Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Special Article

The Year in Cardiothoracic and Vascular Anesthesia: Selected Highlights from 2020

Archer Kilbourne Martin, MD[*,1], Menachem M. Weiner, MD[†], Jared W. Feinman, MD[‡], Himani V. Bhatt, DO, MPA[†], Ashley Virginia Fritz, DO[§], Matthew M. Townsley, MD, FASE[¶,‖], Archit Sharma, MD, MBA[#], Kristin Stawiarski, MD[**], Saumil J. Patel, MD[‡], Elizabeth Y. Zhou, MD[‡], Dylan R. Addis, MD[¶], Lourdes Al Ghofaily, MD[‡], Anita K. Malhotra, MD[††], Miguel T. Teixeira, MD[‡‡], Sudhakar Subramani, MD, FASE[#], Lovkesh Arora, MD[#], Christopher R. Cowart, MD[†], Arun L. Jayaraman, MD, PhD[§§], Harish Ramakrishna, MD, FASE, FACC, FESC[§]

[*]*Division of Cardiovascular and Thoracic Anesthesiology, Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Jacksonville, FL*

[†]*Department of Anesthesiology, Perioperative, and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, NY*

[‡]*Department of Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*

[§]*Division of Cardiovascular and Thoracic Anesthesiology, Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN*

[¶]*Department of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham School of Medicine, Birmingham, AL*

[‖]*Bruno Pediatric Heart Center, Children's of Alabama, Birmingham, AL*

[#]*Department of Anesthesiology, University of Iowa Hospitals and Clinics, Iowa City, IA*

[**]*Department of Cardiology, Bridgeport Hospital, Yale-New Haven Health, Bridgeport, CN*

[††]*Division of Cardiothoracic Anesthesiology and Critical Care, Penn State Hershey Medical Center, Hershey, PA*

[‡‡]*Division of Critical Care Medicine, Department of Anesthesiology, Stanford School of Medicine, Palo Alto, CA*

[§§]*Division of Cardiovascular and Thoracic Anesthesiology, Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Scottsdale, AZ*

THIS SPECIAL article is the 13th in an annual series for the *Journal of Cardiothoracic and Vascular Anesthesia*. 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 past year in the specialty of cardiothoracic and vascular anesthesiology.[1] The major themes selected for 2020 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 2020 begin with an update on valvular disease, with a focus on updates in management of aortic and mitral valve disorders. The second major theme is an update on coronary artery disease, with discussion of both medical and surgical management. The third major theme is focused on the perioperative management of patients with coronavirus disease 2019 (COVID-19), with the authors highlighting literature discussing medical, surgical, and anesthetic considerations for

[1]*Address correspondence to* Archer Kilbourne Martin, MD, Division of Cardiovascular and Thoracic Anesthesiology, Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL, 32224.

E-mail address: Martin.Archer@mayo.edu (A.K. Martin).

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their cardiac care. The fourth major theme is an update in heart failure, with discussion of medical, psychosocial, and procedural aspects of this complicated disease process. The fifth and final theme focuses on the latest analyses regarding survival in heart transplantation. The themes selected for this 13th special article are only a few of the diverse advances in the specialty during 2020. These highlights will inform the reader of key updates on a variety of topics, leading to improvement of perioperative outcomes for patients with cardiothoracic and vascular disease.

Key Words: transcatheter valve replacement; transcatheter valve repair; coronary artery disease; left ventricular assist device; cardiothoracic transplantation; heart transplantation; coronavirus disease 2019; COVID-19

Updates in Valvular Disease

Valvular heart disease affects a significant percentage of the population and remains one of the most common reasons for consultation with a cardiologist or cardiac surgeon.[2] Research is ongoing in an effort to better understand which cohort of patients will benefit from traditional surgical therapies versus minimally invasive approaches and which patients should be managed with medical therapy alone. During the past year, a number of prominent studies have addressed these important concerns.

Prognosis for Patients with Moderate Aortic Stenosis

Aortic stenosis (AS) remains one of the most commonly encountered cardiac pathologies in the elderly population and is associated with significant morbidity and mortality.[3] Current practice guidelines for patients with severe symptomatic AS or patients with severe AS (aortic valve area < 10.0 cm^2) and left ventricular systolic dysfunction (LVSD) are well-established and recommend aortic valve replacement (AVR) for this patient population.[4,5] Guidelines for surgical therapies in moderate AS currently recommend consideration of AVR only when the patient is undergoing cardiac surgery for another indication; however, these guidelines are not as well-established and require further investigation.[4] Previous studies, including those by van Gils et al.[6] and Delesalle et al.[7], found that moderate AS with or without concomitant heart failure is not as benign as previously believed, thus raising the question regarding the potential benefit of AVR in this patient population. However, nearly all relevant studies have had limited numbers of patients or short-term follow-up. Therefore, there remained a gap in the literature for more definitively understanding the prognostic effect of increasing severity of AS to better guide the clinical management of these patients.

Strange et al. sought to answer this question using data from the Australian National Echocardiography Database.[8] Out of a total of 122,809 male patients (mean age 61 $\pm$ 17 years) and 118,494 female patients (mean age 62 $\pm$ 19 years) with measured aortic valve (AV) hemodynamics, 16,129 (6.7%), 3,315 (1.4%), and 6,383 (2.6%) patients had mild, moderate, and severe AS, respectively. The median follow-up was 1,208 days. Not surprisingly, study investigators found that increasing severity of AS was associated with worse one- and five-year mortality. However, what was more provocative was the finding that there was a clear dichotomy of risk in overall survival using age- and sex-adjusted Cox regression models, with no AS (reference) and mild AS (hazard ratio [HR] 1.02; 95% confidence interval [CI] 0.98-1.07; $p = 0.32$) having similar risk profiles and moderate AS (HR 1.19; 95% CI 1.12 -1.26; $p < 0.001$) and severe AS (HR 1.22; 95% CI 1.13-1.31; $p < 0.001$) having similar risk profiles. The overall five-year mortality was 56% and 67%, respectively, in those with moderate AS (mean gradient 20.0-39.0 mmHg/peak velocity 3.0-3.9 m/s) and severe AS ($\geq$40.0 mmHg, $\geq$4.0 m/s, or AV area $<$1.0 cm^2 in low-flow, low-gradient severe AS). The authors found that the threshold of increased risk of longer-term all-cause and valve-related mortality was at approximately a mean AV gradient of 20.0 mmHg and an equivalent peak AV velocity of 3.0 m/s. The authors concluded that there needs to be a reevaluation of the prognostic effect of moderate AS and the potential value of more timely interventions to reduce a high risk of mortality in the medium to longer term.

Even though the study was not without its limitations, including a lack of adjustment for comorbidities, this study has laid an important foundation for future studies on the prognostic effects of moderate AS and its management. In addition, it is still unclear from this study whether moderate AS patients will benefit from AVR.

Minimal Access Versus Sternotomy for Complex Mitral Valve Repair

As advancements continue in minimally invasive cardiac surgery, debates comparing newer versus traditional surgical approaches to treat a wide range of cardiac pathologies are encountered. Moscarelli et al. compared traditional median sternotomy to a minimally invasive approach for repair of complex mitral valve disease (MVD), specifically bileaflet and Barlow's MVD.[9] They examined how each approach affected the long-term outcomes of these patients by studying whether either technique was more or less likely to result in moderate mitral regurgitation (MR) or mitral valve repeat surgery over a period of up to 10 years. This information previously had been examined in several single-center studies at high-volume centers and for which no difference was found between the two approaches.[10,11]

The authors used a pooled meta-analysis of studies reporting follow-up of mitral valve repair (MVR) for complex mitral valve regurgitation and examined two outcomes. The primary outcome was recurrence of MR and need for repeat surgery, and the secondary outcomes were surgery time, reopening for

bleeding, associated tricuspid procedures, failed repair, and in-hospital mortality. Eighteen studies involving more than 1,900 patients were used in total, and no significant differences were found between MR recurrence and need for repeat surgery between the minimally invasive and sternotomy groups (1.7% [95% CI 1.0%-2.9%] *v* 1.3% [95% CI 0.9%-1.8%]; p = 0.22). There also were no statistically significant differences in secondary outcomes. Of note, the minimally invasive group was associated with longer aortic cross-clamp and cardiopulmonary bypass times ($p < 0.01$).

Despite these compelling results, there still is likely to be a considerable amount of resistance to move toward a minimally invasive approach to treating complex MVD. There are a few reasons for this lack of acceptance. The first is the potential for adding unnecessary complexity to an otherwise straightforward surgery. Minimally invasive techniques, even though advancing, still are technically difficult to perform and likely to add complexity without any known functional long-term benefit to the patient.[12] Second is the goal of a curative surgery without encountering complications. Many patients with complex MVD are young and otherwise healthy. As such, they likely are to be cured of their disease with a successful surgery.[13] Therefore, the question remains, should physicians give up a definitive treatment in an effort to move toward a minimally invasive approach for the possibility of better aesthetics and one fewer day in the hospital? Finally, there are no data beyond 10 years for these patients.[10] Many proponents of traditional sternotomy approach note that minimally invasive approaches may not adequately address complex valve lesions with large myxomatous tissue or annular calcifications. These issues may arise when longer-term data become available.[12]

Despite this hesitancy to move away from traditional approaches to fixing conditions such as complex MVD, anesthesiologists must be aware of the fact that there is a clear interest in treating more severe conditions with a minimally invasive approach.[14] Percutaneous techniques have shown some success in treating a wide array of cardiac conditions and will continue to evolve. As such, there is a growing need for investigations that compare long-term outcomes of each approach in order to feel confident that more complex conditions can be addressed in a minimally invasive fashion.[14]

Novel Transcatheter Mitral Valve Prosthesis for Patients with Severe Mitral Annular Calcification

MVD in patients with mitral annular calcification (MAC) long has been a difficult pathology to treat. Because of the difficult anatomy associated with MAC, surgical options traditionally have been limited because replacement of these valves commonly can lead to fatal atrioventricular groove disruption and paravalvular leak.[15] Moreover, many patients who have MVD and MAC commonly are found to have numerous other comorbidities, making them less-than-ideal surgical candidates and, therefore, often are deemed to be too high risk for surgery.[16] Fortunately for these patients, new techniques are on the horizon that may present less-invasive options for MVR in patients with severe MAC.

The concept of a transcatheter approach for MVR to treat MVD in patients with severe MAC was first described in 2013 by Hasan et al., who used a balloon-expanding aortic valve (such as those used in transcatheter aortic valve replacements) to treat mitral stenosis in a patient with severe MAC.[17] Since that time, several reports have described similar techniques, with considerable success.

Sorajja et al. described a new, anatomically designed mitral prosthesis (Tendyne prosthesis; Abbott Vascular, Santa Clara, CA) using a transcatheter approach for MVR to treat patients with MR and severe MAC.[18] The valve is self-expanding, fully retrievable, and repositionable and is implanted via a transapical approach. A total of nine patients, with a mean age of 77 years, were recruited for this study at five different medical centers. Study participants had to meet the following four inclusion criteria: symptoms of heart failure, severe MR (defined using standard American Society of Echocardiography criteria), severe MAC, and prohibitive surgical risk. Of note, patients with severe left ventricular dysfunction, severe tricuspid regurgitation, or pulmonary hypertension were excluded. The authors reported complete relief of MR in all nine patients, stating that seven of them required balloon valvuloplasty before deployment of the prosthetic valve. They reported no device embolization and no mitral gradient after the procedure; and no patients required the use of extracorporeal circulation or other invasive hemodynamic support. One case resulted in technical failure caused by left ventricular outflow tract obstruction after the prosthetic valve became malrotated. This patient later underwent alcohol septal ablation and ultimately experienced a postoperative cardiac arrest, leading to end-organ damage and an eventual hospice admission. Another patient subsequently developed a hemothorax requiring drainage. Of the nine patients, five ultimately were sent directly home, and four were discharged to a nursing facility.

Long-term clinical follow-up was carried out over 28 months. One patient, previously described, died on postoperative day 41 in hospice, and another died of suicide eight months after the trial was completed. The remaining seven patients were free of MR and saw improvement in their symptoms. Two of the study participants ultimately were admitted to the hospital for heart failure during the follow-up period. The authors reported no incidence of major adverse clinical events. This investigation by Sorajja et al. was an optimistic outlook for the future in terms of transcatheter mitral valve replacement for patients with severe MR and MAC. Although this was a small case series with strict inclusion criteria, it highlighted some of the potential benefits of using these techniques in high-risk populations and certainly demonstrated the feasibility of providing relief for these patients.

Updates in Coronary Artery Disease

Coronary artery disease is a significant source of both morbidity and mortality within the adult population worldwide.[19] The spectrum of treatment spans from medical management to a range of invasive procedural and surgical options. Studies

highlighted include updates from major studies covering the entire scope of these clinical concerns.

Invasive Versus Conservative Management for Stable Coronary Disease

The question as to when, if at all, to intervene in stable coronary disease is one that has been examined in many small and large trials without a definitive conclusion being reached. Several large-scale clinical trials of stable ischemic heart disease have demonstrated the effectiveness of lifestyle and pharmacologic interventions in reducing the likelihood of major adverse cardiac events. However, many patients still undergo routine cardiac catheterization and revascularization for stable disease, which have not been demonstrated to confer any mortality benefit.[20–23] The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) sought to address this conundrum, and its initial results were published in the *New United Kingdom Journal of Medicine* in 2020.[24]

This study enrolled patients with stable coronary disease and moderate-severe ischemia, randomly assigning them to an initial invasive strategy of angiography and revascularization plus optimal medical therapy or an initial conservative strategy of optimal medical therapy with the option for later intervention.[25] A total of 5,179 patients were enrolled at 320 sites across 37 countries, with a primary composite outcome of death from cardiovascular causes, myocardial infarction (MI), or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest. The authors found no difference between the initial aggressive and conservative management groups with respect to the primary composite outcome over a median of 3.2 years (event rate of 16.4% and 18.2% at 5 y, respectively, 95% CI −4.7 to 1.0). The study also examined a secondary outcome of death from cardiovascular causes or MI and similarly found no significant difference between the two groups.

One methodologic issue raised by the study findings was how a study examining coronary disease defined "myocardial ischemia." In the ISCHEMIA trial, patients with a positive stress test underwent coronary computed tomographic angiography to diagnose the presence of coronary disease. The trial did not routinely use fractional flow reserve during catheterization as part of its definition, which is more sensitive to lesion-specific ischemia detection and was shown in a previous trial to significantly reduce death, MI, and repeat revascularization.[26] The effect of the completeness and method of revascularization also was not addressed in the initial outcomes of the ISCHEMIA trial nor were any quality-of-life metrics that may have led toward a greater rate of intervention. Although there surely are more data to come from this trial and others on conservative management versus revascularization, the initial results from ISCHEMIA point toward conservative medical therapy as a viable treatment path for at least a subset of patients with stable coronary disease.

Percutaneous Coronary Intervention Versus Coronary Bypass Graft Surgery for Left Main Disease

As percutaneous coronary interventions (PCI) have increased in prevalence over the past several decades for increasingly complex coronary arterial lesions, left main disease remains one of the few lesions for which the majority of patients are referred for coronary artery bypass grafting (CABG). Subgroup analysis of previous studies suggested that PCI may be an acceptable alternative to CABG in patients with left main disease of low or intermediate anatomic complexity.[27] The Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial sought to address whether this was indeed the case. A total of 1,905 patients with low- to intermediate-complexity left main disease randomly were assigned between PCI and CABG, and five-year outcome data recently were published.[28]

At five years, the authors found no difference in the primary composite outcome of death from any cause, stroke, or MI between the PCI and CABG groups (22.0% *v* 19.2%, 95% CI −0.9 to 6.5; p = 0.13). There was, however, a change in whether PCI or CABG was favored depending on the time interval examined within the study. At 30 days, the primary outcome favored PCI (HR 0.61, 95% CI 0.42-0.88); from 30 days to one year, PCI and CABG were equivalent (HR 1.07, 95% CI 0.68-1.70), and from one-to-five years, the primary outcome favored CABG over PCI (HR 1.61, 95% CI 1.23-2.12).[28] The rate of MI alone was greater in the CABG group during the first 30 days but was subsequently greater in the PCI group from one-t-five years, which explains some of this temporal difference; however, the overall rate of MI at five years was not different between the two groups.

These findings somewhat contradict other recently published data examining PCI versus CABG in left main disease. The Nordic-Baltic-British Left Main Revascularization Study (NOBLE) trial, which also used a second-generation drug-eluting stent for PCI, found a significantly increased risk of major adverse cardiac events (all-cause mortality, nonprocedural MI, repeat revascularization, and stroke) in the PCI group at five years, driven mainly by nonprocedural MI and the need for repeat revascularization.[29] Another recently published meta-analysis, which included 4,595 patients with left main disease undergoing PCI or CABG, found no difference in all-cause mortality at five years, but the rates of MI, repeat revascularization, and major adverse cardiac events all favored CABG over PCI for treatment of left main disease.[30] It is important to note that the large number of procedural variables among the aforementioned studies, including type of stent, off-pump versus on-pump CABG, number of arterial grafts, and postoperative care protocols, makes direct comparisons challenging. Nonetheless, although reported mortality rates between PCI and CABG were similar at five years, these studies suggested that the early stroke and periprocedural MI risk in CABG must be weighed against a longer-term increased risk of MI and the need for repeat revascularization after PCI.

Secondary Prevention After CABG Surgery

Surgical coronary revascularization through CABG reestablishes coronary blood flow and thus restores myocardial oxygen supply but does not treat the underlying coronary atherosclerosis. Likewise, CABG does not prevent the continued progression of atherosclerosis in the native coronary arteries or the development of disease in the new bypass grafts. Instead, it is medical therapy instituted after CABG or stenting that attempts to arrest or slow coronary artery disease progression. Ultimately, the objective of secondary prevention is to achieve more durable CABG results, decrease the need for repeat interventions, reduce hospitalizations, improve functional status, and decrease mortality. Guidelines from Europe and North America emphasize the importance of prompt postoperative initiation and continued maintenance of key secondary prevention therapeutics in appropriate patients, including antiplatelet medications, statins, renin-angiotensin-aldosterone system (RAAS) inhibitors, and beta-blockers.[31,32]

Data from Swedish national registries, including the SWEDEHEART Registry (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies), suggested that pharmacy dispensation rates for several of these critical secondary prevention medications decrease over time, with a corresponding increase in mortality.[33] These registry data included 28,448 patients admitted for first-time CABG between 2006 and 2015, with medication exposure status established at six months after discharge and updated every three months. The median follow-up time in this study was 4.9 years. Although baseline dispensation rates were high, they decreased over time, declining from 93.9% to 77.3% for statins, 91% to 76.4% for beta-blockers, 72.9% to 65.9% for RAAS inhibitors, and 93% to 79.8% for antiplatelet drugs. After adjusting for confounders, the authors found a significant inverse association between all-cause mortality and use of statins, RAAS inhibitors, and antiplatelet drugs. Interestingly, the authors found no association between the rate of beta-blockers dispensation and the risk of mortality. Low-income patients had statins and antiplatelet medications dispensed less often, both at baseline and at eight years, than those with higher incomes, and had a steeper decline in the dispensation rate over time. There were important limitations inherent to the retrospective design of this study, including the inability to determine causality. As the authors pointed out, they could not account for numerous risk factors, including lifestyle factors such as tobacco use, exercise habits, and diet. The application of these reported data to other countries was buttressed by two key points that are not unique to cardiovascular medicine—the beneficial health effect of consistent compliance by patients and physicians with evidence-based treatments and the ongoing need to improve cardiovascular outcomes across the spectrum of socioeconomic circumstances.

Arterial Versus Venous Grafts for Coronary Bypass Surgery

The benefit of using a left internal thoracic artery graft in addition to venous grafts for CABG has been well-established and is believed to be because of the superior patency of the arterial conduit. As such, several observational studies have been performed comparing bilateral internal thoracic artery grafts (BIMA) with single internal thoracic artery grafts (SIMA) for CABG and have demonstrated improved long-term mortality when multiple arterial conduits are used.[34,35] The Arterial Revascularization Trial (ART) sought to address this question by means of a multicenter randomized control trial. The authors selected patients with multivessel coronary disease who were scheduled to undergo CABG and randomly assigned them to receive either SIMA or BIMA plus any additional venous grafts that were deemed necessary. The initial five-year data from the ART trial showed no difference between the two groups in either all-cause mortality or the composite outcome of death from any cause, MI, or stroke.[36] The ART trial group recently published the 10-year follow-up outcomes of the study.

At 10 years, there continued to be no significant difference between the two groups in all-cause mortality or the composite outcome of death, stroke, MI, or need for repeat revascularization.[37] However, there were some significant confounding factors in this trial that must be addressed. First, there was a high rate of crossover between the two groups, with 14% of the BIMA group receiving only a single graft and 2% of the SIMA group receiving BIMAs. Perhaps more significantly, 22% of the SIMA group also received a second arterial conduit in the form of a radial artery graft. Whereas radial artery grafts, similar to SIMA grafts, have a longer expected patency than venous grafts, the nearly one-fifth of SIMA patients who received two arterial grafts likely had a significant effect on the ability to detect any statistically significant difference between the two groups. Indeed, when the data were analyzed to compare those who received two or more arterial grafts with those who did not, there appeared to be a meaningful difference in mortality favoring multiple arterial conduits. Whereas the ART trial was neither designed nor powered to judge whether this difference was statistically significant, there currently is a trial under way that is designed to answer this very question.[38]

COVID-19 and Cardiovascular Disease

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 infection is caused by binding of the viral surface spike protein to the human angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is expressed in the lung (principally type II alveolar cells) and is highly expressed in the heart as well, counteracting the effects of angiotensin II in states, with excessive activation of the renin-angiotensin system, such as hypertension, congestive heart failure, and atherosclerosis.[39] COVID-19 interacts with the cardiovascular system on multiple levels,

with increasing morbidity and mortality observed in patients with underlying cardiovascular conditions.[40]

Li et al. addressed the role of cardiovascular disease (CVD) in the progression and prognosis of COVID-19, reporting that COVID-19 patients with CVD showed several more clinical symptoms, lung injury, uncontrolled cytokine storm, and hypercoagulable state compared with patients without a history of CVD.[41] In addition, studies have shown pre-existing CVD to predict mortality in COVID-19 pneumonia patients.[42–44] Cardiovascular damage secondary to COVID-19 includes a wide variety of clinical syndromes including myocarditis, cardiogenic shock, pulmonary embolism, and arrhythmias. These cardiac pathologies also may be caused or exacerbated by pharmacologic therapies administered to treat COVID-19 infection.[45,46]

COVID-19 Drug Therapy and Cardiovascular Implications

As of yet, no comprehensive expert recommendations regarding COVID-19 treatment in patients with pre-existing cardiovascular disease exist, but the input of dedicated multidisciplinary teams to guide selection has been widely recommended. Morawietz et al. suggested that patients with elevated troponin T and triglyceride levels should continue medications related to pre-existing cardiovascular comorbidities, including antiplatelet therapy, beta-blockers, and statins, as a result of their potential to attenuate inflammation, acute lung injury, and cardiovascular complications.[47] Several potential negative drug interactions secondary to therapeutics are possible. First, antiviral or immune response modulator medications may trigger ventricular arrhythmias via QTc interval prolongation. Second, patients with pre-existing disease receiving angiotensin-receptor blockers or angiotensin-converting enzyme inhibitors have upregulation of ACE2, the binding site for SARS-CoV-2. However, this concern, derived from in vitro and animal studies, has not been confirmed in clinical practice.[48]

Adult Cardiac Surgery During the COVID-19 Pandemic: Guidance and Recommendations from

Cardiac Organizations

The worldwide COVID-19 pandemic has had a profound effect on the delivery of cardiac surgical care throughout the world.[49,50] Cardiac patient demographics show a predominant aged population, with frequent comorbidities, and are, thus, at the highest risk for mortality associated with COVID-19. However, it is vital that cardiac surgical teams balance the risk of delaying surgery versus increasing the likelihood of acquiring COVID-19 infection. The pandemic also has affected the logistical operations of surgical care, and factors, such as shortage of blood products and personal protective equipment and limited inpatient hospital resources directed toward the pandemic, need to be considered before utilization of medical care facilities for elective cardiac surgery.

The American Association for Thoracic Surgery and the Society of Thoracic Surgeons recommend templates for physicians and interdisciplinary teams to consider and adapt for their own individual medical center treatment strategies (Fig 1).[51] Their recommendation for postponement of elective cardiac surgery is based on the following principles: protecting the patient, protecting the healthcare team, protecting the individual institution, and protecting society.[51] The template proposed a four-tier system for various cardiac services depending on the inpatient occupancy of COVID-19. If the inpatient load is <30%, minimal reduction in elective surgery is suggested. They also emphasized the importance of collaboration between the cardiac surgical team and Extracorporeal Life Support Organization to provide extracorporeal support for certain COVID patients in an efficient way.[52]

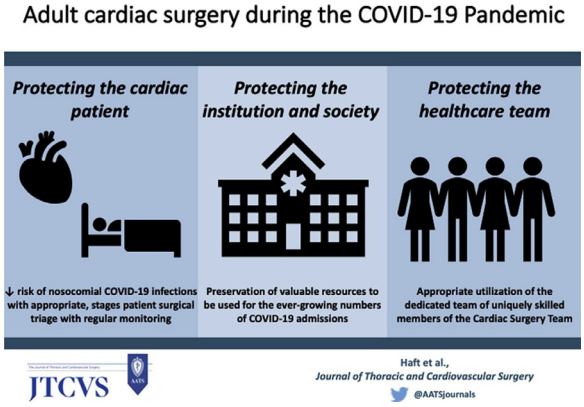

Fig 1. Adult cardiac surgery during the coronavirus disease 2019 pandemic: A tiered patient triage guidance statement.
Used with permission from Haft et al.[51]

The implementation of a tiered system to manage cardiac surgical patients in the setting of the COVID-19 pandemic also is seen in other literature. Patel et al. also provided both a perioperative testing algorithm for SARS-CoV-2 and recommendations for the perioperative care of cardiac surgical patients.[53] They proposed a three-tier system based on acuity of underlying cardiac disease and the pretest probability of COVID-19 infection. In low-acuity patients, their recommendations were to postpone surgery for up to 12 weeks.[53] Cardiac surgery hospitals in Italy's Lombardy region organized "hub centres" to minimize postponement of treatment for cardiovascular patients and "spoke centres" that served as satellites for efficient enrollment of patients seeking cardiac care. The Canadian Society of Cardiac Surgeons suggested a three-tier triage system based on reduction in their routine services, with a shift to emergency cardiac surgeries only if routine services are reduced by 50% or more because of COVID-19 patient surges.[50]

Anesthetic Management of Patients with COVID-19 Infections During Emergency Procedures

The combination of high-frequency aerosol-generating procedures (AGPs), with the strong transmissibility of SARS-CoV-2, presents a novel challenge for anesthesiologists in preventing cross-contamination among equipment, personnel, and

anesthetizing locations. SARS-CoV-2 has been proven to be transmitted through contact with infected surfaces and fluids and with aerosol transmission.[54,55] Examples of AGP include bag-mask ventilation, intubation, extubation, airway suctioning, and cardiopulmonary resuscitation. Even though there is a lack of agreement among guidelines as to the use of airborne precautions during routine care, airborne precautions, including the use of a fitted N95 mask or powered air purifier respirator, universally are recommend for AGP.[56]

Elective procedures generally are deferred for patients with COVID-19, thus resulting in the predominance of procedures presenting as emergencies. Operating room logistics should focus on efficient delivery of care, with minimization of risk to the patient and healthcare staff. Intubation and extubation should be performed by the most experienced person, with full airborne precautions available, ideally in an airborne isolation room that is configured for negative pressure protection relative to the surrounding area. Preoxygenation with 100% oxygen, followed by rapid-sequence intubation, should be performed to reduce aerosolization with mask ventilation. In addition to extensive personal protective equipment among the anesthetic team, the literature recommends the use of a high-efficiency antiviral filter between the mask and breathing circuit.[57] All members of the healthcare team should be well-versed and practiced in the local protocols designed from the latest literature for initiation of care and transport of anesthetized patients with COVID-19.

Updates in Heart Failure

Despite numerous advances in therapy, heart failure continues to remain a significant and increasing problem. It is estimated that there are more than six million patients with heart failure in the United States alone, accounting for 10% of deaths attributable to cardiovascular disease.[58] Mortality and resource utilization remain high, with total costs projected to be almost $70 billion by 2030.[59] Some of these costs are directly attributable to implantation of mechanical circulatory support (MCS) devices. In 2019, INTERMACS reported implantation of more than 25,000 devices, including left ventricular assist devices (LVADs); one-year survival with an LVAD is >80%.[60,61] Highlights for 2020 include discussion of advancements in both device and medical management, two facets of heart failure management that are applicable to the perioperative arena.

Heart Failure: MCS Device Update

Because of increased survival and scarcity of organs for transplantation, implantation of LVADs is becoming more common. Despite the high prevalence in the United States of mental illness in those with chronic health conditions such as heart failure, there has been a lack of research concerning device implantation in such patients. A recent study was the first to investigate psychiatric comorbidity and outcomes after LVAD implantation.[62] Using the INTERMACS database, Mullan et al. identified a total of 2,207 of 22,000 patients who had a psychiatric comorbidity. In addition to having lower quality-of-life scores, an increase in adverse events of hospital readmission, thrombotic events, and infection were observed in this population.[62] Compared with the general population, the prevalence of psychiatric disease in LVAD patients within the database was lower, although a key limitation of the study was the ill-defined nature of "psychiatric comorbidity" within the INTERMACS database. Despite the increase in morbidity, no increase in mortality was observed in patients with psychiatric comorbidities.[62]

Despite the increasing implantation of LVADs within the heart failure population, the most commonly implanted MCS device remains the intra-aortic balloon pump (IABP). Historically, the most common insertion sites have been the femoral and subclavian arteries. Newer techniques have allowed percutaneous placement with fluoroscopic guidance via the axillary artery.[63,64] Placement in the upper extremity is advantageous because of the ability of patients to ambulate and a decreased rate of infections. A recent retrospective study evaluated 195 patients with advanced heart failure who received IABP support via the axillary route.[64] Outcomes evaluated were two-fold—the first was defined as successful heart replacement, including bridge to transplantation or planned permanent MCS device, and the second was defined as failed heart replacement, secondary to either death or unplanned upgrade in MCS. A total of 133 patients underwent successful cardiac replacement. The failure group consisted of 62 patients, with 16 deaths, 18 requiring escalation of therapy, and 28 in whom the IABP was removed because of complications. Adverse events included cerebrovascular accidents (2.5%), left upper extremity ischemia (3.5%), and mesenteric ischemia resulting from malpositioning of the IABP (3%). Use of the axillary approach allowed for longer usage and improved patient ambulation. The percutaneous approach allowed for fewer general anesthetics to be used for placement, which may provide some benefit in the heart failure population.

Heart Failure: Medical Management Update

Treatment options for patients with heart failure with preserved ejection fraction (HFpEF) remain limited. After much success with the incorporation of angiotensin-neprilysin inhibitors (ARNIs) into mainstay therapy for heart failure with reduced ejection fraction (HFrEF), possible use in the HFpEF population is under exploration.

Initial investigations began in 2012 with the Prospective comparison of ARNI with angiotensin-receptor blocker (ARB) on management Of heart failure with preserved ejection fraction (PARAMOUNT) study, a multicenter, phase II trial that enrolled patients with left ventricular ejection fraction ≥45% and New York Heart Association class II to III heart failure

symptoms with elevated N-terminal pro-brain natriuretic peptide.[65] Patients randomly were assigned to receive LCZ686, an ANRI, or valsartan followed by a titration period to target doses of 200 mg and 160 mg twice daily, respectively. The primary endpoint was change in NT-proBNP from baseline to 12 weeks, with significant reduction seen in the LCZ696 group compared with the valsartan group (LCZ696 baseline 783-605 pg/mL compared with valsartan: 862-835 pg/mL; $p = 0.005$). LCZ696 was well-tolerated, with adverse effects similar to those of valsartan.[65]

This favorable outcome provided the basis for the later 2019 Efficacy and Safety of LCZ696 Compared to Valsartan, on Morbidity and Mortality in Heart Failure Patients With Preserved Ejection Fraction (PARAGON-HF) trial that examined a composite clinical outcome of total hospitalizations for heart failure and death from cardiovascular causes.[66] Patients randomly were assigned to receive either sacubitril–valsartan (target dose 97 mg of sacubitril with 103 mg of valsartan twice daily) or valsartan (target dose 160 mg twice daily). Enrolled patients had similar profiles to those in the PARAMOUNT trial, including left ventricular ejection fraction ≥45% and New York Heart Association class II to III heart failure symptoms with elevated NT-proBNP. However, unlike PARAMOUNT, PARGON-HF patients were required to have evidence of structural heart disease. Approximately 35% of enrolled patients had ischemic cardiomyopathy. Despite the previous reductions in NT-pro BNP seen in PARAMOUNT, there only was a trend toward a reduction in the primary outcome (HR 0.87, 95% CI 0.75-1.01; $p = 0.06$), which was driven largely by a 15% reduction in heart failure hospitalizations and 5% reduction in cardiovascular causes of death. When reviewed in the context of 12 prespecified subgroups, there was possible benefit with sacubitril–valsartan in patients with lower ejection fraction and in females. This heterogeneity in outcomes was not seen in the prior HFrEF trials, which showed consistency across all patient groups.[67] However, PARAGON-HF did demonstrate the safety and general tolerability of the sacubitril–valsartan combination in this population. Current heart failure guidelines remain limited to the approved use of ARNI therapy in HFrEF alone.[68] Additional studies are required to clarify select patient populations that may derive the best benefit from ARNI before expanding ARNI use to HFpEF.

Updates in Heart Transplantation

Heart transplantation remains the gold standard of treatment for end-stage heart failure refractory to medical management or MCS devices. Given that the recent literature has discussed the importance and emergence of anesthesiologists as members of cardiothoracic multidisciplinary transplantation teams, an understanding of the new allocation system and latest data regarding variables affecting cardiothoracic transplantation survival are vital for the specialty to successfully integrate with other disciplines.[69,70] Highlights for 2020 include updates on donor factors, recipient factors, surgical factors, and the effect of the new heart allocation system on survival.

Update on Assessing Survival

Survival after heart transplantation continues to improve, with a mean survival after transplantation of 12.5 years, extending to 14.8 years among one-year survivors. The major survival gains are limited to the first six-to-twelve months, with a largely unchanged long-term attrition rate of 3% to 4% mortality per year thereafter. Understanding how survival is assessed after transplantation is crucial given how allocation scores balance waitlist mortality with survival after transplantation. Traditionally, survival has focused on reporting early versus late mortality or at specific time points, such as the annual publication of the International Society for Heart and Lung Transplantation Registry with multivariate analyses on survival after an arbitrary number years after transplantation.

More recently, through temporal decomposition statistical analysis of a large retroactive cohort, Hsich et al. categorized mortality after transplantation into early, constant, and late hazard phases.[71] The risk of death was greatest during the first week after heart transplantation, with a decline over one month, which was influenced primarily by both procedure-related outcomes and the medical condition of the recipient. The constant phase of survival correlated with non-modifiable risk factors such as age, race, and socioeconomic factors. In the late phase, risk of death increased with time, diabetes, obesity, age, and transplantation complications. Using a three-phase mortality paradigm allows for a more precise evaluation of time-dependent risk factors for mortality.[71]

Update on the Influence of Recipient, Donor, and Surgical Risk Factors on Survival

Specific recipient, donor, and surgical characteristics are associated with increased mortality after transplantation in cardiothoracic transplantation and should be recognized to optimize organ allocation and clinical outcomes.[70,72] Recipient end-organ dysfunction, including cardiac, hepatic, renal, or pulmonary failure, has the highest overall correlation with mortality after transplantation at 90 days. At one year, mortality was affected by the need for mechanical ventilation, advanced donor age, or donor ischemic time >4 hours.[73] Late phase mortality, assessed at both five and 10 years, was most affected by recipient and donor ages. Interestingly, the detrimental effect of prolonged ischemic time without other donor risk factors did not affect the five-year survival after transplantation.[74] Overall, recipients who undergo transplantation for ischemic or non-ischemic cardiomyopathy have a better prognosis than those with congenital heart disease (HR 1.722, CI 1.40-2.12; $p < 0.01$), restrictive cardiomyopathy (HR 1.363, CI 1.119-1.661; $p < 0.01$), or repeat transplantation (HR 1.671, CI

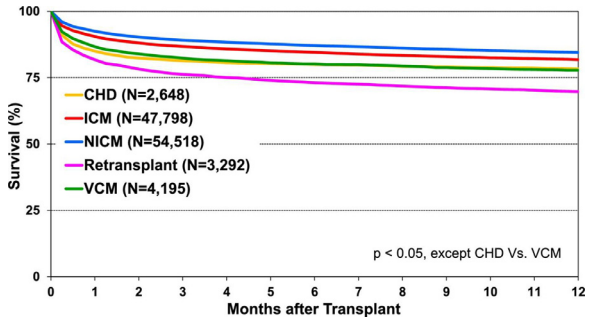

Fig 2. Kaplan-Meier survival within one year of transplantation by diagnosis (adult heart transplantations: January 1985–June 2017). CHD, congenital heart disease; ICM, ischemic cardiomyopathy; NICM, non-ischemic cardiomyopathy; VCM, valvular cardiomyopathy.

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1.337-2.088; p <0.01).[73] The most consistent predictor of mortality in heart transplantation over time was an elevated recipient total bilirubin, with the greatest predictive value of this influencing factor observed early after transplantation.[75]

Understanding recipient sex disparity in heart transplantation is complex but paramount to ensure equitable therapy and organ allocation. Males and females are listed based on criteria that are not sex-specific, yet sex-specific interactions with strong predictors of mortality before heart transplantation have been elucidated.[76] Although sex mismatching of female donors to male recipients appears to result in increased mortality, overall survival after transplantation based on sex alone has yielded contradictory results.[76–78] Currently, female recipients only represent one in four heart transplantations worldwide and appear to receive hearts from higher-risk donors.[79] This has been ascribed to women presenting with end-stage heart failure at an older age, selection, referral bias, and purported poorer outcomes in female recipients.[80–82] Female recipients, however, have significantly greater survival after transplantation than do male recipients (median 12.2 y *v* 11.4 y, respectively). Two large retrospective cohort studies, using international registry data, applied advanced statistical modeling and machine learning to address these conflicting results. Both concluded that, when matched for recipient and donor characteristics, sex was not a significant variable predicting mortality in early postoperative, constant, or late survival of heart transplantation.[71,79]

Heart transplantation survival has improved continually over time; however, complications such as graft failure, rejection, and cardiac allograft vasculopathy can necessitate cardiac retransplantation.[73] Globally, approximately 120 cardiac retransplantations are performed on a yearly basis, accounting for 2.2% of heart transplantations performed in 2016.[75] Heart retransplantation survival rates are lower both in one year (Fig 2) and conditional one-year survival as compared with all comers for index surgery.[73,83] Most commonly performed in the early phase for primary graft failure, cardiac allograft vasculopathy predominates the etiology of retransplantation after the first month of primary transplantation.[83] Barghash et al. recently provided an update on heart retransplantation outcomes, reporting that retransplantation recipients are often younger, hospitalized at the time of transplantation, and more frequently required preoperative use of intravenous inotropic medications or MCS devices compared with primary transplantation patients.[83] They noted that while patients who have been bridged with MCS to retransplantation historically have experienced lower survival rates, examining the latest data revealed similar outcomes in patients who were bridged at least one year after initial transplantation compared with those who underwent repeat transplantation without MCS bridging.[83]

Update on the New Heart Allocation System

In response to an increasing number of heart failure patients transitioned to MCS devices, stabilized hemodynamically, and discharged home to await cardiac transplantation, the United States heart transplantation organ allocation system was modified on October 18, 2018. Before this revision by the Organ Procurement and Transplantation Network's Thoracic Organ Transplantation Committee and the United Network Organ Sharing, the last revision was in 2000. The prior system arguably fostered an environment that allowed for regional and geographic inconsistencies in donor access and increased wait-list times for high-risk candidates.[84,85] The old system used three tiers (status 1A/B and status 2), whereas the new system transitioned to status 1 to 6 (Table 1) while broadening geographic boundaries.[86]

At first review, preliminary assessment of patients undergoing transplantation under the new system (through March 31, 2019) reported a decrease in waitlist mortality but unexpectedly poor survival rates after transplantation, with an increase in repeat transplantation compared with the old system.[87] Cogswell et al. emphasized that these early results represented a small sample size (n = 529) and further evaluation was needed to determine trends in survival.[87] Jawitz et al. sought to build on these preliminary data and determine survival under the new system.[88] Performing a registry update allowed the authors to include a total of 7,119 recipients, with a split of 6,004 under the old system compared with 1,115 under the new allocation system.[88] Recipients undergoing transplantation under the new system were more likely to be bridged to transplantation with temporary MCS devices and have shorter wait-list times and longer graft ischemic times. They were less likely to have durable LVADs, diabetes, and ischemic cardiomyopathy. The comparison of donor characteristics were similar between the two cohorts, with the exception that in the old system the most likely cause of death was head trauma, whereas in the new system the most likely cause was anoxia.[88] Unadjusted Kaplan-Meier survival analysis performed by the authors established a minimal decrease in 90- and 180-day survival with 93.0% and 90.6%, respectively, under the new allocation system, compared with 94.4% and 93.3% under the old system.[88] However, after adjusted analysis was performed to determine independent association between the new allocation system and survival, there was no significant decrease in survival between the old and new systems. Independently identified factors associated with decrease in survival included

Table 1
Comparison Between Older and Revised Heart Allocation Policies

Old OPTN/UNOS Adult Heart Allocation Policy	New OPTN/UNOS Adult Heart Allocation Policy
• Status 1A	• Status 1
• 30-d elective VAD time	• ECMO
• TAH	• Non-dischargeable, surgically implanted, non-endovascular biventricular MCS
• IABP	• MCS + life-threatening VT/VF
• ECMO	
• VAD + complications	• Status 2
• Mechanical ventilation	• Non-dischargeable, surgically implanted, non-endovascular VAD
• Pulmonary artery catheter + multiple inotropes or single high-dose inotrope	• IABP
	• VT/VF, MCS not required
• 1A exception*	• MCS with device malfunction/mechanical failure
	• TAH, BiVAD, RVAD, or VAD for single ventricle patients
	• Percutaneous endovascular MCS
	• Status 3
	• Dischargeable VAD for discretionary 30 d
	• Multiple inotropes or single high-dose inotrope with continuous hemodynamic monitoring
	• ECMO after 7 days; percutaneous endovascular MCS or IABP after 14 days
	• Non-dischargeable, surgically implanted, non-endovascular VAD after 14 d
	• MCS with ≥1 of:
	• Device infection
	• Hemolysis
	• Pump thrombosis
	• Right-sided heart failure
	• Mucosal bleeding
	• Aortic insufficiency
• Status 1B	• Status 4
• MCS beyond 30-d interval	• Dischargeable VAD without discretionary 30 d
• Continuous IV inotropic support	• Inotropes without hemodynamic monitoring
• 1B exception†	• Retransplantation
	• Diagnosis of:
	• Congenital heart disease
	• Ischemic heart disease with intractable angina
	• Hypertrophic cardiomyopathy
	• Restrictive cardiomyopathy
	• Amyloidosis
• Status 2	• Status 5
• Those who do not meet criteria for status 1A or 1B	• Dual organ transplantation candidates
	• Status 6
	• All remaining active candidates

Abbreviations: BiVAD, biventricular assist device; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; IV, intravenous; MCS, mechanical circulatory support; OPTN, Organ Procurement and Transplantation Network; RVAD, right ventricular access device; TAH, total artificial heart; UNOS, United Network for Organ Sharing; VAD, ventricular access device; VF, ventricular fibrillation; VT, ventricular tachycardia.

* Most common status 1A exception categories: ventricular tachycardia/ventricular fibrillation; no intravenous access for inotropes/pulmonary artery catheter contraindicated; congenital; ventricular assist device complications; unable to tolerate inotropes; other/miscellaneous; retransplantation; other (hypertrophic cardiomyopathy, restrictive cardiomyopathy, coronary artery disease, refractory angina, amyloidosis).

† Most common status 1B exception categories: ventricular tachycardia/ventricular fibrillation; congenital; retransplantation CD refractory angina; restrictive cardiomyopathy; unable to tolerate inotropes; ventricular assist device complications; hypertrophic cardiomyopathy; other (amyloidosis, other/miscellaneous, no intravenous access for inotropes/pulmonary artery catheter contraindicated).Used with permissions from Reich et al.[86]

increasing donor and recipient age, extracorporeal membrane oxygenation use before transplantation, previous cardiac surgery, and prolonged graft ischemic time.[88]

Conclusion

The selected themes for the 2020 highlights article summarize diverse aspects and ongoing innovations within the specialty of cardiothoracic and vascular anesthesia. It is likely that these latest studies will not only advance the practice domains for the specialty, but also improve outcomes for all patients seeking cardiothoracic and vascular surgical care.

Declaration of Competing Interest

The authors have no conflict of interest to report.

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