboratory methods. All cardiac anesthesiologists and clinicians involved in the perioperative care of the cardiac surgical patient will certainly use data derived using these new tools for risk stratification and treatment in the near future.

FELLOWSHIPS, TRAINING, AND CERTIFICATION

In response to the exciting challenges in this subspecialty, its future lies in enhancing the training for cardiovascular anesthesiologists. The first cardiac anesthesia fellowships were initiated more than 40 years ago, with Accreditation Council for Graduate Medical Education (ACGME) accreditation beginning in 2006. In the 2012–13 academic year, 74 fellowships are available in the United States, 58 of which are ACGME-accredited. Current ACGME requirements for adult cardiothoracic fellowship training include minimum numbers of valve, CABG, and thoracic aortic procedures; training in TEE; and time spent in the ICU setting with options in other related areas (perfusion, invasive cardiology, outpatient cardiology or pulmonary medicine, research, or pediatric cardiothoracic anesthesia). These requirements are meant to ensure adequate training to prepare individuals to confidently and safely perform and supervise perioperative care for a variety of cardiac and thoracic surgical procedures. However, a thorough knowledge of perioperative care for the patients seen in 2013 will not necessarily translate to care for the patients who will be seen in 2042 (or even in 2015); likewise, the knowledge gained by the first fellows 40 years ago is largely irrelevant to treatment of the patients they see today. What remains relevant, and what is likely to be increasingly relevant in the future, are the less-tangible skills acquired during the year of working within the subspecialty. Those skills, practice-based learning and improvement, systems-based practice, interpersonal and communication skills, and professionalism are identified by the American Board of Anesthesiologists and the ACGME as a part of the “core competencies” of all successful trainees. As surgical procedures and patient disease presentations and comorbidities become more complicated, the organization of the team of professionals involved in perioperative care also becomes more complex. Consider the example of a transcatheter aortic valve implantation procedure in a hybrid operating
room. The multidisciplinary team within the operating room consists of nursing staff, radiology technicians, surgical attendants, anesthesia technicians, anesthesiologists, cardiac surgeons, cardiologists, device representatives, cardiovascular perfusionists, and the patient. The success of the procedure relies on technical skills but, equally important, each individual’s ability to work effectively with diverse team members.

With regard to the more tangible skills a cardiovascular anesthesiologist demonstrates, the establishment of fellowships in the subspecialty led inevitably toward accreditation of those fellowships. Recent history has shown that accreditation of a fellowship often leads to the implementation of subspecialty board examination for certification, particularly for those subspecialties in areas of practice that overlap substantially with physicians in other fields of medicine, such as pain, critical care, sleep medicine, and transesophageal echocardiography. Board certification, as a tool to gain credibility within a larger community of practitioners, has not previously been encouraged for subspecialties of anesthesiology without such competition (pediatric, cardiothoracic, and obstetric anesthesiology). These standards become increasingly necessary as national health care policy is reevaluated. With this precedent, cardiovascular anesthesiology, a recognized subspecialty within ACGME accredited fellowships and therefore with readily defined standards for training, will likely join others in instituting board examinations for certification in the near future. An important question regarding specialty training in the face of greater emphasis on efficiency and cost-effectiveness will be how academic programs can fulfill their educational mission and remain competitive?

CHANGES AND OPPORTUNITIES IN US HEALTH CARE

Finally, it is clear that change will soon occur on a system-wide scale, and that the ability of cardiovascular anesthesiologists to adapt on all fronts will be tested. Changes and therefore opportunities in US health care have not been more apparent at the national and global level since the institution of Medicare more than 5 decades ago. The Patient Protection and Affordable Care Act will change the landscape of medical care, including the practice of anesthesiology. In the United States, while the national debate over government spending continues, the business reality of health care, with underlying issues surrounding health care cost and quality, remains constant. Many important issues remain unresolved, and many models of care redesign and care management have been and are being proposed to help solve these issues. Fee for service is giving way to capitation at a varying pace depending on regional market pressure. Along the way, performance and value are giving way to bundling and shared savings and risk. It is argued that the fiscal solvency of the Federal government depends on the success of care redesign. For example, Don Berwick, former Centers for Medicare and Medicaid Services administrator, has outlined a $2 trillion dollar opportunity in the US health care market between now and 2020 through the elimination of non-value-added costs.

The consequence of health is equally striking. Estimates show that the prevalence of obesity in Americans will grow from 35% to 42% by 2030. This national endemic is projected to lead to a decrease in life expectancy for the first time ever in the United States. Furthermore, this condition will be associated with significant economic costs from diabetes, osteoarthritis, hypertension, and the other clinical derivatives. Health and health care are global issues (eg, polio and maternal mortality in Nigeria, developing hospital systems in India, health insurance schemes in China). Everywhere in the world governments are addressing questions about the financing and delivery of health care in the face of increasing demands and limited resources.
Regardless of politics, legislation, or policy, health care in the United States is rapidly becoming a value-based economy in a manner not seen in more than 5 decades. In a value-base economy, value is defined by unique and differentiating quality.

“Quality is not what you put into a product; quality is what the customer gets out of it.”

—Peter Drucker

Going forward it is likely that the value proposition of specialty care and specialists will be defined differently: value \( (V) = \text{quality (Q)} \times \text{service (S)}/\text{cost (C)} \). Critical questions will need to be asked and answered, such as whether specialists can justify higher marginal costs with higher marginal quality, and whether specialists will shift up the quality axis or down the cost axis, or both. How cardiovascular anesthesiologists respond will shape the specialty. Data-driven evidence will build perceptions and realities of best practice decisions and policy. Only through collecting and sharing outcomes data can meaningful assessment and comparison be possible through comparative effectiveness research.

Specialists and primary care physicians will need to increase integration to increase efficiency and focus on reducing complications, such as readmissions. The subspecialty of cardiovascular anesthesia will need to distinguish itself as critical to this value proposition in this changing environment (eg, they already do this in preoperative clinics, which, in the absence of a universal electronic medical record [EMR], collects outside records before admission for surgery and can avoid duplicate testing and provide valuable succinct information for the anesthesiologist).

Cardiovascular anesthesia, having a distinct and unique body of knowledge within anesthesiology, will lead ways to explore opportunities for clinical integration with partners in medicine and surgery. Value opportunities for cardiovascular anesthesia to assume leadership positions in tomorrow’s care redesign include developing teamwork training and safety standards for the cardiac operating room, patient transition of care and hand-off processes, and patient transport standards. The specialty of cardiovascular anesthesia must take the lead in the science of safety to improve cross-disciplinary communication through identifying opportunities to reduce the risk of error and improve patient outcomes.

Diagnostic perioperative TEE has and will continue to distinguish the subspecialty of cardiovascular anesthesiology. TEE is recommended in the Practice Guidelines for Perioperative Echocardiography by the American Society of Anesthesiologists and Society of Cardiac Anesthesiologists (SCA) for all patients undergoing open chamber cardiac or thoracic aortic surgery in the absence of contraindications. Use during coronary artery bypass surgery is also suggested. In addition, intraoperative TEE has been shown to be beneficial during noncardiac surgery when high-risk cardiovascular disease and surgery might lead to life-threatening hemodynamic, pulmonary, or neurologic compromise. These recommendations for TEE use during cardiac and noncardiac surgery are mirrored in the recent guidelines from the European Association of Echocardiography and the European Association of Cardiothoracic Anesthesiologists. The use of ultrasound in intensive care and emergency medicine has also evolved. In the future, surface ultrasound will be integrated into the everyday clinical practice as ultrasound-assisted examination and ultrasound-guided procedures. The SCA has led and must continue to be out front in the development of criteria for clinical application on TEE use based on research. Furthermore, specific criteria for perioperative TEE training have and are based on clinical research largely performed by cardiovascular anesthesiologists.
In addition, cardiovascular anesthesiology should assume leadership within the health system for blood management and take a leadership role in the coagulation laboratory. In the United States, unneeded services, inefficient delivery, and/or missed opportunities have been estimated to represent nearly 300 billion of the 2.8 trillion dollars spent on health care per year. The lack of guideline adaptation and variability in clinician practice has also been reported to continue to lead to the inappropriate use of blood components. More than 16,000,000 units of red blood cells and more than 5,000,000 units of plasma are transfused per year, with more than 60,000 adverse reactions reported, or 0.25% events per component administered. Blood transfusion continues to be 1 of the top 5 fastest growing procedures in medicine today. Blood transfusions occur in 1 of 10 of all hospital stays that involve a procedure. On the other end of the continuum, bleeding continues to be a major problem and contributor of morbidity in high-risk cardiac and aortic surgery. Knowledge of coagulation medicine and coagulation pharmacology falls easily within the domain of the subspecialty of cardiovascular anesthesiology. The role and value of cardiovascular anesthesia in blood management is self-evident.

Finally, going forward, rapid response management and postcardiac surgery critical care must be defined and shaped by both cardiac anesthesiologists along with cardiac surgeons when appropriate, in this country.

CLOSING THOUGHTS

The future of cardiothoracic anesthesia, simply stated, depends on establishing and maintaining a unique and differentiated quality and identity that promotes and contributes positive value to patients, surgical colleagues, and health system administrators who are all also responsible for seeking value. Cardiovascular anesthesiologists must therefore be prepared to define their value through demonstrating their unique qualities. To do this, they must codify and continue to push the leading edge in education, research, and clinical innovation for the subspecialty of anesthesia, and thereby ensure a role in defining true value as the best. Their value will be based on their ability to accept the challenge to differentiate themselves from others. They face a time in health care of great change with great opportunity.

REFERENCES
