The Year in Cardiothoracic and Vascular Anesthesia: Selected Highlights From 2015

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THIS ARTICLE IS the eighth in an annual series for the *Journal of Cardiothoracic and Vascular Anesthesia*.[1] The authors thank the editor-in-chief, Dr. Kaplan, and the editorial board for the opportunity to continue this series, namely the research highlights of the year that pertain to the specialty of cardiothoracic and vascular anesthesia. The major themes selected for this past year are outlined in this introduction, and each highlight is reviewed in detail in the main body of the article.

The literature highlights in the specialty for 2015 begin with the mitral valve revolution.[2] Surgical intervention is now a reasonable option for asymptomatic severe mitral regurgitation. Recent landmark randomized trials from the Cardiothoracic Trials Surgical Network (CTSN) have further refined the surgical management of mitral valve disease. The role of transesophageal echocardiography (TEE) has remained central throughout these advances, especially now as transcatheter mitral interventions enter clinical practice. The second major theme in the specialty for 2015 is the development of temperature guidelines for the conduct of cardiopulmonary bypass for adult cardiac surgery. These guidelines likely will stimulate further trials to augment the evidence base and also focus attention on temperature management in specialized areas of cardiopulmonary bypass, such as hypothermic circulatory arrest. The third major theme for the specialty is the focus on the right ventricle with respect to clinical outcomes and echocardiography. The themes selected for this eighth highlights article are only a sample of the advances in the specialty during 2015. These highlights likely will further improve important perioperative outcomes for patients with cardiovascular disease.

THE MITRAL VALVE REVOLUTION

Mitral regurgitation (MR) remains a leading valve disease in the developed world, with an incidence that is likely to rise as the population ages.[2–4] The surgical management of MR has evolved progressively since being championed by Alain Carpentier in the 1970s and 1980s.[3–6] Mitral valve (MV) repair is now the preferred surgical intervention for MR and, in major referral centers, it can be accomplished in the majority of patients with minimal mortality in the setting of expert cardiac anesthesia and TEE.[6–8] The MV revolution for MR now has progressed beyond the concept of MV repair to include the transcatheter era.[9] The following examines this journey into new clinical realms, taking into account the latest clinical trials.

Surgical Intervention for Asymptomatic Severe Mitral Regurgitation

Even though there is widespread agreement on the importance of surgical intervention in symptomatic patients with severe MR, there continues to be significant international disagreement regarding early surgical intervention for patients experiencing asymptomatic severe MR.[5] The American College of Cardiology/American Heart Association guidelines designate early MV surgery a class-IIa recommendation; whereas European guidelines are more conservative, with a class-IIb recommendation.[3,5,10] Proponents for this early surgical approach of early intervention argue that the success rate of MV repair in experienced centers may prevent the deleterious effects of myocardial dysfunction due to severe MR.[11] A recent meta-analysis demonstrated that early MV surgery compared with watchful waiting in patients experiencing asymptomatic, severe, degenerative MR significantly reduced all-cause mortality at 10 years (hazard ratio [HR] 0.38;

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95% confidence interval [CI] 0.21-0.71), with no difference in rates of operative mortality (0.7% for both cohorts).[12] This survival benefit due to early MV surgery persisted in patients without atrial fibrillation or pulmonary hypertension, current class-II indicators for MV surgery in contemporary guidelines (relative risk [RR] 0.85; 95% CI 0.75-0.98).[3,10,12] A further advantage of the early MV intervention paradigm is that it significantly increases the likelihood of MV repair (RR 1.10; 95% CI 1.02-1.18).[12] Further randomized trials are required to determine whether surgical intervention truly is indicated in patients experiencing asymptomatic, severe mitral regurgitation. This question is a possible opportunity for the CTSN.

Recent Randomized Trials From the Cardiothoracic Trials Surgical Network

Aside from the success of MV repair in degenerative MR, the treatment of ischemic MR still remains controversial.[3,10,13] The guidelines to date have been derived from an evidence base consisting of small observational and randomized studies that differed in design, study population, and definition of MR.[13,14] Results of 2 significant randomized trials were published in 2014 from the CTSN that provided further clarification.[15,16] Acker et al examined the impact of MV repair versus replacement for severe ischemic MR in 251 patients.[15] No significant differences in left ventricular (LV) reverse remodeling or survival were noted at 12 months.[15] The recurrence of moderate or greater MR at 12 months was significantly higher for MV repair compared with replacement (32.6% *v* 2.3%: $p < 0.001$).[15] The main mechanism for failure of MV repair in this key randomized trial was ongoing MV leaflet tethering.[17] Although a multivariate model was derived to predict the risk of recurrent MR in this setting, there already has been a call for a more definitive surgical approach for MV repair in ischemic MR.[17,18]

In patients with both moderate MR and coronary artery disease, the decision to perform both coronary artery bypass grafting (CABG) and correction of moderate MR has remained unclear.[13,14] In the largest prospective randomized trial to date, the Surgical Treatment of Moderate Ischemic Mitral Regurgitation Trial, Smith et al randomly assigned 301 patients with moderate ischemic MR at 26 sites to CABG alone or CABG plus MV repair.[16] The primary endpoint was the left ventricular end-systolic volume index at 1 year. In patients with moderate ischemic MR, the combination of MV repair and CABG did not result in a higher degree of LV reverse remodeling as reflected by the left ventricular end-systolic volume index (z score 0.50; $p = 0.61$), although the risk of recurrent significant MR was significantly lower in the MV repair cohort (11.2% *v* 31%; $p < 0.001$).[16] Even though MV repair resulted in a reduced risk of downstream MR, it was associated with longer cardiopulmonary bypass (CPB) times ($p < 0.001$), longer hospital stays after surgery ($p < 0.002$), and more neurologic events ($p < 0.03$).[16] At 1 year, the investigators concluded that there was no meaningful advantage to adding MV repair to CABG in patients with incidental moderate MR. Further clinical monitoring of this CTSN trial cohort may demonstrate a net outcome advantage due to reduced downstream MR associated with MV repair.[13,14,16]

A third CTSN trial in patients presenting for MV surgery examined the role of surgical ablation for concomitant atrial fibrillation in this setting.[19] Atrial fibrillation has a prevalence of 30% to 50% in this population and has important outcome effects, such as reduced survival, stroke, and significant economic burden.[20–23] Given that atrial fibrillation is common and important, it hardly is surprising that the CTSN chose it for this randomized trial in which a cohort of 260 patients with chronic atrial fibrillation presenting for MV surgery were randomized with respect to surgical ablation.[19] Furthermore, all patients underwent left atrial appendage ligation, and the ablation cohort further was assigned randomly to pulmonary vein isolation versus a biatrial maze procedure.[19] The primary trial endpoint was freedom from atrial fibrillation in the first year as detected by 3-day Holter monitoring.[19]

Freedom from atrial fibrillation in the first year was significantly enhanced by surgical ablation (63.2% *v* 29.4%; $p < 0.001$). Furthermore, simple pulmonary vein isolation was as effective as an extensive biatrial maze procedure in providing freedom from atrial fibrillation (61% *v* 66%; $p = 0.60$). Although concomitant surgical ablation added no additional outcome risk including mortality (HR 0.76; 95% CI 0.32-1.84; $p = 0.56$), it did significantly increase the risk for a permanent pacemaker (21.5 *v* 8.1 per 100 patient years; $p = 0.01$).[19]

In summary, these 3 recent randomized trials from the CTSN significantly have enhanced the surgical management of patients with significant MR. Given the controversy surrounding asymptomatic degenerative MR, this management decision may lend itself to a landmark randomized CTSN trial, as outlined earlier.

Role of Percutaneous Mitral Valve Interventions

As reflected in both European and American valvular heart disease recent guidelines, there remains inconclusive evidence to guide the surgical management of significant secondary MR.[3,10] Transcatheter mitral techniques may offer expanded treatment options in high-risk cohorts with significant MV disease.[9,24] Although transcatheter devices have borrowed the principles of surgical MV repair, they now include techniques for leaflet resection, neochordal construction, annuloplasty, and edge-to-edge leaflet approximation that have spawned a family of randomized trials with defined endpoints.[2,25–27] While there are multiple devices currently in trials for feasibility, the MitraClip device (Abbott, Abbott Park, IL), modeled after the surgical edge-to-edge repair (Alfieri stitch), has been used extensively with more than 19,000 applications worldwide.[9,24] A randomized trial that evaluated MitraClip in degenerative MR resulted in commercial approval of the device in the United States in 2013.[28,29] The anesthetic approach for this procedure already has been discussed extensively in the *Journal*.[29,30] The Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II randomly assigned 279 patients with severe degenerative MR to transcatheter MitraClip repair or open surgical repair.[28] The primary trial endpoint for efficacy was a composite of freedom from the following 3 outcomes at 12 months: death, MV surgery, and severe MR.[28] The primary trial endpoint for safety was a composite of major adverse