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The Year 2020 in Review: Coronavirus Disease 2019 Cloud and Its Impact Excelling the Clinical Practice

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> The three fundamental units as cornerstones of 20th-century innovation: the bit, the atom, and the gene.
>
> —Walter Isaacson (biographer)[1]

The year 2020 has been an "unusual" year, in every way, for everyone. As if the only consistency has been the "inconsistent." These inconsistencies have been met with both resilience and resistance alike. Not only has it been the year of the pandemic but also the year of societal unrest; introspection; recouping diversity, ethics, and equality; and domestic violence. During the worldwide lockdown and distancing, while active laboratories and research (other than coronavirus disease 2019 [COVID-19]) came to a standstill, the year 2020 saw an unprecedented rise in research papers, even aside from COVID science.[2] Submissions in journals by publisher Elsevier alone found a 58% increase from February to May of 2020 when compared with the same period in the year 2019. This rise has been explained by more available time due for researchers to work on completing their manuscripts owing to the lockdown; evolution of robust preprint servers like medRxiv, SSRN, and Research Square; and push for a faster review process by journals.

The editors of *Seminars in Cardiothoracic and Vascular Anesthesia* (*SCVA*), keeping this in mind, decided to come up with this current issue to summarize all the salient publications that happened in the year 2020 broadly into 6 categories pertinent to the readership, namely, cardiothoracic anesthesiology, anesthesia for congenital heart disease (CHD), thoracic transplant anesthesiology, cardiothoracic critical care, abdominal organ transplantation, and cardiothoracic surgery.

A literature review on cardiothoracic anesthesia by Clendenen et al discusses preoperative iron therapy, acute kidney injury, postoperative pain, anticoagulation after transcatheter aortic valve replacement (TAVR), mechanical circulatory devices, and machine learning.[3] The authors conclude in their review that for cardiac surgery, preoperative iron supplementation may increase hemoglobin that may potentially translate to improved outcomes. A recent prominent randomized controlled trial (RCT), although performed for major abdominal surgery (PREVENTT), did not demonstrate preoperative intravenous (IV) iron to be superior to placebo in reducing the need for blood transfusion when administered to patients with anemia 10 to 42 days prior to surgery.[4] Two primary composite end-points were studied, namely, blood transfusion/death and number of transfusions from randomization until 30 days after index operation. Another recent study in cardiac surgery patients showed a significant reduction in transfusion by following a central venous saturation-guided restrictive strategy.[5] Previously, the TRICS trial in patients for cardiac surgery demonstrated that a restrictive strategy for transfusion based on hemoglobin <7.5 g/dL was noninferior to liberal strategy for those with hemoglobin <9.5 g/dL.[6] After cardiac surgery, blood volume reduction is about 18%, red blood cell volume 38%, while plasma volume only 8%, implying hemoglobin may after all not be the best trigger for transfusion.[7,8] This brings us back to the same questions with yet uncertain answers: What is the best trigger for transfusion? Does the rise in hemoglobin preoperatively translate to improved outcomes? How do we measure deficit in oxygen-carrying capacity: by anemia (low hemoglobin), by regional oxygen saturation, by red cell mass indexed to patient`s size, or by oxygen-debt (SaO_2 minus SvO_2, lactate rise)? Cardiac surgery-associated acute kidney injury (CSA-AKI) is a vexing problem in about 40% patients with 3% needing renal replacement therapy.[9] Authors report a novel tool, the soluble urokinase receptor for predicting CSA-AKI. This may be blocked by a monoclonal antibody leading to the prevention of AKI. As reiterated by Vijayan, while biomarkers and preclinical identification of potential AKI remain under aggressive investigation, clinically speaking, only prevention, the

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timing of dialysis, and follow-up to prevent chronic kidney disease remain the keystones.[10] Of note, early initiation (within 24 hours) of kidney replacement therapy for patients with AKI in intensive care unit did not improve outcomes and was found to be associated with increased hypotension and hypophosphatemia.[11] Regarding analgesia for cardiac surgery, the authors drive home a few pertinent points: liberal prescription of narcotics, opioids sparing techniques, regional analgesia, and methadone. The majority of elective adult cardiac surgery happens in older age groups. Putting a perspective to the context of analgesia clinically, it is fair to assume that analgesia and delirium are often inseparable. As shown in the DEXACET trial, both postoperative delirium and requirement of morphine-equivalents were lower in patients receiving scheduled acetaminophen with propofol or dexmedetomidine.[12] It is often a clinical dilemma for the practitioner to practice opioid-sparing multimodal analgesia, and yet avoid polypharmacy to spare delirium. Considering this, the concept of using methadone may be potentially promising, although more studies are needed. As the therapeutic TAVR advances exponentially, the uncertainty with optimal anticoagulation strategy expands too. The authors compare and contrast 3 trials, GALILEO, POPular, and PARTNER 2. Taking a step back, compared with surgical-AVR, the TAVR valve is increasingly predisposed thrombosis and degeneration due to (1) neo-anatomy (axis of left ventricle outflow tract, annulus, and sinuses of Valsalva) and eccentric distortion over time leading to mechanical stress and fluid-dynamic effects on leaflets and stent; and (2) intrinsic limitation of leaflet material.[13] Futuristically, more personalized and customized TAVR valves (size, design, and material) may be the correct answer rather than trying to find a "fit-all" anticoagulation strategy. As the authors mention, the studies on use of mechanical circulatory support devices for cardiogenic shock, acute respiratory distress syndrome (ARDS), and sepsis have shown that extracorporeal membrane oxygenation (ECMO) may have a more beneficial role to play than realized yet. Apparently, also the intra-aortic balloon pumps (IABPs) maybe more efficacious than temporary left ventricular assist device given the lesser complications for cardiogenic shock after myocardial infarction. On similar lines, Baudry et al showed 42% survival on patients with electrical storm undergoing ablation.[14] Delineating benefit from harm while interpreting "real-world" trials could be challenging.[15] In clinical science, in order to attain best outcomes, the inflection point of deprivation of potential benefits from undertreatment versus engendering potential harm from overtreatment could be extremely difficult to identify. The best possible resource could be a RCT, but conducting RCT on these complex clinical scenarios may again be challenging. Authors summarize studies showing improved "prediction" based on deep-learning (artificial intelligence [AI]). However, and rightly so, they do mention a word of caution on the utility of these AI-based algorithms for clinical care. One such large-scale study by Escobar et al showed successful automated identification of adults at risk for in-hospital clinical deterioration in a nonrandomized, stepped-wedge study design.[16] Although this was not a technically RCT, and had its limitations, it is a step forward in medical science.[17]

Landsem and colleagues[18] highlight the congenital heart developments seen in year 2020. Children have presented with Kawasaki-like symptoms, myocardial injury, and cardiogenic shock, while vaccination strategy remains uncertain for COVID-19. A recent report did mention that adults with CHD are at a higher risk, particularly cyanotic heart disease (odds ratio = 13.2, 95% confidence interval [CI] = 2.4-68.4).[19] As for developments in surgery for CHD, they highlight the recent modifications in surgical technique in Norwood surgery, and adaption of STAR-perfusion strategy (sustained all regional perfusion) in place of deep hypothermic circulatory arrest (DHCA). For Fontan surgeries, dealing with the atrioventricular valve regurgitation and minimizing complications post-Fontan held the center stage. As the authors have indicated, the incidence of heart transplantation in single-ventricle patients (Fontan circuit) is approximately 0.003%, which may be due to high waitlist-mortality and de-listing due to Fontan complication. We would like to reiterate that owing to these issues, there has been a major push toward ventricular assist devices (VAD) for single-ventricle physiology patients, either to reduce waitlist deaths, and maybe delay onset of Fontan failure symptoms by improving end-organ dysfunction.[20,21] A parallel concept has been the possibility of a "Stage 4" palliation, implantation of VAD, in the failing single-ventricle patients.[22] Failing single ventricle could be after immediate stage 1 repair of Norwood procedure, or after Stage 2 repair of Norwood procedure or a longer term failing of Fontan circulation. Conceptually, Fontan circulation remains a physiological "paradox." Initially developed to treat cyanosis in children with complex CHD, it has been a mainstay of staging therapy for the past 50 years for children born with one "rudimentary" ventricle. After the creation of total cavo-pulmonary connection (Fontan circuit), there is a persistent elevated central venous pressure about 3 times normal (approximately 15 mm Hg), which is needed to maintain forward flow. Over the years, this may lead to either systolic heart failure or diastolic heart failure, or side-effects of persistent elevated central venous pressure, like liver fibrosis, renal dysfunction, protein-losing enteropathy, lymphatic dysfunction, and so on. In extremis, these conditions may be labeled as Fontan failure. These are situations where the role of more permanent VAD are being investigated. Candidacy for VAD in a single-ventricle physiology patient needs several factors like size, anatomy,

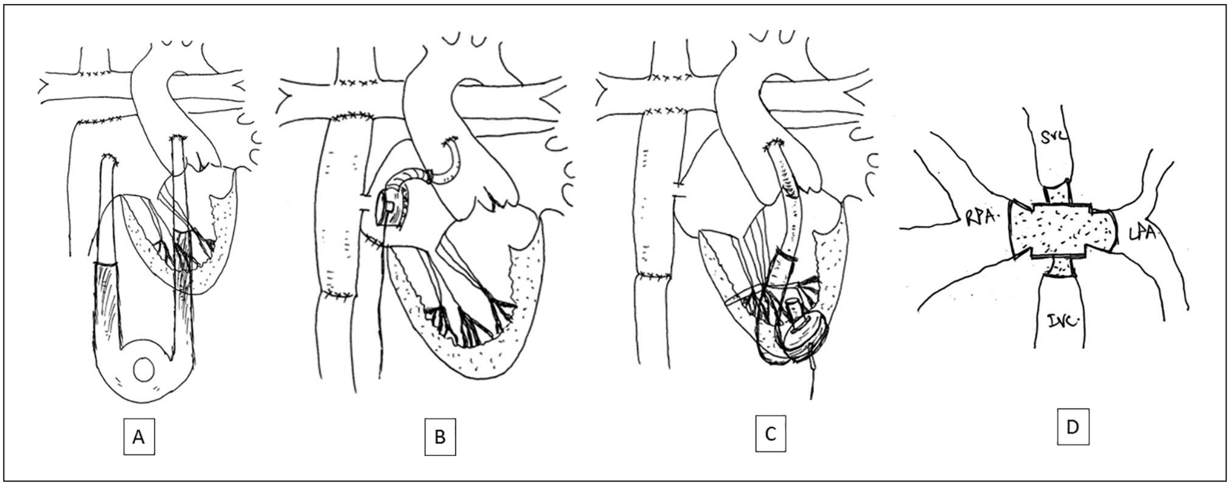

Figure 1. Ventricular assist devices (VAD) for single-ventricle physiology. (A) Pneumatic pulsatile Berlin Heart device in patient with superior cavo-pulmonary connection. (B) Continuous axial flow HVAD device (HeartWare) with inflow in atrium and outflow in aorta in total cavo-pulmonary connection (TCPC). (C) Continuous axial flow HVAD device (HeartWare) with inflow in ventricular apex and outflow in aorta in TCPC. (D) Viscous impellar pump configuration for subpulmonic support and improved end-organ function in failing Fontan circulation.

physiological limitations, and subtype of Fontan failure to be considered. Depending on size of patient, existing anatomy of heart, reason for VAD placement, and magnitude of support needed, it can be one of either the configurations (Figure 1):

1. External pump with cannulas in atrium and aorta
2. Internal pump with outflow on aorta with inflow either on atrium or apex of ventricle
3. Pump only at the cavo-pulmonary junction

Systemic VAD use in Fontan patients as reported from ACTION registry showed that VAD was implanted in 45 patients with mean age group of 10 years. Seventy-six percent implantation were as bridge to transplantation, of which at 1 year of device implantation almost 70% received a successful transplantation.[20,21] The authors also continue to summarize recent literature on neurocognitive development in children with CHD. They did find that full-scale IQ was reduced in single-ventricle CHD children when compared with 2-ventricle CHD children. Higher neuroapoptotic rate and release of Nestin (biomarker) was seen in DHCA than antegrade cerebral perfusion groups. However, utility of near-infrared spectroscopy in gauzing neuronal injury continues to be equivocal.

Gilliland et al[23] review the noteworthy publications in cardiothoracic anesthesiology for the year. They elaborate the research in 4 areas, ECMO for out-of-hospital cardiac arrest (OHCA), intensive care unit sedation, fluid therapy, and advances in heart and lung transplantation (LTx). The utility of extracorporeal cardiopulmonary resuscitation (ECPR) has been on the rise. Authors highlight another study that shows optimistic outcomes of ECPR for OHCA suffering ventricular fibrillatory arrest. A study by Baudry et al[14] did report 42% 6-month survival in drug-refractory electrical storm patients. However, as pointed out in our correspondence, it is extremely complex to analyze survival and may depend on multiple factors after ECMO.[15,21] The overall survival to discharge in adult after ECPR is 42% as reported by the Extracorporeal Life Support Organization (ELSO; https://www.elso.org/Registry/Statistics/InternationalSummary.aspx). Other than vascular injury, major complications of ECMO are hemorrhage, intracranial bleed, infection, and thrombosis. Marinacci et al observed only a 25.5% survival to discharge after ECPR, and that arrest rhythm and etiology seemed to be insufficient predictors of outcome.[25] ECMO is associated with a high rate of neurologic injury, which could be a hemorrhagic stroke or anoxic injury during the cardiac arrest.[26] One way to mitigate the hemorrhagic injury is ideal anticoagulation. Majority of the times, patients are on heparin infusion but alternatively bivalirudin may be utilized. Other than standard activated clotting time measurement, anti-Xa activity level could be a prognostic marker of hemorrhage. In a recent study, a group of bleeding patients had an anti-Xa level of 0.38 IU/mL, while the group of nonbleeding patients had a level of 0.33 IU/mL (P = .01), and furthermore, a level of >0.46 IU/mL (P = .0006) was associated with survival on ECMO without bleeding.[27] In order to mitigate infection, especially ventilator-associated pneumonia in patients with ECMO after cardiac arrest, another strategy studied is "'awake ECMO" where patients are not anesthetized for peripheral ECMO placement and thereafter.[28] After propensity matching, the

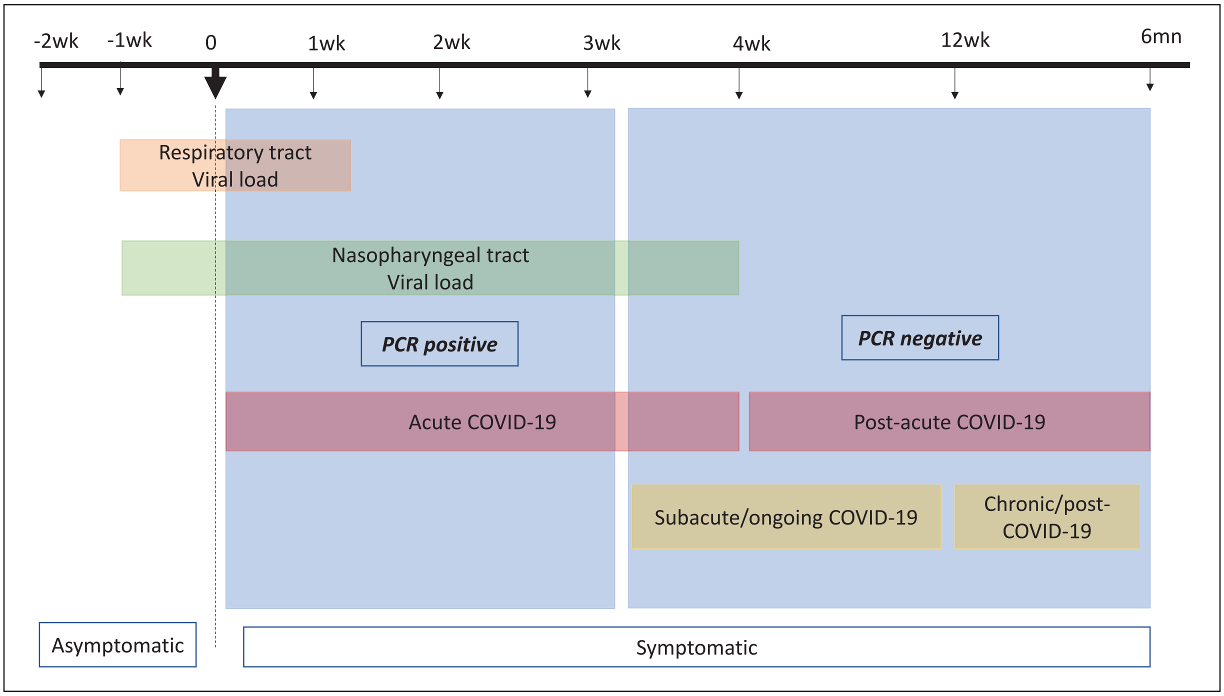

Figure 2. Timeline for COVID-19 manifestations.

investigators found much lower rates of pneumonia in awake-ECMO group (35% vs 59%, $P = .017$), as well as reduced 60-day (20% vs 41%, $P = 0.018$) and 1-year (31% vs 54%, $P = .21$) mortality rates. "Cooling" after cardiac arrest has been widely studied. Although cooling is routinely utilized in conduct of cardiopulmonary bypass during cardiac surgeries, it has not been well studied in association with ECMO, which in theory may have potential benefit on overall survival. Jacquot et al intend to study moderate hypothermia (33-34 °C) in patients on ECMO after cardiogenic shock in a multicenter RCT.[29] Any fluid that has more sodium chloride than 0.9% (physiologic) may be known as "hypertonic." One therapeutic strategy for addressing diuretic-resistance in treatment of acute decompensated heart failure is addition of hypertonic saline along with loop diuretic. This helps overcome the plateau achieved in water and sodium excretion with loop diuretics only.[30,31] In another retrospective cohort of acute decompensated heart failure patients, hypertonic saline solution (HSS) was associated with increased diuretic efficacy, fluid loss, and metabolic improvement.[32] In contrast, the study highlighted here is essentially a negative trial that failed to demonstrate claimed benefits of HSS. Further trials are warranted to tease out whether it was the incorrect setting, inappropriate patients selection, or the amount, and/or duration of HSS therapy that resulted in insignificant results.[33] Implementation of "Awakening, Breathing, Co-ordination, Delirium monitoring and management, and Early mobilization (ABCDE)" has improved duration of mechanical ventilation, length of stay, and cost.[34] Current scientific understanding of delirium indicates a multifactorial causation, namely, age, major surgery, anesthesia, psychoactive medications, end-organ failure, and drug toxicity.[35] A simple one-drug solution may not at all be the answer after all, as was expected of dexmedetomidine trials. Authors then continue to focus on heart and lung transplantation. As witnessed by entire transplant community in the United States, with the revision in heart allocation system, more patients are seen undergoing primary heart transplantations often with IABP in situ.[36] Also, there has been a steady rise in donation after cardiac death (DCD) heart donors, although duration of pulselessness was not well studied. As a matter of fact, a recent study looking retrospectively at over 650 patients in whom a transient resumption of at least one cycle of cardiac activity was seen in 14% patients after withdrawal of life-support. All these events occurred within 4 minutes 20 seconds after the period of pulselessness.[37] COVID-19 continues to remain and prevail almost in all the articles in this issue of *SCVA*. Now that we have the majority patients recovering from COVID-19, several of them continue to have one or the other symptom like persistent dyspnea, persistent fatigue, malaise, cognitive clouding well after 4-week when they are polymerase chain reaction test negative.[38] This has been labeled as "post-acute COVID-19 syndrome" (Figure 2). The authors here highlight some exciting and novel work on COVID-19 patients with severe ARDS treated with therapeutic LTx.[39] Although they quote instances of LTx in acute-COVID-19 situation, could post-acute COVID-19 syndrome with lung damage (fibrosis) potentially become another indication for LTx? Time will tell.[40] Subsequently, the authors review some studies with outcomes of LTx. Of note, once again, they quote a study claiming VA-ECMO for LTx to have lesser primary graft failure (PGD) and improved outcomes as compared to conventional cardiopulmonary bypass. Bilateral sequential LTx with no circulatory support will probably still stand out to be the best option.[41] Finally, authors conclude with reviewing the current evidence-based drugs for COVID-19 treatment, dexamethasone and remdesvir.

Abrams and Wilkey[42] summarize the literature on thoracic organ transplant in the past year. Once again, preoperative optimization takes a central role as authors present a retrospective study looking at preoperative anemia as a potential prognostic marker for poor outcomes after LTx, making erythropoietin and iron supplement as an option for treatment. Since end-stage lung disease needing LTx have a variety of etiology ranging from pulmonary fibrosis, to chronic obstructive pulmonary disease, to cystic fibrosis, could it be that anemia is merely an epiphenomenon and not a marker? Pulmonary fibrosis patients may have right ventricle (RV) dysfunction, chronic obstructive pulmonary disease may have polycythemia, while cystic fibrosis may have malabsorption. In a recent RCT trial in heart transplant recipients, IV iron treatment did not improve peak oxygen consumption in patients compared with placebo.[43] Also, the PREVENTT trial, for major abdominal surgery, did not find IV iron preoperatively to be superior to placebo for reducing the need for perioperative transfusion.[4] Coronary artery disease could present a unique challenge for patients undergoing LTx.[44] It was observed that majority patients who had had a coronary artery bypass grafting (CABG) in past received single-LTx, off-pump. Balancing kidney dysfunction with LTx has never been simple. Although double organ transplant (lung and kidney) may be an option, but may not necessarily improve mortality. Not surprisingly, the authors quote literature where increased transfusion was associated with increased poor outcomes (PGD) after LTx. Once again, this refreshes the age-old questions around transfusion: How much is too much? Are alternatives to fresh frozen plasma like prothrombin complex concentrate and factor VII better options? How best to monitor coagulation (thromboelastography, rotational thromboelastometry, point-of-care)? And foremost, as mentioned before, what are the best triggers for transfusion? High LTx volume centers (>25 per year) continue to demonstrate less incidence of PGD, and more successful rescue as well. These results again encourage the ongoing debate that should our health policy be directed toward creating “centers for excellence” for certain complex surgeries[45]? And if that is the case, which procedures to consider, and how to balance health care costs? These authors once again reiterate issues and opportunities related to LTx and COVID-19. While immunosuppression in transplanted patients and susceptibility to COVID-19 has been an issue, more recently investigators are considering LTx as a potential therapy for COVID-19-induced pulmonary fibrosis.[40] In the field of heart transplantation, the authors quote a study that found morphologic RV as the foremost cause for heart failure needing transplantation in adult-CHD (ACHD) patients. This does go along with the fact that even with single ventricle repair (Fontan physiology) it is usually the morphologic RV that starts showing signs of systolic failure after about early adulthood. They also mention a study in which outcomes in recent era in ACHD patients were similar to non-ACHD patients after a heart transplant if they had 1 or less of 3 risk factors: body mass index >25 kg/m^2, total bilirubin >1.2 mg/dL, glomerular filtration rate <60 mL/min/1.73 m^2. As stated before, failure of Fontan circulation could be diastolic failure or another extreme effect on other organ systems like lymphatic drainage, liver, protein losing enteropathy, and so on, and hence the need for device therapy (VAD) to support failing Fontan to stage them to a heart transplant.[22,21] Heart donation after cardiac death continues to be a topic of interest. Authors mention a bench study in porcine model with mitochondrial transplant in DCD heart after reperfusion showed improved myocardial function as compared with placebo. Of recent, organelle transfusion has attracted enormous attention. Although several studies have claimed benefits like myocardial function, prevention of spinal ischemia, and so on, there remains the need to identify exact biological mechanism of action. It is still unclear how an intracellular organelle can be useful when injected into the systemic bloodstream; or how does it detect the target tissue, be it the myocardium or spinal cord; or what should be the precise dose or amount of mitochondria that needs to be injected.[46] In the quest to achieve ideal and efficacious DCD donor, authors also highlight another study where donor heart were managed on normothermic perfusion after harvest keeping the ischemia time to 27 to 35 minutes, and avoiding the cold machine reperfusion entirely with good outcomes. Expanding device therapy and understanding of heart failure has led to advent of various devices and various configurations of device placement. Biventricular failure continues to remain a major challenge. Some studies have been performed looking at 2 simultaneous VAD placement, one for left ventricle and one for RV, while others looking at total artificial heart (TAH), which is a device with 1 controller and 2 pumps, one for each ventricle. Issues with TAH are that it is a dedicated device in which the entire ventricles are removed, so patient has to be a transplant candidate. Also, incidence of renal failure is higher possibly due to loss of atrial tissue (and ANP). For bi-VAD, although the ventricular tissue does not need to be removed, there are several challenges: ideal location for the inflow cannula, the right atrium or the RV; ideal length of inflow to project into the chamber, or the outflow graft length and diameter to avoid overflow into the pulmonary artery; ideal technique to deal with the moderator band and the indwelling pacing leads; mitigating risk of thrombosis; and last, dealing with 2 controllers.[47] Renewed interest in TAH has been revived with the advent of the bioprothetic TAH.[48] The authors here highlight couple TAH-related outcome studies. Graft placement, driveline positioning, and older age groups continue to be challenges with TAH placements. Ever since the publication of "diametrically opposite" COAPT and Mitra-FR trials for treatment of secondary mitral regurgitation with percutaneous edge-to-edge repair, in order to reconcile the results, a phenomenon of proportionate and disproportionate functional mitral valve regurgitation (MR) has been explained.[49-51] Simplistically put, those patients with mixed etiology for severe MR benefitted, while those with severe MR mostly or entirely from heart failure and dilatation of LV did not benefit from the percutaneous edge-to-edge therapy.[51,52] Authors here elaborate the study which showed promising results like reduction in New York Heart Association class, avoidance of VAD, and increased longevity on the waitlist in patients who were treated with percutaneous edge-to-edge procedure while waiting for heart transplantation. Also, another retrospective study was published recently that showed reduction in 1-year survival and lower in-hospital mortality for patients presenting with mitral regurgitation and cardiogenic shock undergoing percutaneous edge-to-edge repair during index hospitalization.[53] This relatively novel modality of therapy may potentially have several implications that are gradually being unfolded.

Wang et al in their comprehensive narrative review highlight and summarize multiple publications salient to solid organ transplantation.[54] They start with scoping review describing the influence of COVID-19 on various "life-saving" versus "life-enhancing" organ transplantation. Through the reviewed articles, they critically discuss the balance between the need, availability, risks for such transplantation surgeries amid the unprecedented times of COVID-19 pandemic. The authors do note that in the field of pancreatic transplantation, simultaneous kidney and pancreas may be the way to move forward even for diabetes type 2 with end-stage renal disease (ESRD), rather than restricting it to only type 1 diabetics with ESRD. For intestinal transplantation, better survival and enteric autonomy has been observed in patients with duodenum or jejunum to ileum or colon anastomosis, and cecal and ileo-cecal valve preservation. Cardiac risk stratification continues to remain a highly debated topic in the field of kidney transplantation. Authors yet again quote studies that were unable to justify neither improved outcomes with prior revascularization nor cost-effectiveness for such interventions. Interestingly enough, a study by Matthews et al retrospectively looked at patients preoperatively revascularized prior to their liver or kidney transplant surgeries.[56] Surprisingly, they found that outcomes after CABG in pre-kidney and pre-liver transplants versus nontransplant groups were poor (30-day mortality 14.3% vs 2.8%; P = .009). Also, despite revascularization, majority patients never underwent the desired transplant surgery altogether. In field of liver transplantation, the potential for machine perfusion in "saving" marginal livers keeps growing. The drug terlipressin may have some potential advantages over vasopressin due to its splanchnic vasoconstriction property, early graft dysfunction was identified to be associated with lower oxygen content in the anhepatic and neohepatic phases, and sarcopenic obesity was found to be associated with increased mortality after liver transplantation. Quest for ideal method of providing pain-free surgery progresses along with fascial plain blocks for kidney transplantation, and also intrathecal opioids with low-dose naloxone infusion for hepatectomies. As in all fields of medicine, traditional statistical methodologies are being challenged by AI and deep neural network analysis. Risk indices for liver transplantation like MELD (Model of End-stage Liver Disease), SOFT (Survival Outcomes Following Liver Transplant), BAR (balance-of-risk), and DRI (donor-risk index) once again scored inferior to AI-based analysis. However, standardization, uniformity, and replication may be needed before the implementation of machine learning in human medicine.[17,57]

Reece et al[55] explicitly elaborate the effects of COVID-19 on the specialty of cardiac surgery. As recently revealed in the analysis of national vital statistics for the year 2020, the largest cause of death was cardiovascular diseases.[58] Overall, there has been an increase of 17.7% deaths when compared with 2019, with heart disease deaths going up by 4.8%, which is the largest rise since 2012. The reason for these increased mortality, due to diseases other than COVID-19, is presumably a collateral damage; people unwilling to go to hospitals from fear of being exposed to the disease; hospitals being overwhelmed by COVID-19 patients; specialized staff being deployed to manage COVID-19 patients; and limited hospital supplies. As highlighted by the authors, an analysis from the STS database showed that mid-Atlantic region suffered a decline of over 70% in cardiac surgery. Even the mortality for CABG patients in this region went up significantly. Amid statewide restrictions, resource allocation, and personal safety concerns, the heart transplantation program offered by United Network for Organ Sharing (UNOS) suffered too. Initially, the evaluation for donors were put on hold by UNOS, then local procurement was encouraged to limit exposure. The authors summarize studies looking into ECMO for therapy for COVID-19 patients with severe ARDS. ELSO maintains an active dashboard of COVID-19 patients undergoing ECMO therapy. As of date, there are over 6200 patients of COVID-19 (suspected or confirmed) who have undergone ECMO (https://www.elso.org/Registry/FullCOVID19RegistryDashboard.aspx; accessed April 13, 2021). Authors briefly mention their experience as a collective effort between 5 university hospitals, without revealing the results of the analysis yet. Survival on ECMO for COVID-19 patients as quoted by the authors is about 52%. A German registry-based study quoted 1% patients needing ECMO after severe COVID-19.[59] Also recently published is the possibility of LTx as a therapy for severe ARDS from COVID-19.[40] Mechanical ventilation, ECMO, and LTx all these are extremis measures for severely critically ill patients. Under normal conventional situations, this may be a step-wise escalation of therapy. However, in the midst of an ongoing pandemic with scarce resources, growing demand and challenging resource-allocation or manpower, consensus-based ethical principles, outcome-oriented utilitarian principles, and rights-oriented egalitarian principles may see a conflict.[60] Triaging patients and rationing therapy where thresholds have been crossed in both direction multiple times during this dynamic persistent pandemic, unlike any single mass casualty, has been a lesson learnt by all health care systems.[60,61]

While year 2020 was dominated by the unprecedented prodigious SARS CoV-2 (severe acute respiratory syndrome coronavirus 2), resulted in the death of more than 2.9 million people worldwide (https://coronavirus.jhu.edu/map.html; accessed on April 15, 2021), and caused an economic devastation, on an optimistic note there has been significant advances that will shape the next decade in science. Overall, harnessing the immense power of clean energy by nuclear fusion, the power of quantum computing, investment in geo-engineering to address climate change, and advances in CRISPR biotechnology for medical therapeutics are few notable advances. Basic tenets of scientific principles involve rigor and reproducibility. In our field of cardiovascular surgery, anesthesiology, and intensive care, the past year has seen quest for novel therapy, debates, and reproducibility. *Novel ideas* of treatment for COVID-19, vaccine, drugs, ECMO, even lung transplantation. Mechanical circulatory devices usage was expanded for cardiogenic shock for sepsis, ECPR, and electrical shock. *Debate* on utility of iron therapy prior to surgery, and superiority of IABP over ECMO for cardiogenic shock evolved. Expansion of domino transplantation of pancreas with kidney was considered even in type 2 diabetics with renal failure. Quest for optimal analgesia for cardiac surgery and neurological outcomes continue especially in CHD patients. *Reproducibility* of AI-derived algorithms have continued. Looking at the silver lining as induced by the COVID-19 cloud, in science, the promotion of collaboration among scientists, promotion of open-science, sharing research data, the evolution of preprint and paywall-free publishing, and addressing issues surrounding work-life balance will persist and pursue to advance science and benefit humankind as it did in conquering COVID-19.

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