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Focused Topic Series: Impact of COVID-19 on Cardiothoracic Surgery

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Innovations—The COVID-19 Pandemic

Innovations
2020, Vol. 15(4) 295
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The current issue of *Innovations* has dedicated the Focused Topic Series section to the coronavirus disease 2019 (COVID-19) pandemic. The COVID-19 pandemic resulted in a significant impact on our everyday life and clinical practice. In this issue, we put together a special collection of insightful Editorials from authors who experienced the pandemic firsthand. The experience with COVID-19 was slightly different around the globe with different degrees of burden. However, multiple publications revealed that the effect on surgical volumes, education, and safety was almost universal. The topics that we chose to highlight are not directly related to decrease in surgical volume and personal safety. In their Editorial, Frankel et al. detail the necessary considerations and steps for returning to elective cardiac surgery practice. Elective cases during this time represent a special challenge from the patient safety standpoint and from the hospital resources perspective. Appropriate planning is therefore necessary prior to the initiation of a fully functioning elective cardiac surgery program. Dr Bobby Yanagawa and a group of surgeons from multiple institutions assembled a COVID-19 educational playbook for cardiothoracic surgery residency programs. Much is going to be learned about education during this time and it is important to learn from the experience of highly respected surgeon educators in order to maintain and improve our training capacity for the younger generation. The use of extracorporeal membrane oxygenation (ECMO) to treat COVID-19 patients is under constant debate and evolution. We chose to include the perspective from Europe and from the United States regarding indications and management of ECMO circuits in general and more specifically for COVID patients. The group from the University of Maryland prepared a very interesting Editorial on heart and lung transplantation and the specific challenges associated with such procedures during the pandemic.

In this issue we also chose to publish content that is not associated with COVID-19. We included a review article on sternal

closure using cerclage versus cable closure, sternal stability, and infection. We find this review important since median sternotomy is still performed even in minimally invasive heavy programs and the advantages and disadvantages of the different closure techniques is important. In the Original Articles section, we chose to publish an interesting experimental model of the mitral valve and a comparison between video-assisted thoracoscopic surgery and thoracotomy for segmentectomy in lung tumor patients. Stand-alone surgical ablation for atrial fibrillation is on the rise and one of the hottest debates is whether to perform hybrid surgical ablations as a single stage or sequentially. The contribution by Matteucci et al. is important to enhance our ability to understand the ablation process and the expected outcome. The outcome of the Florida sleeve technique in patients with tricuspid and bicuspid aortic valves and a provocative article on temporary pacemaker wires in minimally invasive procedures complete the Original Articles section. In their How-To-Do-It Article, Kaleda et al. share a technique for central venous cannulation during minimally invasive aortic valve replacement. Finally, our Case Reports section includes a very diverse set of cases with some excellent take-home messages and practical technical information.

On behalf of our Editorial Team, I hope that you will find this new issue useful in improving your knowledge and practice. We share with you the hope that the negative impact of COVID-19 will diminish quickly, and that new treatments and vaccination avenues will be found soon.

Niv Ad, MD

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Charting a Safe and Expeditious Course Back to Elective Cardiac Surgery During the COVID-19 Pandemic

Innovations
2020, Vol. 15(4) 296–299
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DOI: 10.1177/1556984520930066
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"The compass of accurate knowledge directs the shortest, safest, cheapest course to any destination." – Claude C. Hopkins

The novel coronavirus disease 2019 (COVID-19) pandemic has swept across the United States, leaving a wake of unprecedented disruption. At the front lines, hospitals have swiftly enacted large-scale structural and organizational changes in order to meet the unique challenges of the pandemic. Based on the recommendations of the Centers for Medicare and Medicaid Services (CMS),¹ most hospitals across the United States have significantly curtailed all non-emergent procedures in an effort to conserve resources for a potential surge in severe COVID-19 infections. Consequently, cardiac surgeons have found themselves in uncharted waters due to indefinite cancellation of elective cardiac surgery. At the same time, while some patients with surgical-level cardiovascular disease have been left unable to access definitive treatment, others are avoiding the hospital altogether for fear of infection.^{2–4} What has become clear amidst the flux and uncertainty of the pandemic is that we must find a way to remain available to our patients by charting a safe and expeditious path toward resumption of elective cardiac surgery.

At the urging of the federal government,⁵ hospitals across the nation have slowly begun to plan for phased reopening of elective surgery. Although guidance statements such as those from the American College of Surgeons exist,⁶ the unique position of cardiac surgery within the spectrum of all elective surgery warrants specialty-specific considerations. Our patients are particularly tenuous and face an elevated risk of morbidity and mortality while waiting for surgery. Escalation of a case from elective to urgent based on clinical deterioration is not uncommon in our field. Elective cardiac surgery also requires substantially more resources (e.g., mechanical ventilation, blood products, inotropic medications, intensive care beds) compared to many of the other surgical subspecialties. Finally, the deleterious effects of cardiopulmonary bypass on the lungs may render these patients especially vulnerable to severe COVID-19 infection; however, evidence on this subject is purely speculative. Taken together, these unique challenges underscore the need for a specialty-specific roadmap. In the context of limited evidence at this time, we provide initial considerations for programs embarking on paths toward phased reopening of elective cardiac surgery.

Phase I—Preparation

A central requirement of most guidance statements regarding the resumption of elective surgery is confirmation of a sustained decrease in the rate of new COVID-19 cases in a given area for at least 14 days. It would, therefore, be remiss not to emphasize the critical importance of testing at this point. In hindsight, what will likely be recognized as the single greatest flaw in our national response to the COVID-19 pandemic was our inability to provide sufficient testing. Our limitations on this front have contributed to profound variation in estimates regarding the peak and duration of COVID-19 surge based on epidemiologic predictive models.^{7–10} While speculating on this data as it applies to a given geographic region may be a Sisyphean task, hospitals may ultimately find greater return on investment by developing a robust internal infrastructure for real-time data collection and analysis in order to triangulate between regional COVID-19 burden, hospital resource capacity, and backlog of elective cases. With such infrastructure in place, hospitals will be positioned to assess continued safety and make proactive rather than reactive adjustments as they progress through staged reopening of elective cardiac surgery.

In order to safely and sustainably resume elective cardiac surgery, programs must first ensure that their hospitals have the requisite resources and personnel. Programs will be tasked with the challenge of gradually increasing capacity to address the mounting backlog of time-sensitive cases in systems that may have been significantly depleted of resources due to the pandemic. Therefore, programs that have experienced profound disruption should not feel compelled to resume elective cardiac surgery immediately. Hospitals must confirm they can provide

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a sufficient number of adequately trained personnel and appropriate staffing ratios for all perioperative phases. It is also imperative for hospitals to have an adequate supply of personal protective equipment for their staff. Protecting the members of the surgical and perioperative teams, as well as the patients, must be a top priority throughout this process. This will require concerted attention to all phases of the personal protective equipment supply chain, including regional and national supply, daily burn rate, as well as policies and procedures to minimize waste.

Phase 2—Outpatient Diagnostic Testing

With the requisite infrastructure in place and in compliance with evolving local public health policy, programs may embark on phased reopening of elective cases. The first phase should center around reestablishing and optimizing the preoperative workup process. This phase can be initiated with minimal strain on inpatient hospital resources while additional perioperative process planning is underway. Many patients who were originally scheduled for surgery but were delayed may require repeat laboratory or imaging tests, history and physical exam, and/or a renewed consent. Protocols will need to be established to determine which patients should be seen again in the clinic by a surgeon versus those who could be seen in a general preoperative clinic or via telemedicine. Regardless, efforts should be made to accomplish as much of the preoperative workup in as few visits as possible in order to minimize the risk of potential transmission. In certain cases, this will require considerable coordination, especially for patients who require invasive tests such as cardiac catheterization or for patients who require staged tests such as those with renal insufficiency who require multiple intravenous contrast administrations.

Cardiac surgery programs should aim to create individualized perioperative COVID-19 testing algorithms in order to maximize the efficiency of available testing capacity. At a minimum, all patients scheduled for elective cardiac surgery should be tested for COVID-19 within 72 hours prior to surgery as part of standard preoperative workup. Careful consideration should be directed toward the management of patients who test positive for COVID-19 during the preoperative phase. Preliminary retrospective data suggest unacceptable morbidity and mortality in patients who underwent elective noncardiac surgical procedures and developed COVID-19 infection postoperatively.^{11,12} Therefore, patients scheduled for elective surgery who test positive should have their surgery canceled if safe to do so and be sent home to self-isolate with instructions to return to the hospital for further evaluation following recovery. A similar approach may be appropriate for patients who test negative but have significant exposure history, given the high false-negative rates associated with current polymerase chain reaction (PCR) tests.¹³ If feasible, hospitals could consider establishing a dedicated multidisciplinary team of infectious disease doctors, cardiologists, cardiac surgeons, and anesthesiologists charged with surgical planning and close monitoring of these patients

(both for their COVID-19 status as well as their underlying cardiovascular condition). As we deepen our understanding of COVID-19 infection, we may need to adapt these algorithms and consider the role of repeat PCR testing, serological testing, and serial imaging in determining the optimal timing for elective cardiac surgery in a patient who has previously tested positive for COVID-19.

In addition, hospitals will need to establish an appropriate policy for testing of health-care workers. Initial testing in the United States has been limited to symptomatic individuals; however, there is inadequate evidence to support this strategy. In fact, a recent study showed that approximately 44% of infections are transmitted during the primary patient's presymptomatic phase.¹⁴ This is highly concerning given the sheer number of individuals involved in the care of cardiac surgery patients. There are significant limitations to the current antibody assay technology including assay-to-assay variability along with limitations to our understanding of the implications of a positive titer. Nevertheless, serology may prove to be especially useful in this context. For example, if a positive titer is found to confer immunity to subsequent infections, hospitals may be able to use exposure history and serostatus to strategically staff units and operating rooms in a manner that bolsters infection control. Unfortunately, no testing algorithm is infallible. Given the high false-negative rates associated with current PCR tests,¹³ hospitals may also need to devise a system for contact tracing within the hospital in order to prevent localized outbreaks.

Phase 3—Elective Surgery

Once a thorough mechanism for identification and management of patients who tested positive for COVID-19 during the preoperative workup is in place, programs may begin to resume elective surgery. Given the variation in time-sensitivity of cases between surgical subspecialties, a governance committee including administrators, surgeons, anesthesiologists, and intensivists could be established to create a prioritization policy for elective cases. This committee could also establish a predetermined capacity goal for resources dedicated to the operating rooms to accommodate a potential surge of patients with COVID-19 infection without compromising the safety of postoperative patients.

Several valuable guidance statements for the triage of time-sensitive elective cases^{15,16} along with a resource prediction instrument for cardiac surgery from the Society of Thoracic Surgeons¹⁷ have been made available recently. Other programs have developed similarly useful models for resource allocation. For example, the Texas Medical Center has created an online dashboard that allows hospitals to monitor regional COVID-19 burden, personal protective equipment needs, and ventilator and intensive care unit bed capacity.¹⁸ In addition, a multicenter team developed a simple mathematical model to estimate the time required to clear the backlog of elective cardiac surgery cases based on variable levels of postsurge surgical volume.¹⁹ These can serve as preliminary support tools as hospitals

develop their own individualized prediction models. These initiatives also highlight the value of regional centralization of data. Similar platforms to share data and best practices between programs will be invaluable to our collective progress. Hospitals may need to accept a shift in paradigm to one where collaboration will rule over competition when it comes to providing their communities with access to safe elective cardiac surgery during the COVID-19 pandemic.

At this stage, hospitals should also incorporate strategies to mitigate the risk of postoperative nosocomial infection, especially as they take on more complex cases that require prolonged length of stay. For example, given the curtailed surgical volume and decreased census at most hospitals, it may be possible to bypass the pre- and postoperative anesthesia care units altogether in order to accomplish this aim. In addition, routine postoperative testing and procedures can be ordered more judiciously and medication administration can be clustered when feasible.

Programs should also develop algorithms for the diagnosis and management of postoperative patients with suspected COVID-19 infection. In a retrospective series of patients who underwent elective thoracic surgery and developed COVID-19 infection postoperatively,¹² the authors highlight some of the diagnostic challenges in the postoperative setting and advocate for liberal use of computed tomography scans at the onset of symptoms while awaiting confirmatory testing. In line with these recommendations, hospitals may consider a low threshold of suspicion for COVID-19 infection in patients after cardiac surgery, with early and serial testing at as many time points as necessary.

Programs should also dedicate ample consideration to the importance of visitation policy in our field. Given the gravity of our surgeries, many patients wish to have their families present during their recovery. Unfortunately, allowing unrestricted visitation potentially poses risks to our vulnerable patient population and undermines the value of preoperative testing to identify COVID-19 infection. Accordingly, most hospitals have adopted strict visitation policies, and will likely need to find creative solutions such as tablets with video chat technology or accommodations for a single family member to stay with the patient in the hospital postoperatively.

Phase 4—Business as Usual

In order to resume business as usual, we will need to ensure either (1) negligible transmission in the community or (2) negligible risk of severe infection in postoperative patients. Meeting the first condition in the absence of a safe and effective vaccine is unlikely. While hundreds of vaccine candidates are in development,²⁰ we must consider the fact that the timeline to bring an efficacious vaccine to market is unknown, but possibly on the order of years if it were to mirror historical timelines. On the other hand, although new potential treatments emerge almost daily, none are currently supported by high levels of evidence. It is imperative that we as a specialty lead by example and practice patience and promote evidence-based

medicine. This is not the time to peddle mechanistically intriguing potential treatments or needlessly wasteful, ineffective practices, but rather the time to demand rigorous studies rooted in safety and efficacy.

As difficult as it may be, we will need to temper our eagerness and momentum and steel ourselves to the reality that in contrast to the previous phases, which may have been separated by weeks or months, progression to this final phase could last much longer. In the meantime, embracing adaptive strategies to provide safe cardiac surgery in this new landscape will likely prove to be a more fruitful venture than attempting to restore our old sense of normal.

Conclusions

The path toward phased reopening of elective cardiac surgery will require patience, humility, and frequent recalibration in response to emerging data. Programs should implement dynamic COVID-19 testing protocols, examine capacity, and create prioritization policies in order to ensure safety and sustainability. At all phases during the pandemic, we must be transparent with our patients and maintain the highest standard of surgical care all the while maintaining preparedness for a potential surge in COVID-19 cases. In the face of this challenge, it is worth remembering that as a specialty, we are tasked with similarly high-stakes decisions daily when we counsel our patients, carefully balancing the risks of surgery against the risks of untreated disease. We are therefore uniquely qualified to captain this ship and chart a safe and expeditious course back to providing elective cardiac surgery for our patients.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Nguyen serves as a consultant for Edwards LifeSciences. All other authors have nothing to disclose with regard to commercial support.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Cardiothoracic Surgical Residency Programs: A Pandemic Playbook

Innovations
2020, Vol. 15(4) 300–305
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DOI: 10.1177/1556984520937656
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Bobby Yanagawa¹, MD PhD, Erin Mills Iannacone², MD, Tsuyoshi Kaneko³, MD, Fraser Rubens⁴, MD MSc , and David T. Cooke⁵, MD

The current generation of medical educators has experienced acquired immunodeficiency syndrome, severe acute respiratory syndrome (SARS) coronavirus, avian influenza, Ebola, and other pandemics. Even so, the coronavirus disease 2019 (COVID-19) has been unique in terms of sheer size, scale, and acuity in terms of impact on global societies, patient lives, and healthcare burden.^{1,2} Our residency programs, like our overall healthcare systems, were largely unprepared for the impact of COVID-19. In cardiothoracic surgery, during the initial days and weeks, the more immediate clinical care for infected and potentially infected patients were front and center.

Several weeks into the pandemic, residency programs continue to address key questions of how to balance safety and service for trainees and how to ensure that their education continues, many in their own unique ways. Residency programs have been forced to adapt through experimentation, incorporating new technologies and establishing new partnerships within an expedited timeframe. Our professional societies and our respective post-graduate medical education offices have provided much needed guidance and leadership. Additionally, many of us have used previous experiences with past pandemics and improvised with the availability of our new armamentarium of online telecommunications tools. We have learned some important lessons—what works and what does not—and have established new rules of engagement for our trainees. Once this pandemic is over, we may or may not embrace the “temporary” residency education measures resulting in permanent changes to cardiothoracic residency training. Only time will tell. Finally, by planning ahead, we hope to be better prepared for the next pandemic.

To document our experiences, challenges, and solutions for issues of cardiothoracic surgery residency education during this pandemic, we brought together a working group of cardiac and thoracic surgical program directors and educational leaders from the USA and Canada to share their experiences with COVID-19, including challenges, unique solutions, and unmet needs. We share these insights in the framework of 10 issues for cardiothoracic surgery residency education.

Resident Safety

The role of a resident straddles that of a learner as well as that of a clinician or caregiver and this raises interesting questions

during times of a pandemic. That role is fluid and often depends on the nature of the service, the individual, and the surgical system, whether the resident is early or late in their training, the task that is being performed, and others. For instance, during the acquired immunodeficiency syndrome epidemic, residents actively cared for human immunodeficiency virus (HIV)-infected patients. Most (77%) residents revealed that it was an excellent educational experience. As a stark reminder of the potential risks, a significant number were exposed to blood-contaminated needlestick from an HIV-seropositive patient (9%).³ On the other hand, during the Ebola epidemic, most US and Canadian residency programs limited patient contact with possible Ebola-infected patients to staff/faculty only.⁴ These experiences have shaped our current approach to balance the valuable patient care residents provide as well as the educational opportunity versus the risk of transmission to our residents.

We believe there are several principles that should be applied to maximize the physical safety of residents during the pandemic. The first is to optimize the efficiency of patient contact to limit unnecessary and redundant patient encounters, particularly by very junior trainees, to both limit the risk of transmission to healthcare staff and preserve limited personal protective equipment (PPE) resources. Needless to say, some hard-hit areas of COVID-19 needed residents as a workforce and be actively engaged in patient care. At the Brigham and Women’s Hospital, the cardiothoracic surgery team was reorganized into

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2 separate teams during COVID-19, the rationale being that if one team gets infected, the other team may still be available. This is often referred to as platoon coverage/rounding. Also, only 1 resident was allowed per operating room case, and only 1 individual rounding in a COVID+ patient's room at a time as opposed to platoon coverage/rounding.

Second, proactive steps should be taken to protect residents who could be considered high risk. Pregnant trainees, trainees with a newborn at home, and immunocompromised trainees, or those who are in any particular at-risk subpopulation should be excused from COVID-19-related clinical duties as the risk would outweigh service or educational benefits. Furthermore, programs may consider alternate housing for trainees who are at high risk of transmission to their families. During the COVID-19 pandemic, the State of California and UC Davis offer vouchers for residents to stay at an adjacent hotel if they are worried about exposing their families. Similarly, at select hospitals at the University of Toronto, hotels were made available for any healthcare worker, including residents, free-of-charge to those who live with vulnerable family members.

Third, educators should be the residents' advocate to ensure that PPE is properly deployed and available. The importance of PPE has been a focus during this pandemic, and programs should set an example of the correct application of PPE for recognized procedures (intubation, tracheostomy, procedures causing air leak, and so on) based on the best available evidence and reassess protocols as appropriate. Looking ahead, programs should ensure sufficient PPE to protect all trainees with stockpiles on hand for pandemics and to ensure that trainees are adequately trained in the process of safely donning and doffing PPE.

Finally, it is essential that educators retain the role of primary supervisor, overseeing safety at every stage. In the USA, the Accreditation Council for Graduate Medical Education (ACGME) advised programs that:

"Any resident or fellow who provides care to patients will do so under the appropriate supervision for the clinical circumstance and the level of education of the resident [or] fellow. Faculty members are expected to have been trained in the treatment and infection control protocols and procedures adopted by their local health care settings."

Resident Redeployment to Non-Cardiothoracic Units

Cardiothoracic residents have critical care skill sets that may be particularly valuable in the management of patients with COVID-19. However, redeployment may challenge our ability to fulfill our educational mandate for several reasons. First, faculty may not be in proximity to provide ongoing supervision and evaluation. This will require proactive work on the part of faculty to communicate regularly with residents to ensure that the academic environment is optimized by a mandated culture

of teaching and evaluation wherever the residents are working. Second, critical care work may be perceived as duplication in training particularly with senior residents. The residency program director must do their utmost to prepare training objectives during the redeployment and to provide ongoing opportunities for teaching such as full access to academic days and simulation. Finally, redeployment may threaten other rotations necessary for the time-based fulfillment of training certification. In Canada, the Royal College has recognized this challenge and they have provided guidelines to training programs to best balance how we will meet this need to avoid the potential of having to prolong training. The Royal College has signaled a willingness to recognize redeployment rotations as valid components of training as long as programs have optimized the academic quality of the rotation including formative and summative assessments. Finally, redeployment should occur only when necessary, and residency programs should coordinate with the hospital leadership to make this determination. The need for redeployment should be continually reassessed with the aim of returning the resident to their home service as soon as possible.

Academic Education and Online Learning

Before COVID-19, the integration of online communications platform into residency education was slow and in-person, academic rounds were the norm. At the height of the pandemic, all academic teaching was immediately placed on hold. Virtually every residency program has quickly turned to online resources such as Zoom and Microsoft Teams to continue teaching (Table 1). Many of us have been surprised at the seamless transition from in-person PowerPoint presentation to online sessions, particularly for our generation of trainees who are adept at the use of online tools. This format has resulted in positive unintended consequences that bode well for the quality of training. First, most programs have reported that faculty attendance has been better than average. Second, online sessions may allow more robust discussion and question and answer sessions as participants may not feel the stress of speaking in front of a large group as they might in person. Third, there is a convenience factor as residents can log on from virtually anywhere—personal laptop, smartphones, or from any hospital desktop. Fourth, no additional investment in infrastructure and no additional formatting are needed as talks on PowerPoint can be shared instantly with a "Share Screen" function. Finally, the talks can be shared with other centers or recorded to allow for their review by residents. Importantly, it is incumbent on residency program directors to work with their IT department and residents to take all possible steps to verify that such online platforms protect patient confidentiality. There are also well-validated online learning materials offered by the Thoracic Surgery Directors Association (TSDA) free of charge (<https://tsda.org/resources/resources-for-residents/>).

The Harvard Business Review offers expert tips on the optimal use of these meeting and communication tools.^{5–8} Some main points are as follows:

1. Have a meeting facilitator.
2. Be as interactive as possible.
3. Engage participants at all locations to ensure discussion understanding and alignment.
4. Have all participants share their video and audio to prevent disengagement.
5. Provide an agenda to participants.
6. Share content as much as possible via video conferencing and using online tools.
7. Allow verbal or visual cues, such as raising a hand to indicate a question.
8. Test equipment before the meeting.
9. Have a backup communication plan (e.g., connection via speaker phone).

Finally, educational rounds function to teach but also offer a social network for learners. During the SARS outbreak of 2003, Toronto experienced 253 suspected or probable cases of SARS, of which 40% were healthcare workers.^{9,10} In the aftermath of the SARS outbreak in Toronto, we learned that the cancellation of rounds and the restrictions placed on social interactions with other healthcare workers created majorly a sense of isolation in the trainees.⁹ Thus, every effort should be made to replace traditional teachings, rounds, and journal clubs with an online equivalent.

Online Surgical Simulation

Most surgical simulation involves learners congregating in a simulation center with a preceptor who provides immediate, real-time feedback.¹¹ Individual institutions can create online simulation programs, but this requires significant expertise and investment in time and infrastructure.

There are several online surgical simulation programs that are in various stages of development and trial. Brewer et al.

created 4 “cognitive” surgical modules (i.e., sternotomy, cannulation, decannulation, and sternal closure) on a free downloadable app.¹² This app was utilized by over 5,000 individual users worldwide. As a proof of concept, 16 trainees randomized to use of the app versus traditional learning experienced higher learning assessment scores.¹² My Virtual Anastomosis (Johnson & Johnson, Ethicon, Bridgewater, NJ, USA) was developed by Prof Paul Sergeant to provide a standardized curriculum and assessment platform for trainees, enabling continuous practice and learning based on the portable and cheap Arroyo anastomotic simulator (www.myvirtualanastomosis.com). This is a comprehensive curriculum that incorporates component tasks, supports deliberate practice, and most importantly, distance coaching/assessments of video-recorded anastomoses by Prof Paul Sergeant. The success of My Virtual Anastomosis has led to the development of My Virtual Aortic Root and My Virtual Mitral Valve modules, which, together, have already been accessed by thousands of surgeons globally. The TSDA offers a free, online simulation curriculum ranging from coronary anastomoses, to aortic valve replacement to management of aortic dissection including equipment setup, conduct, and assessment tools (<https://tsda.org/education/tsda-cardiac-surgery-simulation-curriculum/>). They report the feasibility of a home curriculum of aortic and coronary anastomoses using a low fidelity simulator.¹³

In summary, the initial success of online simulation initiatives supports that online courses and trainee-driven practice should be strongly considered as permanent adjuncts to cardiothoracic residency education.

Resident Wellness and Stress Management

Cardiothoracic surgery residency is intense and can lead to burnout. Residents learn how to care for patients in high-stakes, high stress environments. This may be compounded by the challenges of trainee abuse and sexual harassment that was shown to occur in more than half of women and a quarter of men.¹⁴ In this milieu, the stress of a pandemic may precipitate

Table 1. Commonly Available Online Teaching and Communication Platforms.

Online platform	Pro	Con
Zoom (zoom.us)	<ul style="list-style-type: none"> • Easy and convenient • Can be used from desktop, laptop, or cell phone • Screen sharing by both the conference manager and guests • Meetings can be recorded 	<ul style="list-style-type: none"> • Security is in question
GoToWebinar (gotomeeting.com)	<ul style="list-style-type: none"> • Easy and convenient • Can be used from desktop, laptop, or cell phone • Managers can take control of a participant's device • Documents can be shared in real time • Meetings can be recorded • Can host large meetings, up to 1,000 attendees 	<ul style="list-style-type: none"> • Requires a fast and reliable internet connection
Microsoft Teams (microsoft.com)	<ul style="list-style-type: none"> • Good security • Text-based communication 	<ul style="list-style-type: none"> • Must have a Microsoft account

burnout, as reflected by decreased job satisfaction, frustration, depression, and even suicidal ideation.¹⁵ Concerns may include fear of contracting the disease at work, fear of transmission to coworkers, family, and friends, worry about the well-being of elderly parents, and concern regarding their future. Trainees are also acutely concerned with the impact of the pandemic on their ability to finish their residency. Questions that have arisen include how they will make up for lost operative time, will extension of training be necessary and, how the loss of operative experience will impact their technical competency. Finally, social isolation during the COVID-19 pandemic can add loneliness and depression particularly if a trainee is isolated from family and friends.

Most residency programs have institutional wellness programs in place. In all residency programs there are regular bi-yearly one-on-one meetings between residents and the program director. During COVID-19, some programs have instituted weekly or monthly check-in meetings with the faculty and trainees. Trainees should have an opportunity to connect with others and inquire about the hospital/residency updates. Programs may also consider proactive consultation options with professional therapists and counselors.

Interviews and Recruitment

In-person interviews with residency applicants provide the opportunity to tour the hospital, meet the faculty and fellows in a relaxed environment, and experience the city of the institution. The residency program also gets a chance to meet the applicants in person and gain insight into their poise and personalities. In the coming year, it is also anticipated that medical student electives on cardiothoracic surgery rotations will not be feasible, no longer providing this opportunity to evaluate potential recruits.

This year, many programs were unable to complete all of their residency applicant interviews in person. At Weill Cornell Medicine, applicants were first sent a presentation showcasing the faculty, case complexity, specialized programs, and research. The applicants had Zoom interviews with the faculty as well as a separate session with the current fellows. Follow-up sessions with faculty were encouraged for interested applicants. There are other resources for these formats to help educators. The Association of American Medical Colleges offers insight on conducting interviews during the pandemic.¹⁶ In addition, Varghese et al. and the TSDA offer a virtual interview primer.¹⁷

It is unclear what effects these changes will have on the ranking process. For some, it may be difficult to gage an unfamiliar applicant without direct contact to experience all of the personal attributes that otherwise make them a good fit. This may be compounded further for applicants with families who have additional concerns extrinsic to the training program. When the question of whether remote interviews would likely become part of the new normal was discussed among faculty, the majority hoped for a return to the classic courting process

between programs and applicants. In addition, it is unclear what, if any, effect virtual interviews have on implicit bias. Although detailed analysis will be necessary, the interview process will likely return to the old format with some exceptions.

Examination and Licensing

Due to the COVID-19 pandemic, in the USA, the American Board of Thoracic Surgery (ABTS) has delayed the Certifying Exam (Oral Board) from June to October. The Qualifying Exam (Written Board) is still on schedule. The TSDA (representing US Program Directors) and the ABTS are in constant communication. Similarly, in Canada, to comply with COVID-19 social isolation, the Royal College of Physicians and Surgeons of Canada has decided to forgo the in-person oral examination and to hold only a written examination, to be written in each major city in September (normally written in May).

The certification process in Canada is overseen by the Royal College of Physicians and Surgeons. As in the USA, after completion of mandatory rotations and on the recommendation of their Program Directors, trainees must pass both the written and oral components of the certification exam. This year, the Royal College has elected to award certification on the basis of the written component only. This will place a heightened need for program directors and residency program committees to bear the responsibility that they have no concerns related to the competency of their candidate. As a consequence, residency program committees should plan to have thorough, well-documented discussions as it relates to graduating residents to support their decisions.

The criteria for licensure across jurisdictions may vary between our 2 countries. Whereas in the USA, many states provide licensure for “board eligible” candidates, this has not been a practice in Canada. However, with the delay of the examination, this may introduce a challenge to some candidates. Many trainees carry a financial load from schooling and it is unclear how this will be addressed. Commitments to commence work may have to be delayed, thus creating challenges to the individual service and hospital. As the majority of Canadian trainees also complete fellowship programs in the USA, it is unclear how the current crisis will change these plans.¹⁸

Generally speaking, we recommend that at the completion of training, all trainees should be given some form of general licensure as they may no longer have access to funding related to their residency and they will need to bill for clinical services. Most jurisdictions have negotiated such a process so that newly graduated residents can bill for services such as assisting and working in intensive care. In summary, each program director should be in close communication with licensing bodies to lobby for their concerns. If a significant exam or licensing delay is needed, a temporary license as a board-eligible status should be sought.

Operative Experience

In most jurisdictions, nonurgent cases such as coronary artery bypass graft for stable ischemic heart disease, valve repair/replacement in asymptomatic patients, repair of asymptomatic ascending aortic aneurysm (<5.5 cm), and surgical treatment of atrial fibrillation have been deferred. On the other hand, training programs are accredited based on volume and diversity of cases. Such standards are challenged during a pandemic when nonurgent and nonessential cases are not performed or performed in a limited manner. Most US and Canadian programs have minimum numbers for specific cases in their logs that are needed to graduate. During the COVID-19 pandemic, most centers have experienced an almost complete halt of nonurgent cardiac and thoracic cases. This has been the primary concern for the current trainees.

If a slowdown is protracted or there is a second wave of COVID-19, specialties may need to consider an extension of resident training to redo core surgical rotations. However, it is not clear that there are resources to support such an extension and it may fall upon the individual training programs to redouble their efforts to achieve competency objectives in the shorter time frame. The lack of exposure currently also may cause a domino effect in impacting all subsequent residency training years. The alternative would be to have the impacted residents to graduate with some minimal set of skills and “learning on the job.”

In the USA, ACGME, ABTS, and TSDA are in close communication regarding the major concern for graduating residents of insufficient case logs. The ACGME has directed all of their Residency Review Committees that

“It is up to the program director, with consideration of the recommendations of the program’s Clinical Competence Committee, to assess the competence of an individual resident/fellow as 1 part of the determination of whether that individual is prepared to enter the unsupervised practice of medicine.”

For instance, if a chief resident/fellow is short of their minimum case thresholds, and their program director and residency program committee decide that they are competent for graduation, their situation will be reviewed on a case-by-case level by the ABTS, and determine if they are board eligible, despite being short of recommended case thresholds. If the program director feels the patient is not ready, or the ABTS does not think the resident/fellow meets board eligibility, then they will need to extend training. It is up to the residency to find funding for salary and benefits.

In a similar manner, the Royal College of Physicians and Surgeons has provided its support to residency programs to modify training to more reflect competency as opposed to time-based rotations. Greater flexibility will be granted to programs to modify rotations as they see fit as long as this is accompanied by documentation and consensus and a commitment to quality of care.

Research

Due to the impact of low case volumes, many residents are quarantined away from the hospital with no clinical duties. Wet laboratories are considered nonessential and as such were closed. Clinical research has also been halted. On the other hand, this is a unique time to engage in clinical outcomes research that can be performed primarily online using local and large database projects, including case reports and series, systematic reviews and meta-analyses, and so on. There are also substantial funds available for COVID-19-based research. In summary, this is an opportunity to set up conference calls and to write grants focused on the impact of COVID-19 in a cardiothoracic surgical population, including COVID-19-related health disparities and social determinants of health.

Communication and Leadership

The COVID-19 crisis has highlighted the critical role of program directors as the stewards of the health and education of our trainees. We have a responsibility to communicate as leaders on their behalf with the hospital leadership, the individual postgraduate medical education offices, the professional societies, and local and federal governmental agencies. We must also commit to providing up-to-date consistent information and disclosure to our trainees. During the SARS outbreak of 2003, Toronto trainees experienced significant anxiety both from the uncertainty and changing information on the mode of transmission but also from the inconsistency in interpretation of public health directives and the lack of communication between healthcare institutions.¹⁰ Consistent and strong leadership and communication are the key.

Conclusions

We have attempted to provide some guidance for residency programs to address the teaching and well-being of residents while still providing care for our patients. Overall, we must balance our responsibilities of patient care during the pandemic and our commitment to train safe competent surgeons. Individual decisions must be personalized. Whereas the majority of our excellent candidates will succeed and gain tremendous life-experience, there may be situations where trainees were struggling prior to the pandemic and this hiatus may critically impede their momentum to succeed. This pandemic has spurred innovations in virtual learning, simulation, and meetings, to provide new ways for the trainees to stay focused and these innovations may positively change the way we teach. The wellness of the trainees is a major reported issue and must be followed carefully. Finally, it will be crucial for our individual residency training programs and professional societies to prepare for the next pandemic. The collective knowledge we gained must be passed on for future trainees. Based on all the topics discussed, we call on our professional societies to offer

guidelines or a pandemic manual to assist programs to manage each unique training environment.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Extracorporeal Membrane Oxygenation for COVID-19

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Introduction

The current coronavirus disease 2019 (COVID-19) pandemic represents an international public health crisis unprecedented in modern times with death rates in highly impacted countries approaching in excess of 400 deaths per one million persons.¹ Acute respiratory failure is a prominent clinical feature of patients with severe COVID-19, in part due to similarities between viral surface proteins of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and those involved in human pulmonary surfactant synthesis (Fig. 1).² While underlying molecular pathways that mediate the pathophysiology of COVID-19 have yet to be completely defined, it is clear that the disease can affect multiple organ systems resulting in devastating clinical sequelae.

Patients with acute respiratory distress syndrome (ARDS) and persistent hypoxemia despite recruitment maneuvers, escalation of positive end-expiratory pressure, and proning may benefit from veno-venous (VV) extracorporeal membrane oxygenation (ECMO). ECMO has been used increasingly to support patients with severe ARDS and also has demonstrated utility for treatment of ARDS related to H1N1 influenza.³ Recent data from the Extracorporeal Life Support Organization (ELSO) Registry demonstrate a 65% survival rate for patients supported with VV ECMO.⁴

First pioneered in the late 1960s, ECMO was initially utilized for treating neonates and infants with cardiopulmonary failure but was successfully translated to adult patients in 1972.^{5,6} Since then, a number of improvements in oxygenators, cannulas, pumps, and clinical strategies have contributed to increasingly broadened use of ECMO. A 2009 landmark study of intensive care unit patients with confirmed H1N1-associated ARDS in Australia and New Zealand found ECMO survivorship to be 79% with a median of 25 days of mechanical ventilation.³ This observation contributed to an exponential increase in the use of ECMO for acute respiratory failure, specifically with the use of VV ECMO in the 2013 H7N9 avian influenza A pandemic several years later.⁷ A subsequent outbreak in the next year of Middle East respiratory syndrome coronavirus (MERS-CoV) suggested

superior clinical outcomes in patients receiving ECMO compared to those who did not, with 65% mortality compared to 100% mortality for those receiving conventional therapy.^{8,9}

While the precise role has yet to be defined, VV ECMO is currently being utilized to treat many critically ill patients with COVID-19-related respiratory failure. According to the ELSO COVID-19 registry at time of this writing, 1,042 patients confirmed to have COVID-19 have been cannulated for ECMO and 237 out of 445 (53%) whose outcome have been determined have been discharged alive.¹⁰ At our institution we have seen an increase in the use of ECMO in the setting of the COVID-19 pandemic. In the first 5 months of 2020 we have supported 100 patients on ECMO, 33 of which have been for respiratory disease due to COVID-19.

Cannulation Strategies

Veno-venous ECMO

In patients with predominantly impaired gas exchange as often observed in COVID-19, VV ECMO is appropriate. VV ECMO extracts blood from the venous system, generally via the vena cava or right atrium, performs gas exchange, then returns blood to the venous system while simultaneously allowing mechanical ventilatory pressures to be safely reduced. In turn, this decreases risk of ventilator-induced lung injury (VILI) from barotrauma, hyperinflation, and reduces sedation requirements while potentially improving hemodynamics by reduction in

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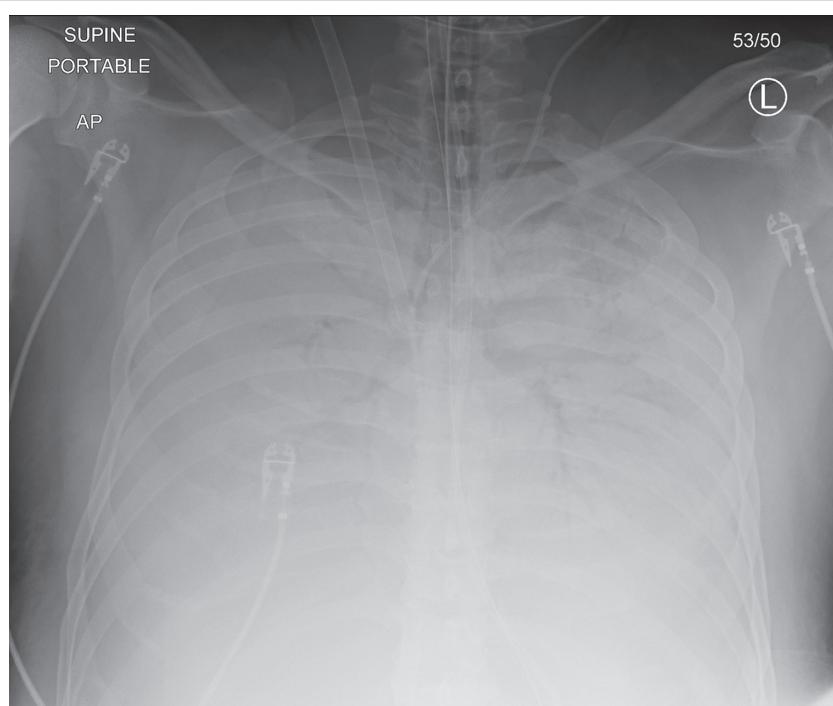


Fig. 1. Chest x-ray of a patient with COVID-19 on ECMO. The lung fields are opacified and ECMO is necessary for life-sustaining gas exchange. COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation.

intrathoracic pressure. Increased blood oxygen content improves myocardial perfusion, reduces pulmonary vascular resistance, and right ventricular strain, thereby resulting in improved hemodynamics.

Our institution preferentially performs femoral vein-right internal jugular vein cannulation. A percutaneous approach that employs ultrasound guidance is often used at the bedside without need for fluoroscopy. Cannulas are secured at the skin. A 25 French (Fr) femoral venous drainage cannula is commonly employed. Return cannulas ranging from 19 to 23 Fr are employed in the right internal jugular position. The use of large cannulas may facilitate higher flows, thus potentially achieving improved oxygenation, however at an increased rate of intracranial hemorrhage.¹¹ In smaller patients, should partial or total venous obstruction occur from the cannula, extremity edema and venous thrombosis may result. Alternative cannulation strategies may similarly be efficacious, particularly in patients who require mechanical support for the right ventricle. Dual lumen cannulas such as the Protek Duo can provide both VV ECMO and right ventricular mechanical support. These strategies typically require fluoroscopy or transesophageal echocardiographic guidance and may be less desirable in the setting of a viral pandemic. We have not utilized these cannulas and do not recommend their use unless there is a compelling reason.

ELSO has established guidelines for the implementation of prolonged extracorporeal life support for adult patients with respiratory failure.¹² Per their recommendations, optimal

ECMO outcomes are obtained when initiated early after respiratory failure according to the criteria listed in Table 1.^{13–15}

Veno-arterial ECMO

Veno-arterial (VA) ECMO offers hemodynamic support as well as gas exchange, conferring greatest benefit in patients who develop significant impairment in cardiac output. This has been used only sparingly in COVID-19 but has potential utility for patients with myocardial infarction or myocarditis causing cardiogenic shock.¹⁶ There have been a significant number of ST elevation myocardial infarctions reported in patients with COVID-19 possibly due to the virus' potential to replicate within cardiomyocytes and pericytes resulting in viral myocarditis, although this is an ongoing area of study.^{17,18} To our knowledge, only one case of cardiogenic shock secondary to COVID-19 myocarditis has been successfully managed with VA ECMO.¹⁹

Cannulation can be performed percutaneously at the bedside. Our practice generally utilizes a 25 Fr venous drainage cannula, with arterial cannula sizes ranging from 17 to 21 Fr for adult patients. To avoid leg ischemia, we routinely place a 6 Fr reinforced distal perfusion catheter percutaneously under ultrasound guidance. Of note, if cardiac output is initially robust or improves substantially and pulmonary gas exchange remains poor, ejection of deoxygenated blood from the heart can cause selective upper body hypoxemia (North-South or Harlequin syndrome), which

can lead to coronary or cerebral ischemia.²⁰ Development of pulmonary edema or echocardiographic evidence of left ventricular distension should prompt consideration left ventricular venting. A number of strategies, including direct surgical venting, the use of temporary left ventricular assist devices, and atrial septostomy, can be employed to vent the left ventricle.

Hybrid ECMO Strategies

Hybrid strategies may be useful for patients with significant hypoxemia and some degree of cardiac dysfunction resulting in hemodynamic compromise that is not resolved by correcting hypoxemia and hypercarbia. One case report describes a patient rescued from cardiogenic shock following poor response to cannulation for VV ECMO with left femoral 25 Fr drainage and left internal jugular 20 Fr return cannulas. Subsequent addition of a 15 Fr arterial limb to the right femoral artery improved arterial flow and significantly diminished pressor requirements with normalized lactic acid levels.²¹ Such a strategy would be useful for patients initially cannulated for VV ECMO that develop myocarditis or thrombotic complications resulting in coronary ischemia. Conversely, hypoxemia may be alleviated by adding a right internal jugular inflow cannula should hypoxemia develop in a patient initially supported on VA ECMO.

ECMO-Assisted Cardiopulmonary Resuscitation for Cardiac Arrest

ECMO may be a useful adjunct to conventional cardiopulmonary resuscitation in the setting of refractory cardiac arrests.²² Unfortunately, ECMO-assisted cardiopulmonary resuscitation (ECPR) may not be practical for COVID-19 patients because of the extra time required to don protective equipment for all members of the team and transport equipment into the room.²³ Further, patients with COVID-19 who have refractory cardiac arrest tend to have a grave prognosis and the risk–benefit profile does not favor performing ECPR. Ethical considerations and expectations should be discussed early with patients and their surrogate(s) during the hospital course. Our institution requires patients or family members to discuss expectations for ECMO therapy during the initial few days on ECMO.

Complications of ECMO Therapy

ECMO is associated with serious complications that include bleeding, stroke, ventilator-associated pneumonia, catheter-related blood stream infections, metabolic derangements, limb ischemia, and brain death in cases of severe brain injury.²⁴ Bleeding is the most common severe complication during ECMO occurring in up to 70% of VA ECMO patients.^{25–27} Procedures such as chest tube insertion and nasal gastric tube insertion also lead to much higher complication rates in patients on ECMO for COVID-19 because of increased bleeding risk. Severe inflammation and dysregulation of the coagulation cascade are factors that may lead to increased complication rates for ECMO when used

for patients with COVID-19 compared to other disease processes.

Special Considerations

Personal Protective Equipment

Guidelines from the World Health Organization (WHO) recommend combined droplet and contact precautions for patients with COVID-19. The US Centers for Disease Control and Prevention (CDC) have suggested that airborne precautions are necessary.²⁸ Because our understanding of the infectivity of SARS-CoV-2 is incomplete, there remains controversy about what level of personal protective equipment (PPE) is necessary.²⁹ Regardless, all suspected patients should be treated as positive until tests have confirmed negative viral status. Routine hand hygiene prior to and following contact with suspected or confirmed COVID-19-positive patients, materials, or surfaces with either soap and water or alcohol-based disinfectants remains universally endorsed for all levels of patient care.³⁰

As ECMO is often initiated as a bedside sterile procedure, PPE should be collected and then donned in the correct order. Following an initial round of hand hygiene, sterile gown should be donned, then N95 respirator, powered air-purifying respirator (PAPR) with high-efficiency particulate arrestance filter, sterile gloves, then a second sterile gown and gloving, taking care to overlap with the cuff of the gown at each step. When doffing, the order is to remove external and internal gown into both layers of sterile gloves, then to remove PAPR, keeping the respirator worn until exited from the contaminated area. Appropriate training and fit testing should be provided to all personnel prior to patient care, with additional staff present outside of designated hot zones to ensure correct donning and doffing procedures. The additional time necessary to comply with these procedures should also be considered, as time-sensitive encounters may be complicated by correct PPE application. Similarly, when procedures such as bronchoscopy or tracheostomy are being performed, appropriate PPE and practices must be utilized (Fig. 2, Fig. 3).

Personnel

Implementation of multidisciplinary ECMO teams has been documented to improve clinical outcomes for patients with ARDS compared to decentralized and informal chains of command.³¹ When initiating ECMO for COVID-19-positive patients, personnel should be limited to reduce personal risk of acquiring the virus and to minimize rates of transmission and with clearly designated roles. Our general strategy utilizes 2 physicians in sterile garb for cannulation, 1 intensivist, 1 nurse, and 1 ECMO specialist or perfusionist for cannulation and initiation. Centers may adjust to their needs accordingly.³²

Patient Selection and Exclusion Criteria

Appropriate patient selection and timing of ECMO initiation is crucial to achieving favorable outcomes in ECMO; however, this process is in evolution for COVID-19. Terminal conditions, severe central nervous system compromise, and do-not-resuscitate orders preclude treatment with ECMO. According to ELSO guidelines, patients with extensive comorbid disease and advanced age should be scrutinized, while patients requiring mechanical ventilation in excess of 7 days should be excluded.²³ Once initiated, if cardiopulmonary function does not improve over a reasonable period of time, care may be deemed futile. ELSO has issued guidelines for the institution of ECMO in respiratory failure (Table 1). At our institution we employ similar criteria.

Postcannulation Care

Ventilation Strategies

COVID-induced acute respiratory failure represents one of the chief insults secondary to infection. According to the Surviving Sepsis Campaign (SSC) COVID-19 panel in conjunction with the WHO and CDC, clinical care guidelines have been offered to address the oxygenation and ventilation of COVID-19 patients.³³ For those who fail to respond to noninvasive ventilation including high-flow nasal cannula or noninvasive positive pressure ventilation, invasive mechanical ventilation is necessary. The SSC advocates low tidal volume (V_T) ventilation V_T 4 to 8 mL/kg of predicted body weight over higher tidal volumes defined as V_T >8 mL/kg and targeting a plateau pressure (P_{PLAT}) of <30 cm H₂O, as more aggressive ventilation pressures have been documented as causing VILI and contributing to multiorgan failure in patients with ARDS.³⁴ Interventions should focus on higher positive end-expiratory pressure (PEEP) as tolerated, with patients observed for signs of barotrauma for PEEP >10 cm H₂O. Limiting driving pressure is key to reducing VILI, as this is the key determinant of VILI and highly predictive of mortality in ARDS.³⁵ PEEP may be titrated at the bedside and, when optimized, driving pressure should be at its lowest level to achieve a particular tidal volume. Fluid support should be used conservatively as COVID-associated cardiac failure either alone or in combination with ARDS has been documented to cause as many as 40% of COVID-19 deaths.³⁶ Judicious fluid administration may be required to help prevent renal failure. Prone positioning for ventilation has also been demonstrated to be useful in ARDS and is recommended for 12 to 16 hours but should be used in conjunction with diligent observation for the development of pressure ulceration. Paralytic agents should be used as necessary and partial paralysis along with deep sedation is often helpful to improve ventilator synchrony and reduce work of breathing. Intermittent dosing should be used when possible, reserving continuous infusion for those with persistent ventilator dyssynchrony. These principles are also employed after a patient has been canulated for ECMO.

Anticoagulation

Early observations suggest that COVID-19 patients are hypercoagulable and require increased anticoagulation, with some data suggesting that heparin administration may be beneficial.³⁷⁻⁴⁰ Patients have elevated fibrinogen and factor VIII levels that likely contribute to hypercoagulability. These changes can be further exacerbated by ECMO, which also leads to increased factor VIII. Before initiating a loading dose of heparin, baseline laboratory data should be obtained if possible including complete blood count, prothrombin time (PT), activated partial thromboplastin time (aPTT), d-dimer and fibrinogen levels, activated clotting time (ACT), and antithrombin activity. Viscoelastic testing may be utilized in some centers and can be helpful in identifying hypercoagulable states in patients with COVID-19. Anticoagulation protocols vary, and some centers preferentially use direct thrombin inhibitors.⁴¹⁻⁴³ There is no compelling data to support a single approach and heparin remains the gold standard anticoagulant. At our center, we have

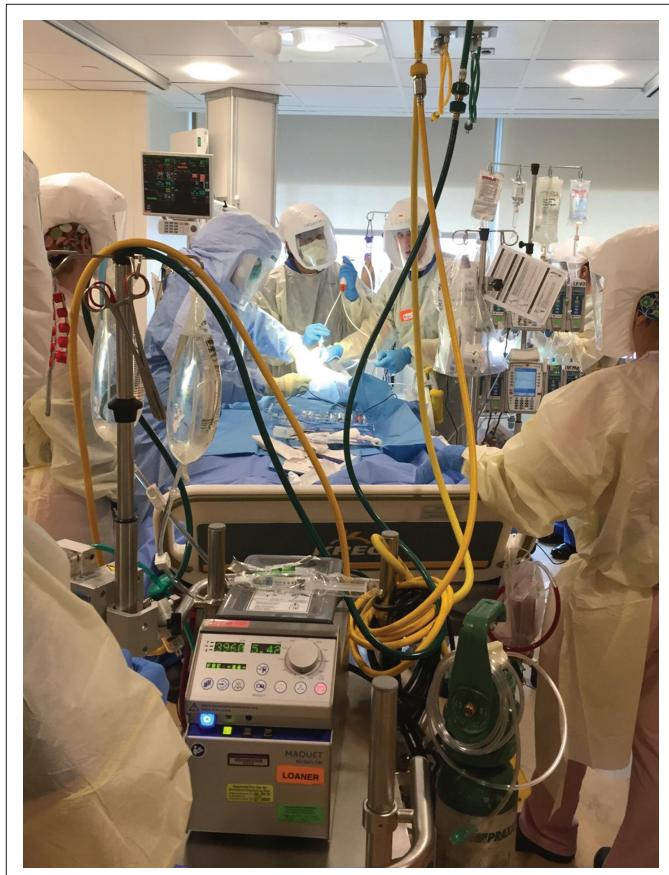


Fig. 2. Performing bedside tracheostomy on COVID patient. Appropriate PPE is critical for any contact with patients with confirmed or suspected COVID-19. During the tracheostomy, ECMO flow and sweep are increased and the ventilator is intermittently paused when the airway is open to help prevent aerosolization. COVID, coronavirus disease; ECMO, extracorporeal membrane oxygenation; PPE, personal protective equipment.



Fig. 3. Cannulation for ECMO in a patient with COVID-19. VV ECMO, used in this case, is appropriate for most patients with COVID-19, where impaired gas exchange is the predominant problem. A femoral venous cannula and right internal jugular cannula were used in this case. Appropriate PPE is also an important consideration. COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; PPE, personal protective equipment; VV, veno-venous.

increased our aPTT goal to 60 to 80 for VV ECMO due to concerns for hypercoagulability. Values are checked every 6 hours until a consistent, stable level is reached, and then every 6 hours thereafter.

Routine monitoring for heparin-induced thrombocytopenia and thrombosis should be performed with platelet counts and skin assessments. Acquired hypofibrinogenemia may be observed in high consumption states as in disseminated intravascular coagulation and should prompt investigation for large volume thrombosis. Typically such low fibrinogen states are associated with increased bleeding risk and warrant necessary precaution. Patients with pronounced coagulopathy prior to initiation of ECMO or known heparin resistance should receive appropriate blood products including fresh frozen plasma, cryoprecipitate, or platelets as indicated. Laboratory data suggesting increased risk of thrombosis, as measured by elevated d-dimer levels, increased fibrinogen, or as observed changes in

thromboelastogram should prompt careful monitoring of the ECMO circuit, particularly the oxygenator.⁴⁴

Medical Therapies

Data on medical therapy for COVID-19 are currently in evolution. Initial therapy with corticosteroids has been discouraged for generalized use in a recent meta-analysis by the SSC and previous studies have demonstrated a possible role in promoting increased viral shedding in coronavirus strains other than SARS-CoV-19.^{33,45} Still, corticosteroids may benefit patients with septic shock or who are worsening without other suitable options. Use of acetaminophen for antipyresis and broad-spectrum antimicrobial coverage for opportunistic secondary infections are also strongly encouraged by most professional societies. Intravenous immunoglobulin and convalescent plasma may be useful but have previously proven ineffective in modulating morbidity or mortality in other viral respiratory infections or have proven too difficult to pool in sufficient quantities to provide on clinically meaningful scales.^{46,47}

Antiviral Drugs

Limited data exist to support efficacy of antiviral therapy in COVID-19; however, this represents an area of ongoing investigation. Chloroquine and its metabolite hydroxychloroquine have previously been studied for their effects on the related SARS-CoV virus responsible for the SARS pandemic of 2003. Some Chinese centers have initiated recommendation guidelines for the implementation of chloroquine and hydroxychloroquine, although care should be taken in monitoring for cardiotoxic prolonged QTc changes that have been well documented with its use.^{48,49} Preliminary data from the Brazilian CloroCovid-19 trial have identified increased adverse events and cardiotoxicity with increased dosing of chloroquine in severe COVID-induced ARDS including QTc prolongation and myocarditis.⁵⁰ To date there remains insufficient evidence to recommend use at this time, with the National Institutes of Health (NIH) currently recommending against use of high-dose chloroquine or hydroxychloroquine as of this writing.⁵¹⁻⁵⁴

Lopinavir either alone or in combination with ritonavir as an adjunctive agent to inhibit metabolism of lopinavir has not been proven effective either in symptom abatement or mortality reduction.⁵⁵ Only nominal benefits including modest reductions in fever were observed in nonrandomized data on 47 patients receiving lopinavir/ritonavir combination therapy.⁵⁶

Remdesivir is a similarly structured nucleoside analog to lopinavir previously studied in the treatment of Ebola and Nipha viruses. Therapeutic administration has demonstrated reductions in viral titers as early as 12 hours after administration of therapy with improved respiratory status and reduced pulmonary infiltrates on radiography in rhesus macaque models.⁵⁷ In a statement by the NIH, it was reported that the Adaptive COVID-19 Treatment Trial (ACTT) sponsored by the National Institute of Allergy and Infectious Diseases was able

Table I. ELSO Guidelines for the Implementation of Prolonged Extracorporeal Life Support for Adult Patients with Respiratory Failure.**Initiation of ECMO should be considered according to the following criteria:**

1. Consideration should be given in hypoxic respiratory failure with associated mortality equal to or greater than 50% and indicated in those whose mortality is 80% or greater. Fifty percent mortality risk is associated with $\text{PaO}_2/\text{FiO}_2 < 150$ on $\text{FiO}_2 > 90\%$ and/or equivalent risk stratification scores (Murray score 2 to 3, AOI score 60, or APSS score 3) while 80% mortality risk is associated with $\text{PaO}_2/\text{FiO}_2 < 100$ on $\text{FiO}_2 > 90\%$ (and/or Murray score 3 to 4, AOI > 80, or APSS 8) despite optimal care for 6 hours or less.
2. CO_2 retention on mechanical ventilation despite high plateau pressure in excess of 30 cm H₂O.
3. Severe air leak syndromes.
4. Intubation requirement in pre-lung transplant patient.
5. Immediate cardiac or respiratory collapse (including PE, blocked airway, or nonresponsive to optimal care).

Relative contraindications resulting in suboptimal outcomes following ECMO therapy include:

1. High mechanical ventilation settings for 7 days or more, including $\text{FiO}_2 > 90\%$ or plateau pressure > 30 cm H₂O.
2. Major pharmacologic immunosuppression (absolute neutrophil count < 400/mm³).
3. Recent or expanding CNS hemorrhage.
4. Nonrecoverable or terminal injury (CNS injury, terminal malignancy).
5. Increasing age associates with increasing risk of poor outcome.

The above guidelines have been set forth according to the ELSO respiratory support guidelines v1.4 dated August 2017 which are available at <https://www.elso.org/Resources/Guidelines.aspx>.¹² Per ELSO guidelines, optimal ECMO outcomes are obtained when initiated early after respiratory failure within 1 to 2 days according to these criteria. Mortality scores include the Murray Score for Acute Lung Injury, AOI, APSS.

Abbreviations: AOI, Age-Adjusted Oxygenation Index; APSS, Acute Physiology of Stroke Score; CNS, central nervous system; ECMO, extra corporeal membrane oxygenation; ELSO, Extracorporeal Life Support Organization; PE, pulmonary embolism; PPE, personal protective equipment; VV, veno-venous.

to demonstrate 31% faster time to recovery in patients receiving remdesivir than those who received placebo, with a median time to recovery of 11 days.⁵⁸ Similarly, in a double-blind randomized controlled trial of 1,063 hospitalized adults, a 10-day course was superior to placebo in shortening time to recovery with estimated mortality at 14 days 7.1% in the remdesivir group compared to 11.9% in the placebo group.⁵⁹

Tocilizumab is an anti-IL-6-receptor human monoclonal antibody currently used in the treatment of rheumatoid and systemic juvenile idiopathic arthritis, which modulates release of proinflammatory cytokines and has been proposed as a possible modulator of COVID-19 symptomatology.⁶⁰ SARS-CoV-2 has demonstrated similar cytokine profiles to SARS-CoV and MERS-CoV, with the constellation of these symptoms now referred to as cytokine release syndromes.⁶¹ The drug is currently under investigation for its potential role in the treatment of SARS-CoV-2.⁶² Single-center experiences and early reports from multicenter trials are promising, suggesting increased likelihood of survival but are not as yet definitive.^{63,64}

Conclusions

The emergence of SARS-CoV-2 has led to a global pandemic resulting in large numbers of cases of respiratory failure. ECMO can be life saving for select patients with refractory cardiopulmonary failure. VV ECMO is the appropriate configuration for most patients with predominantly respiratory failure, although VA ECMO or hybrid strategies may be appropriate for patients with impaired cardiac output. Regionalization of care to high-volume ECMO centers is most likely to lead to improved outcome as management of COVID-19 patients on ECMO is complex and requires a team-based approach. As experience with COVID-19

grows, ECMO is likely to have an important role in caring for severely ill younger patients with few comorbidities.

Acknowledgments

We wish to thank the countless nurses, therapists, and other healthcare providers who risked their lives every day to care for the critically ill patients afflicted with COVID-19.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: David J. Kaczorowski has ownership and intellectual property interest in ECMOTEK, LLC.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Cardiac and Pulmonary Transplant Considerations During COVID-19 Pandemic

Innovations
2020, Vol. 15(4) 313–315
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DOI: 10.1177/1556984520937007
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Coronavirus disease 2019 (COVID-19) has dramatically and rapidly impacted health care in 2020. Every aspect of health care has been affected, but there has been a unique strain on organ transplantation. Each facet of transplantation is faced with unique challenges, including donor evaluation and procurement, recipient considerations, intraoperative management, and posttransplant care. We review the impact on transplant rate and pre-, intra-, and postoperative donor/recipient considerations.

Thoracic Organ Transplant Rate

The strain that COVID-19 has placed on the health care system has impeded the performance of thoracic organ transplants. Compared to the pre-COVID (January 1 to March 14, 2020) mean heart transplant rate in the United States of 72 ± 8 heart transplants/week, there were 58 ± 12 transplants/week performed during the COVID era (March 15 to May 16, 2020; Fig. 1). Weekly transplant rate varied during this period, with a maximum decrease of 40% (April 5 to 11, 2020) compared to pre-COVID. Interestingly, transplant rate has rebounded in May 2020 with 83 (115% of pre-COVID mean) heart transplants performed from May 10 to 16, 2020 (*Data from United Network for Organ Sharing, Accessed May 20, 2020*).

Heart transplantation rate varied by region during the COVID-restricted era, with some regions maintaining their transplant rate and others with a significant decrease. For instance, while the Northeast region performed only 1 heart transplant between April 12 and 18, 2020 (pre-COVID mean: 9 ± 2 heart transplants/week), the Southeast region performed 16 heart transplants during the same week (pre-COVID mean: 17 ± 3 heart transplants/week).

Trends were similar in lung transplantation, with a decrease in lung transplantation rate from 57 ± 7 transplants/week pre-COVID to 37 ± 11 transplants/week during the COVID-restricted era (Fig. 2). Lung transplantation rate in the United States also nadired from April 5 to 11, 2020 with a 67% decrease relative to pre-COVID. Similar to heart transplantation, the Northeast region transplant rate most severely impacted during this time period. In fact, between March 22 and April 25, 2020, only 2 total lung transplants were performed in this region.

A number of factors may have contributed to these observations. These include donor considerations and availability, as well as concern over the danger of travel for organ procurement. Given the need for immunosuppression, the potential for recipients to become infected is another factor that may be a barrier to transplant. Both donor and recipient hospital resources and case counts may impact the ability to proceed with transplantation. Regional variability in the timing and density of COVID-19 cases may account for some of the observed differences in regional transplantation rates.

Recipient and Waitlist Considerations

Patients on the waitlist for heart and lung transplantations are at risk of acquiring the disease prior to transplantation, from the donor organ, during the perioperative period, or after discharge. Since the incubation period for COVID-19 is 2 to 14 days, there is potential risk for asymptomatic transmission and, therefore, the risk of acquiring the disease must be weighed against the benefits of transplantation for each individual patient.

The International Society of Heart and Lung Transplantation (ISHLT) recommends that patients with active COVID-19 should be inactivated on the waitlist.¹ After a patient has recovered from the illness, ISHLT recommends at least 14 days after initial diagnosis and 2 successive negative polymerase chain reaction (PCR)-based tests at least 48 hours apart prior to transplantation.

Prior to transplantation, intensive care unit capacity, availability of resources and staff, location of postoperative care of transplant patients, and crossover of healthcare workers between COVID-positive and transplant patients must be weighed. Moreover, since waitlisted patients could be

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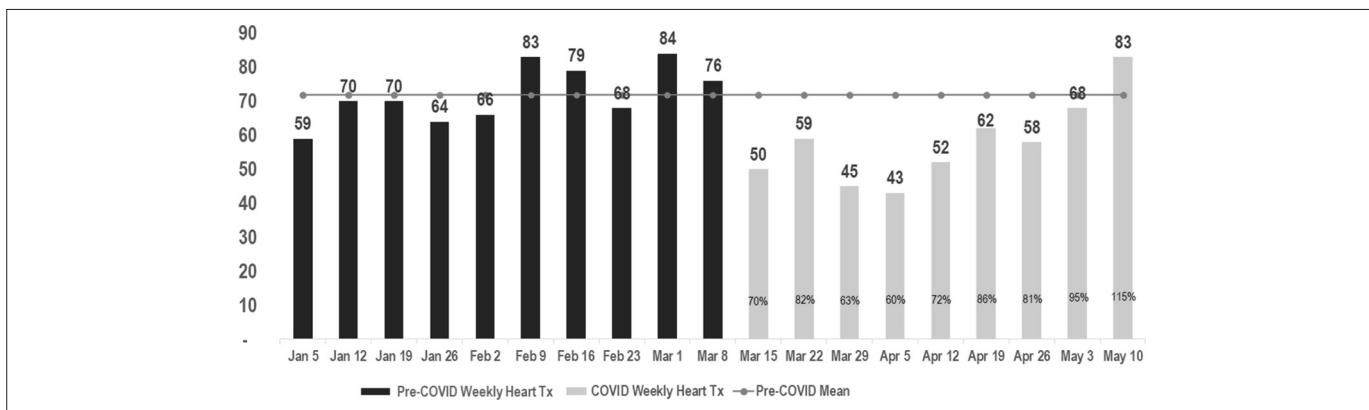


Fig. 1. Rate of heart transplantation in the United States in 2020, prior to the COVID pandemic (blue) and during COVID pandemic (yellow). The pre-COVID mean heart transplants/week (red line) was 72 transplants/week. Percentage of pre-COVID transplant rate is provided within yellow bars. Data from United Network for Organ Sharing, Accessed May 20, 2020. COVID, coronavirus disease.

asymptomatic with the disease, a PCR-based test to rule out infection in the recipient should be considered. The availability of rapid testing can allow potential recipients to be screened immediately prior to transplantation.

Donor Precautions, Evaluation, and Procurement

According to the American Society of Transplantation, donors should be screened epidemiologically, and by clinical history for suspected COVID-19 infection.² Therefore, a donor with known exposure to COVID-19 within 14 days, or any signs or symptoms consistent with COVID-19 should not be considered for transplantation. Signs of viral pneumonitis on chest computed tomography, including ground glass opacification, should be interpreted in the clinical context of the patient.

PCR-based testing of nasopharyngeal swab, tracheal aspirate, or bronchoalveolar lavage (BAL) should be performed within 3

days of procurement, when feasible. While tracheal aspirate and BAL have a higher sensitivity than nasopharyngeal swab, bronchoscopy should only be performed with adequate personal protective equipment (PPE). Serologic testing may provide additional information, but interpretation of these tests in reference to active or previous disease is currently unclear. Therefore, the American Society of Transplantation provides no recommendation regarding testing or interpretation of serologic tests. For donors who have recovered from COVID-19, resolution of symptoms greater than 28 days prior to procurement and serial negative tests suggest that organs from these donors are likely to be safe to use.

During donor procurement, attempts should be made to minimize number of personnel who are traveling, and when possible, organs should be procured by a local recovery team. If remote organ procurement is performed, efforts should be made to minimize contact of the procurement team to COVID-19 patients at the donor hospital. A route through the hospital that avoids units that house patients known to be infected with

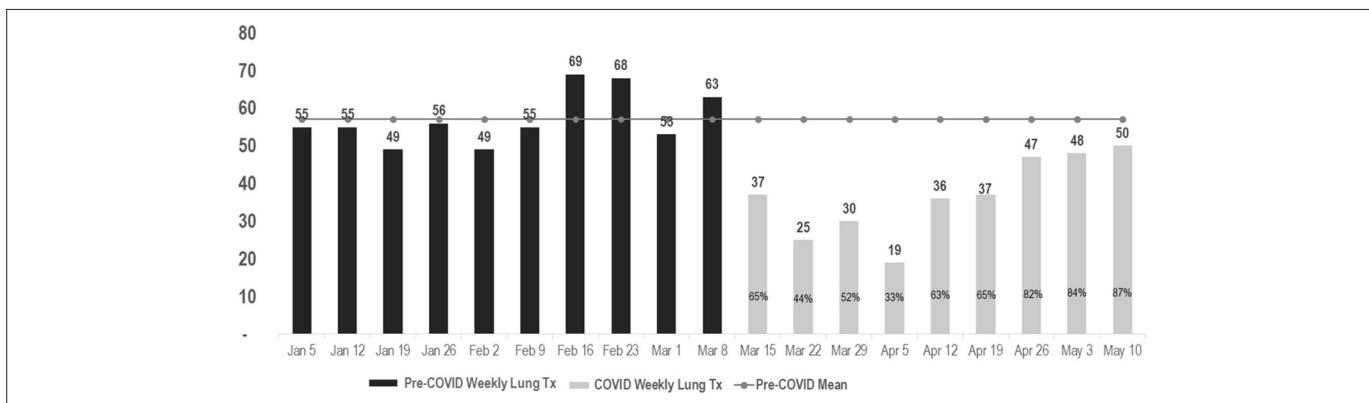


Fig. 2. Rate of lung transplantation in the United States in 2020, prior to the COVID pandemic (blue) and during COVID pandemic (yellow). The pre-COVID mean lung transplants/week (red line) was 57 transplants/week. Percentage of pre-COVID transplant rate is provided within yellow bars. Data from United Network for Organ Sharing, Accessed May 20, 2020. COVID, coronavirus disease.

COVID-19 should be considered. The procurement team should wear a surgical mask, and consider wearing an N-95 mask, during transport. Since the airway is exposed during pulmonary procurement and implantation, adequate PPE is necessary during donor pneumonectomy and implantation.

Posttransplant Considerations

It is currently unknown whether thoracic organ transplant recipients are at increased risk of acquiring COVID-19 or developing severe disease. At a single institution in New York, 28 heart transplant recipients presented for acute care associated with COVID-19. Seven (25%) required intubation, 3 (11%) required new dialysis, and 7 (25%) died.³ Moreover, data from the National Health Service registry demonstrated that organ transplant recipients who developed COVID-19 had a hazard ratio for death of 4.27 after multivariable adjustment.⁴ This hazard for death was second only to advanced age above 70 years.

Current consensus guidelines from the ISHLT include¹:

1. No changes to induction immunosuppression from the institution's standard protocol
2. Continue maintenance immunosuppression regimens without modifications for COVID-19 prophylaxis
3. Defer routine surveillance biopsies in patients with stable allograft function (>3 months from transplant, no history of rejection, no history of positive crossmatch, not sensitized)
4. Home spirometry monitoring in place of going to a pulmonary function test laboratory
5. Minimize social interactions after transplantation, as recommended by the Centers for Disease Control and Prevention

Treatment and monitoring for transplant patients who acquire COVID-19 is largely similar to the general population. For asymptomatic or mild disease, patients should be on home quarantine for 2 weeks without any changes to immunosuppression. For moderate or severe disease, patients should be treated with supportive care including ventilatory support and careful consideration for extracorporeal membrane oxygenation, as appropriate. In patients with moderate or severe disease, the ISHLT recommends consideration to holding mycophenolate mofetil or azathioprine with close monitoring for rejection.

No specific pharmacologic or treatment protocols have been shown to be particularly effective in transplant recipients who

acquire COVID-19. Therefore, outside of supportive care, pharmacologic or other treatment strategies should only be administered in the setting of a clinical trial, with close attention to drug-drug interactions associated with transplant-specific medications. Given the high mortality associated with COVID-19 infection in transplant patients, the development of treatment strategies for this vulnerable patient population represents a subject that mandates further investigation.

Conclusions

COVID-19 has dramatically impacted thoracic organ transplantation, with a sharp, region-specific decrease in rate of heart and lung transplantation. Specific recipient, donor, and posttransplant considerations are necessary to safely perform organ transplantation during the COVID-19 pandemic, and risks of transplantation must be weighed against the benefits.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Has Venoarterial ECMO Been Underutilized in COVID-19 Patients?

Innovations
2020, Vol. 15(4) 316–320
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DOI: [10.1177/1556984520939076](https://doi.org/10.1177/1556984520939076)
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Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic that has affected more than 5,400,000 people in over 180 countries worldwide with more than 40,000 reported deaths.^{1,2} Typical presentation of severe forms of COVID-19 is bilateral pneumonia and, in some patients, an acute hypoxic respiratory failure that can represent a significant therapeutic challenge for physicians.^{3–8} In these severe patients with profound hypoxemia and a near-normal respiratory system compliance, at least in the very early phase,⁹ different clinical scenarios can be observed, ranging from normal breathing (i.e., “silent” hypoxemia) to bilateral patchy ground-glass opacities requiring oxygen supply. Gattinoni et al. suggested that the different COVID-19 patterns are related to the interaction of many factors, including the viral load, the host response, the physiological reserve and existing comorbidities, time between the onset of the disease and the presentation to the hospital, as well as provided therapies.¹⁰ Whether the interactions between these factors can really result in 2 different phenotypes of respiratory failure (i.e., the “L type,” characterized by low elastance, low ventilation-to-perfusion ratio, and low recruitability and the “H type,” characterized by high elastance, high right-to-left shunt, and high recruitability) remains to be demonstrated.^{11,12} Nevertheless, in some patients, the use of mechanical ventilation, even if adjusted on patient’s phenotype, fails to provide an adequate systemic oxygenation and rescue therapies might be needed.

Role of Extracorporeal Membrane Oxygenation in COVID-19

Although it remains unclear which factors determine the progression of COVID-19-related acute respiratory failure to refractory hypoxemia to the “lung-protective” strategies (i.e., severity of the disease itself; negative intrathoracic pressure during spontaneous breathing; interstitial lung edema secondary to the increased lung permeability due to inflammation; loss of lung perfusion regulation due to the microvascular thrombosis; hypoxic vasoconstriction), the institution of extracorporeal membrane oxygenation (ECMO) can be a valuable strategy to

avoid lung damages caused by aggressive mechanical ventilation (i.e., ventilator-induced lung injury) or inappropriate triggering (i.e., patient self-induced lung injury) and to promote pulmonary healing. Indeed, during the ECMO run, ventilatory settings may include the lowest positive end-expiratory pressure, the lowest tidal volume to reduce plateau airway and driving pressures, and the lowest respiratory rate, all reducing the mechanical power.¹³

The initial reports on the use of ECMO in COVID-19 patients has been associated with very limited cohorts and poor outcomes.^{14,15} Despite this discouraging start, the extracorporeal support in COVID-19 respiratory failure had shown a worldwide spread.^{16–18} In particular, the Extracorporeal Life Support Organization (ELSO, Ann Arbor, MI, USA)¹⁹ and the American Society for Artificial Internal Organs (Beverly, MA, USA)²⁰ recently published guidelines about the role of ECMO in this specific patient population. Also, the World Health Organization interim guidelines for the management of severe COVID-19 and the Surviving Sepsis Campaign guidelines both suggested the use of venovenous (V-V) ECMO in patients with persisting hypoxemia despite conventional treatments.^{21,22} Nevertheless, no large report on the effectiveness of such strategy has been reported so far, and indication, optimal management, and potential complications of ECMO therapy in

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COVID-19 patients are actually poorly defined. Moreover, when compared to the previous outbreaks of emerging viral disease such as H1N1,²³ Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Syndrome (MERS) coronavirus related to Acute Respiratory Distress Syndrome (ARDS),²⁴ COVID-19 has been associated with an increased incidence of cardiovascular complications, such as “acute cardiac injury” (i.e., increased troponin values) and/or pulmonary embolism.

ECMO and Inflammatory Burden in COVID-19

As it is well known, COVID-19 is also characterized by a hyperinflammatory state with an increase of markers of inflammation like interleukin 6 and ferritin directly linked with high mortality. The underlying pathophysiology of this inflammatory disease could be strictly related with an endothelial injury and dysfunction that induce a vascular barrier breach with consequent tissue edema, activation of coagulation pathways, and consequent thrombosis that deregulated inflammatory cell infiltration (severe endothelial distress syndrome). At the same time, ECMO per se, with its large and continuous surface, causes a systemic activation of coagulation and inflammation pathways by the increasing shear stress and the interactions between the foreign material and blood components.²⁵ The interplay between ECMO and COVID-19 inflammatory state is an unbalance from procoagulant/hypercoagulant state and anti-coagulant conditions related to the necessary administration of unfractionated heparin required for the ECMO run.²⁶

While several authors have reported a relevant reduction in mortality with higher dosage of heparin in COVID-19, it is too early to gather definitive conclusions, and extreme attention to the coagulation profile during ECMO should be instituted in this particular clinical condition.

Infection triggers a complex host response and the inflammatory activation may lead also to a hyperpermeability of vasculature, which can ultimately induce vasoplegic shock.

In this scenario, the administered fluid is rapidly redistributed into the extravascular compartment leading to only transient improvement in hemodynamic parameters such as cardiac output and increasing adverse consequences in patients with already diminished respiratory reserve due to pulmonary infiltrates.

A restricted or “preventing” overload strategy might be advantageous, or the earlier application of renal replacement therapy (RRT), especially in those patients with more severe volume overload, progressive alkalosis, suboptimal diuretic response or diuretic refractoriness, and development of acute kidney injury, might be considered for optimization of volume status.

In the most severe form of COVID-19, a cytokine storm could be present and hemoabsorption therapy may be used to decrease cytokine levels and to control the pro-inflammatory response by the maintenance of the vascular barrier function.²⁷

Hemoabsorption or RRT could be used alone or in combination with extracorporeal circuit, and even if there is no recommendation for clinical use in the actual guidelines for management of sepsis and septic shock, it could represent a promising approach.

The multifaced presentation of COVID-19 poses a challenge not only in the indications of ECMO but also in its management.

Cardiovascular Complications in COVID-19

Up to one-third of COVID-19 patients who are admitted to the intensive care unit will develop cardiogenic shock, acute cardiac injury, arrhythmias, and/or acute cardiomyopathy. The mechanisms of these cardiac complications remain poorly understood in clinical practice and these phenomena are probably multifactorial. Some authors suggested an acute myocarditis (i.e., viral invasion of myocardial cells), in particular for young patients, while others a form of stress cardiomyopathy (i.e., cytokine-mediated with microvascular dysfunction).²⁸ Another important cause of cardiogenic shock could be acute pulmonary embolism with acute right ventricular (RV) failure, which could result either in low cardiac output or sudden death.²⁹ All of these conditions are enhanced by preexisting cardiovascular diseases.³⁰

In these cases, the benefits of V-V ECMO to confer lung protection are not sufficient to support the failing heart and concomitant tissue hypoxia and might need a shifting mode to venoarterial (V-A) ECMO support or of a hybrid venoarterovenous (V-VA) ECMO. In the literature, there are currently no reported case series on the use of V-A ECMO in coronavirus outbreaks.

Has V-A ECMO Been Underused in COVID Pandemic?

Whereas the mortality of the majority of COVID-19 patients appears to be related to the development of multiorgan failure, complicating acute hypoxic respiratory failure, or superimposed bacterial infections with sepsis, V-V ECMO remains the most frequently applied extracorporeal strategy, being used in 91% of the cases. Indeed, the preliminary data provided by the ELSO and European ELSO ongoing registries showed that less than 5% of the ECMO runs in COVID-19 patients were treated with V-A configuration.^{31,32} Moreover, ECMO-assisted cardiopulmonary resuscitation (ECPR) was used in only 1% of COVID-19 cases in the ELSO registry; ECPR can be considered in carefully selected cardiac arrest patients who fail to obtain return of spontaneous circulation during conventional CPR and have a high likelihood of survival in case of restored circulation. However, because of the very poor outcomes being reported in severe COVID-19 patients and the considerable risk of infection transmission to responding staff, most of the centers interrupted their ECPR program and deprived these patients from a potential life-saving intervention.¹²

Considering the frequent occurrence of cardiovascular complications in COVID-19 patients and the challenging discrimination between a cardiac and a respiratory etiology of hypoxemia in this setting, it is critical to recognize whether cardiac and pulmonary involvement coexists in these patients and provide the most effective ECMO configuration accordingly. In particular, cardiovascular ECMO support should be considered in 2 main scenarios:

1. Persistent hypoxemia that may evolve into RV dysfunction or failure (i.e., due to hypercapnia, acidosis, pulmonary hyperinflation, airway resistance, hypoxia, and thrombosis).
2. Cardiogenic shock of different origin with the coexistence of respiratory failure.

Importantly, cardiovascular ECMO support may include some hybrid configuration, such as V-AV mode (i.e., extra return cannula is inserted to improve the oxygenation in case of moderate cardiac dysfunction with high peripheral metabolic requirement and severe lung injury) or VV-A mode (i.e., an

extra drainage cannula would provide an optimal biventricular unloading with concomitant high-flow ECMO, which would be effective in case of severe hypoxemia and high cardiac output; Fig. 1).³³

From the available data reported until now, we can only postulate a possible underuse of the V-A modalities (i.e., 5%) when compared to the high incidence of cardiovascular complications (i.e., 20% to 30%). The reasons for this lower application of V-A configuration are related to the complexity of an arterial cannulation, the requirement of a backup from cardiovascular surgeons, the lack of experience in low-volume centers with V-A use, and the lack of recognition of cardiac dysfunction in this setting. The rate of conversion from V-V to V-A modes in COVID-19 has been only 3%, but it could have been much higher if a more accurate hemodynamic evaluation of these patients would have been done. We encourage international registries to analyze the cardiac function in COVID-19 ECMO patients to better define the potential role of V-A mode in this disease.

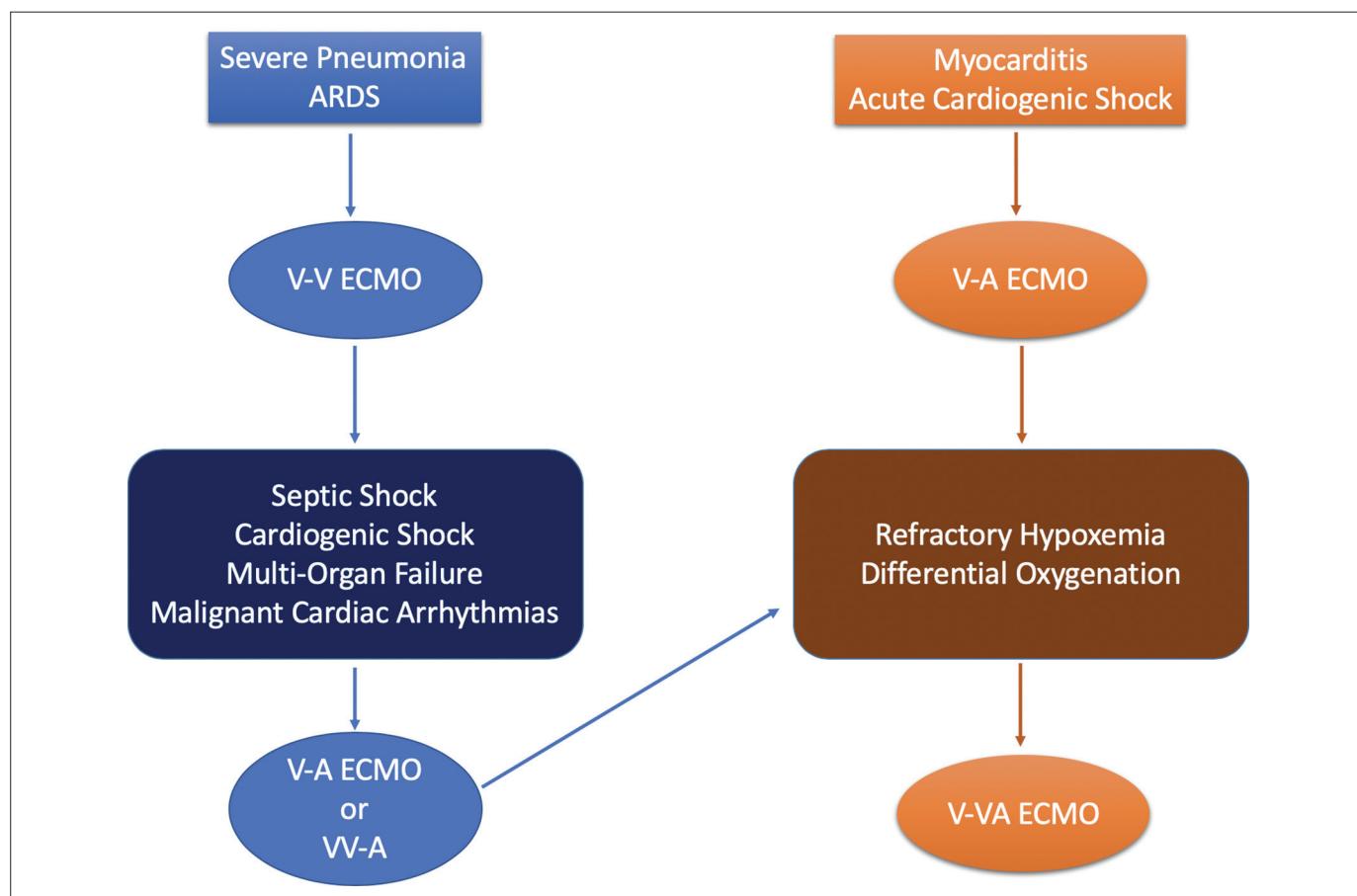


Fig. 1. Different ECMO configurations in COVID-19 according to initial presentation or progress of the disease. ARDS, acute respiratory syndrome; ECMO, extracorporeal membrane oxygenation; V-A, venoarterial; V-V, venovenous; V-VA: veno-venoarterial; VV-A, venovenous-arterial.

Conclusions

The overall impact of the COVID-19 pandemic on potential ECMO use is currently unclear and an urgent need exists to enhance our understanding of the role of ECMO in management of severely ill patients.

Some have advocated restricting mechanical support to V-V rather than V-A ECMO. Each patient must be considered on a case-by-case basis, with great attention regarding candidacy in the context of advanced age, and those comorbidities that portend to a reasonable poor prognosis.

More data are coming from the 2 large multicenter studies on the use of ECMO in COVID-19 patients promoted by ELSO and the European Group of ELSO which is leading to redefinition and reassessment of the real actual global ECMO capacity and capability.^{31,32}

Outbreaks of emerging infectious disease, such as COVID-19, represent an important step to improve our knowledge in ARDS and its different phenotypes in order to provide a better indication about the type of ECMO, target populations, as well as optimal time of implant.

Finally, the need for a multidisciplinary approach to this delicate population together with a more flexible and dynamic reassessment is essential.³⁴

This outbreak of infectious disease could enable an improved understanding of ARDS and a more precise use of therapeutics as ECMO and different configurations with a tailor-made treatment.

outcome and cause of deaths, doubts about an underutilization remain.

6. Several features of COVID-19 patients undergoing ECMO have also been increasingly appreciated and peculiar of this virus-induced patient compromise.
7. The main features and characteristics of ECMO in COVID-19 are need of high-flow V-V ECMO, awareness of those V-V cases with a rapid deterioration which may require conversion to an associated circulatory support (V-A, VV-A), need of prolonged support particularly to enhance lung recovery, and the need of enhanced anticoagulation due to the hypercoagulative state.
8. Several other configurations for cardiorespiratory support, “tailored” ECMO, have been utilized, but in a very limited rate (<1% to 2%).
9. In many ECMO centers, these procedures have been limited due to the lack of beds, dedicated personnel, lack of equipment or supply of disposables due to quick consumption, and an unexpectedly high number of patients potentially requiring such a treatment.
10. For the future, dedicated centers should receive adequate empowerment and resources and be better organized to improve the treatment of the severely ill requiring ECMO, including patient transport. Sicker patients should be centralized to allow access to such treatments, not excluding a full use of a patient-tailored algorithm for best support.

Take-Home Messages

1. Infectious outbreaks such as coronavirus disease 2019 (COVID-19) have been an unprecedented challenge in the treatment of virus-based pandemic due to the high rate of patients with severe compromised respiratory and cardiovascular systems.
2. The ethical and organizational circumstances, particularly the limited resources available during such an outbreak, have highlighted several shortcomings in the hospital network and patient management, including personnel availability and protection.
3. Despite initial skepticism, extracorporeal membrane oxygenation (ECMO), either veno-venous (V-V), or with a reduced use, venoarterial (V-A), has been increasingly applied in COVID-19 patients.
4. ECMO, however, remains a resource-intensive form of respiratory and circulatory support, which should be considered in special circumstances, with indications and selection criteria, which may vary according to the above mentioned shortcomings.
5. V-A ECMO represents, so far, a marginal quote (<5%) of extracorporeal support, apparently indicating a low incidence of cardiocirculatory compromise in COVID-19 patients. However, based on patient

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: F.S. Taccone, M. Belliato, M.M. Malfertheiner, and M.L. Broman received honoraria from EUROSETS. R. Lorusso is consultant for Medtronic and LivaNova, and Medical Advisory Board Member of EUROSETS and PulseCath.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Wire Cerclage Versus Cable Closure After Sternotomy for Dehiscence and DSWI: A Systematic Review and Meta-Analysis

Innovations
2020, Vol. 15(4) 321–327
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DOI: 10.1177/1556984520938155
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Abstract

Objective: Cable closure has been introduced as a potential alternative to traditional wire cerclage (WC) for closure of median sternotomy. To evaluate whether cable closure improves patient outcomes, we conducted a systematic review and meta-analysis of the literature. **Methods:** Ovid versions of Medline and Embase, and Google Scholar were used for the literature search. This yielded 7 studies ($n = 2,758$), which compared traditional WC to cable closure systems. Outcomes included deep sternal wound infection, sternal dehiscence, postoperative pain score, and sternal wound infection. **Results:** We found significantly lower incidence of sternal dehiscence for cable closure compared to WC (risk ratio [RR] 0.14, 95% confidence interval [CI]: 0.03 to 0.59, $P < 0.01$, $I^2 = 0\%$) but no difference in DSWI (RR 0.97, 95% CI: 0.39 to 2.42, $P = 0.95$, $I^2 = 33\%$). Cable closure was also associated with lower pain when compared with the WC group (mean difference -1.04 points, 95% CI: -1.89 to -0.19, $P = 0.02$, $I^2 = 87\%$). **Conclusions:** This study suggests that cable closure results in less incidence of sternal dehiscence and pain compared to WC. Nonetheless, there remains a limited number of studies on this topic and further high-quality studies are required to confirm the results of this meta-analysis.

Keywords

median sternotomy, cable closure, wire cerclage, deep sternal wound infection, dehiscence

Central Message

Cable closure mechanisms may serve as an alternative to traditional wire cerclage by reducing incidence of dehiscence and lowering pain scores following median sternotomy. Additional prospective studies with larger sample sizes are required for more conclusive results.

Introduction

Median sternotomy remains the most commonly performed bone osteotomy, allowing for excellent exposure and quick access to the pericardial structures in patients undergoing cardiac surgery.^{1–3} Wire cerclage (WC) remains the dominant form of sternal closure due to ease, familiarity, speed, and cost-effectiveness.² However, in many other surgical specialties, rigid fixation with plates or devices is commonly used for bone fracture stabilization.⁴ Unlike other means of bone fixation, there is concern with WC regarding improper bone union and sternal instability,⁵ which can lead to clinically important concerns such as sternal dehiscence. A very serious complication of sternotomy is deep sternal wound infection (DSWI). Although it only occurs in approximately 1% of cases, DSWI carries a high mortality rate of 14% to 47%.^{3,6}

In an effort to enhance sternal healing, alternate closure techniques such as cable closure techniques have been

investigated in cardiac surgery. Cable closure systems include biosynthetic cable tie systems and multifilament cable wiring

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systems. As a result of a larger contact surface area, cables are thought to provide additional resistance to tension forces on the sternum and reduce the likelihood of cutting into the sternal bone.⁵ While some studies suggest that cable closure may be associated with improved pain scores and sternal stability, studies to date have been small and underpowered in detecting differences for key clinical endpoints. Herein, we undertook a comprehensive meta-analysis to compare clinical events of dehiscence and DSWI when using cable closure techniques as compared to WC in sternal wound closure for patients who underwent median sternotomy. Additional clinical outcomes assessed included pain score and sternal wound infection.

Methods

Systematic Review of the Literature

Ovid versions of Medline and Embase were searched from 2000 to May 25, 2018. The key words used in the search were “sternum” or “sternal” followed by “closure,” “cable,” “zip-fix,” or “cable-tie” (see Supplemental Material for detailed version). Duplicates of studies were removed by assessing the list of authors, study period, and institutions of the studies. Google Scholar was also searched for additional studies. The inclusion criteria were human studies in the English language that directly compared WC with cable closure and reported at least 1 outcome classified as sternal wound incompetence (any sternal wound infection, DSWI, and dehiscence). Exclusion criteria were conference abstracts, case reports, non-English studies, and studies that did not directly compare the cable closure and WC closure mechanisms. Then, 2 investigators (D.T. and A.D.) independently screened the titles and abstracts on this topic from the literature search to obtain full articles that matched the inclusion and exclusion criteria. Disagreements were discussed by investigators until an agreement was reached.

Quality Assessment and Data Abstraction

The quality grade (low, moderate, and high) associated with each observational study was evaluated by the “Grading of Recommendations, Assessment, Development and Evaluations” approach⁷ and the randomized clinical trials (RCT) were assessed

using the Cochrane risk of bias tool.⁸ The number of participants, study year, type of closure systems compared, patient baseline characteristics, risk factors for sternal infections, and reported outcomes were abstracted from all the studies.

Outcomes

DSWI was the prespecified primary outcome of this meta-analysis. It was reported during follow-up based on diagnostic criteria that are consistent with guidelines outlined by the US Centers for Disease Control and Prevention Criteria. Secondary outcomes included any sternal wound infection, and pain rating scales as measured by the 11-point “visual analog scale”^{2,9} or “the Modified Brief Pain Inventory Short Form.”⁵

Analysis

A random-effects meta-analysis was performed using the *meta* and *metafor* packages in RStudio (R version 3.5.1; R Development Core Team, Vienna, Austria). For the binary outcomes abstracted, summary crude results were determined and the Mantel-Haenszel method was used where the relative risk ratios (RR) were calculated from event rates. For pooling the continuous outcomes, summary crude results were determined and the inverse variance method was used to weight and analyze the mean differences (MD). In the analysis, heterogeneity was reported as being low ($I^2 = 0\%$ to 25%), moderate ($I^2 = 26\%$ to 50%), or high ($I^2 > 50\%$). A 95% confidence interval (CI) was used to report all results as pooled weighted results of 2 subcategories (RCTs and adjusted/unadjusted observational studies) and overall. Statistical significance was assumed for $P < 0.05$. To assess the appropriateness of combining the 2 cable closure systems (ZipFix and Pioneer) into a single class for analysis, a subgroup analysis was conducted.

Results

Description of Selected Studies and Quality Assessment

A total of 387 unique citations were obtained following the literature search through Medline and Embase databases (Supplemental Fig. 1).¹⁰ A Google Scholar search yielded 1

Table 1. Details of Studies Used in Analysis.

Authors	Country	Study year	Study design	Device	Cable closure (n)	WC (n)
Marasco et al. ⁹	Australia	2018	RCT	ZipFix	57	60
Nezafati et al. ²	Iran	2018	RCT	ZipFix	168	158
Dunne et al. ⁶	Australia	2016	RCT	Pioneer	135	137
Stelly et al. ¹¹	USA	2015	Unadjusted observational	ZipFix	300	309
Melly et al. ⁵	Switzerland	2013	Unadjusted observational	ZipFix	95	498
Oh et al. ³	Korea	2014	Adjusted observational	Pioneer	392	392
Ozen et al. ¹²	Turkey	2014	Unadjusted observational	Pioneer	24	32

Abbreviations: RCT, randomized controlled trial; WC, wire cerclage.

additional study that matched the inclusion criteria. After a review of the title, abstract, and then the entire article, 7 studies remained (Table 1) with a total of 2,758 patients. Three of the studies were RCTs ($n = 716$), 1 was a propensity-matched observational study ($n = 784$), and 3 were unmatched observational studies ($n = 1,258$; Table 1). No overlap was found between studies. Within the RCTs, one of the studies was of high quality,⁶ while 2 of the studies were moderate quality due the risk of detection bias^{5,9} (Supplemental Table 3). All 3 studies adequately reported the outcomes needed; however, the sample sizes were small, which increases the risk of bias.^{2,6,9} The duration of follow-up for the RCTs ranged from 1 to 16 months. All

observational studies were retrospective and 3 of the 4 were unmatched.^{5,11,12} The overall quality of the observational studies was moderate (Supplemental Table 4).

We performed a pooled analysis of binary and continuous baseline risk factors (Table 2, Table 3). The studies had comparable baseline characteristics in the experimental and control groups; patients undergoing WC were 0.8 years younger and both groups had the same mean body mass index. The baseline characteristics that were reported by more than 3 studies (Table 2, Table 3) showed no significant differences between the cable closure and WC groups.

Table 2. Pooled Analysis of Binary Baseline Characteristics for Cable Closure Versus Wire Cerclage Analysis.

	Cable	WC	RR	P-value
Male (n = 6)				
RCT	248/360 (69%)	248/355 (70%)	1.01 [0.92, 1.10]	0.87
Adjusted/unadjusted observational	428/716 (60%)	458/733 (63%)	0.96 [0.88, 1.04]	0.27
Pooled	676/1076 (63%)	706/1088 (65%)	0.98 [0.92, 1.04]	0.48
Diabetes (n = 7)				
RCT	148/360 (41%)	137/355 (39%)	1.07 [0.88, 1.29]	0.52
Adjusted/unadjusted observational	277/811 (34%)	436/1231 (35%)	1.07 [0.93, 1.21]	0.34
Pooled	425/1171 (36%)	573/1586 (36%)	1.07 [0.96, 1.19]	0.23
Hypertension (n = 4)				
RCT	108/168 (64%)	95/158 (60%)	1.07 [0.90, 1.27]	0.44
Adjusted/unadjusted observational	511/787 (65%)	837/1199 (70%)	1.02 [0.96, 1.07]	0.55
Pooled	619/955 (65%)	932/1357 (68%)	1.02 [0.97, 1.08]	0.42
Lung disease (n = 6)				
RCT	36/360 (10%)	37/355 (10%)	0.96 [0.62, 1.49]	0.87
Adjusted/unadjusted observational	86/419 (21%)	170/839 (20%)	0.97 [0.49, 1.94]	0.94
Pooled	122/779 (15%)	207/1194 (17%)	0.99 [0.70, 1.40]	0.94
Stroke (n = 3)				
RCT	13/168 (8%)	10/158 (6%)	1.22 [0.55, 2.71]	0.62
Adjusted/unadjusted observational	19/487 (4%)	44/890 (5%)	1.09 [0.41, 2.92]	0.86
Pooled	32/655 (5%)	54/1048 (5%)	1.15 [0.65, 2.05]	0.63
Renal disease (n = 5)				
RCT	20/168 (12%)	23/158 (15%)	0.82 [0.47, 1.43]	0.48
Adjusted/unadjusted observational	241/811 (30%)	255/1231 (21%)	1.09 [0.95, 1.26]	0.23
Pooled	261/979 (27%)	278/1389 (20%)	1.07 [0.93, 1.23]	0.33
Smoking (n = 6)				
RCT	187/360 (52%)	173/355 (49%)	1.06 [0.92, 1.21]	0.42
Adjusted/unadjusted observational	228/419 (54%)	495/839 (59%)	1.00 [0.79, 1.27]	0.97
Pooled	415/779 (53%)	668/1194 (56%)	1.01 [0.90, 1.14]	0.81
Osteoporosis (n = 3)				
RCT	4/192 (2%)	2/197 (1%)	2.07 [0.38, 11.13]	0.40
Adjusted/unadjusted observational	2/300 (1%)	2/309 (1%)	1.03 [0.15, 7.27]	0.98
Pooled	6/492 (1%)	4/506 (1%)	1.54 [0.43, 5.50]	0.51
BIMA grafts (n = 5)				
RCT	22/360 (6%)	18/355 (5%)	1.20 [0.65, 2.20]	0.57
Adjusted/unadjusted observational	23/487 (5%)	40/890 (4%)	1.21 [0.71, 2.08]	0.48
Pooled	45/847 (5%)	58/1245 (5%)	1.20 [0.80, 1.81]	0.37
Reoperation (n = 4)				
Adjusted/unadjusted observational	59/811 (7%)	84/1231 (7%)	0.79 [0.37, 1.70]	0.55
Pooled	59/811 (7%)	84/1231 (7%)	0.79 [0.37, 1.70]	0.55

Abbreviations: BIMA, bilateral internal mammary artery; RCT, randomized controlled trial; RR, risk ratio; WC, wire cerclage.

Table 3. Pooled Analysis of Continuous Baseline Characteristics for Cable Closure Versus WC Analysis.

	Cable mean	WC mean	MD [95% CI]	P-value
Age (years)				
RCT (3 studies)	63.5	62.9	0.64 [-0.92, 2.20]	0.42
Adjusted/unadjusted observational (4 studies)	63.8	62.9	0.86 [-0.21, 1.93]	0.11
Pooled (7 studies)	63.7	62.9	0.79 [-0.09, 1.67]	0.08
BMI (kg/m²)				
RCT (3 studies)	29.3	28.9	0.42 [-1.13, 1.96]	0.60
Adjusted/unadjusted observational (4 studies)	27.7	27.8	-0.16 [-0.71, 0.38]	0.55
Pooled (7 studies)	28.2	28.2	0.02 [-0.57, 0.61]	0.95

Abbreviations: BMI, body mass index; CI, confidence interval; MD, mean difference; RCT, randomized controlled trial; WC, wire cerclage.

Wound Complications

Of the 7 studies in this analysis, all 3 RCTs, 1 matched observational study, and 2 unmatched observational studies reported DSWI. There was no significant difference in DSWI (Fig. 1) postoperatively between cable closure and WC (1.4%, 2.3%, RR 0.97, 95% CI: 0.39 to 2.42, $I^2 = 33\%$; Table 4). One RCT and 2 unmatched observational studies reported dehiscence. The analysis indicated a significantly lower incidence of dehiscence (Fig. 2) when the cable closure mechanism was used as compared to the traditional WC (0.2%, 3.0%, RR 0.14, 95% CI: 0.03 to 0.59, $I^2 = 0\%$; Table 4).

Two RCTs and all 4 observational studies reported events sternal wound infection (SWI). The difference in incidence of

SWI was not statistically different between cable closure and WC groups (2.8%, 4.3%, RR 0.78, 95% CI: 0.45 to 1.34, $I^2 = 18\%$; Table 4). In reporting outcomes, one of the studies pooled “infections or dehiscence” and “major wound complications” together while others separated these outcomes.³ In this case, they were classified under SWI.

Secondary Outcomes

All 3 of the RCTs reported a pain score, and in each case, the group with the cable closure mechanism reported significantly lower pain (Fig. 3) than the WC group (2.3 points vs 3.3 points, MD -1.04 points, 95% CI: -1.89 to -0.19, $I^2 = 87\%$; Table 5).

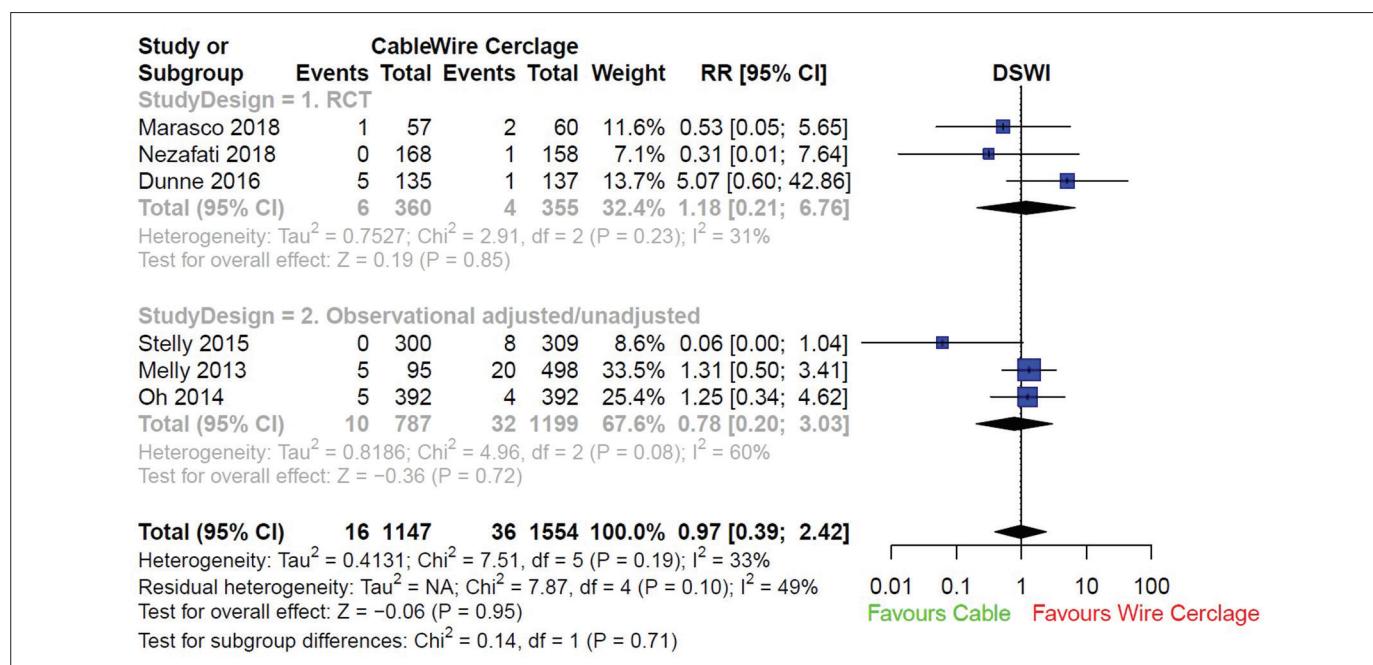


Fig. 1. Forest plot for relative risk of incidence of DSWI for cable closure versus wire cerclage closure groups, subgrouped according to study design. CI, confidence interval; DSWI, deep sternal wound infection; RR, risk ratio; RCT, randomized controlled trial.

Table 4. Binary Outcomes for Cable Closure Versus Wire Cerclage.

	Cable	WC	RR [95% CI]	P-value
DSWI (6 studies)				
RCT/Adjusted	11/752 (1.5%)	8/747 (1.1%)	1.27 [0.49, 3.32]	0.62
Unadjusted	5/395 (1.3%)	28/807 (3.5%)	0.36 [0.01, 10.04]	0.55
Pooled	16/1,147 (1.4%)	36/1,554 (2.3%)	0.97 [0.39, 2.42]	0.95
Dehiscence (3 studies)				
RCT/Adjusted	0/168 (0.0%)	5/158 (3.2%)	0.09 [0.00, 1.53]	0.10
Unadjusted	1/324 (0.3%)	10/341 (2.9%)	0.16 [0.03, 0.87]	0.03
Pooled	1/492 (0.2%)	15/499 (3.0%)	0.14 [0.03, 0.59]	<0.01
Any sternal wound infection (6 studies)				
RCT/Adjusted	18/617 (2.9%)	15/610 (2.5%)	1.13 [0.51, 2.50]	0.77
Unadjusted	11/419 (2.6%)	48/839 (5.7%)	0.58 [0.30, 1.11]	0.10
Pooled	29/1,036 (2.8%)	63/1,449 (4.3%)	0.78 [0.45, 1.34]	0.36

Abbreviations: CI, confidence interval; DSWI, deep sternal wound infection; RCT, randomized controlled trial; RR, risk ratio; WC, wire cerclage.

Results for additional clinical endpoints of mortality, hospital length of stay, mechanical ventilation time, and operating room times are included in the Supplemental Materials.

Subgroup Analysis

The subgroup analysis showed no significant differences between the 2 cable closure systems used in the analysis for both dehiscence and DSWI (Supplemental Fig. 7, Supplemental Fig. 8). There was also no significant difference reported between the 2 devices for pain (Supplemental Fig. 9).

Discussion

In this meta-analysis comparing cable closure systems to WC for sternal wound closure following sternotomy, cable closure

was associated with reduced incidence of sternal dehiscence and resulted in lower reported pain scores as compared to WC.

While DSWI is only reported in 0.3% to 5.0% of patients, there are high associated mortality and morbidity rates.⁶ DSWIs have been deemed a “never” event by Medicare in the United States and related readmissions are no longer reimbursed by Medicare.^{13–15} Thus, recent RCTs comparing cable closure devices to traditional means of sternal closure for DSWI and related outcomes are extremely relevant. Two initial RCTs comparing cable closure to WC showed conflicting results, prompting our group to perform this meta-analysis. In the earlier of the 2 RCTs with 326 patients randomized to cable closure or WC, the authors found reduced sternal dehiscence and improved pain scores.² In contrast, in the more recent RCT of 118 patients, there was more movement of the sternum on

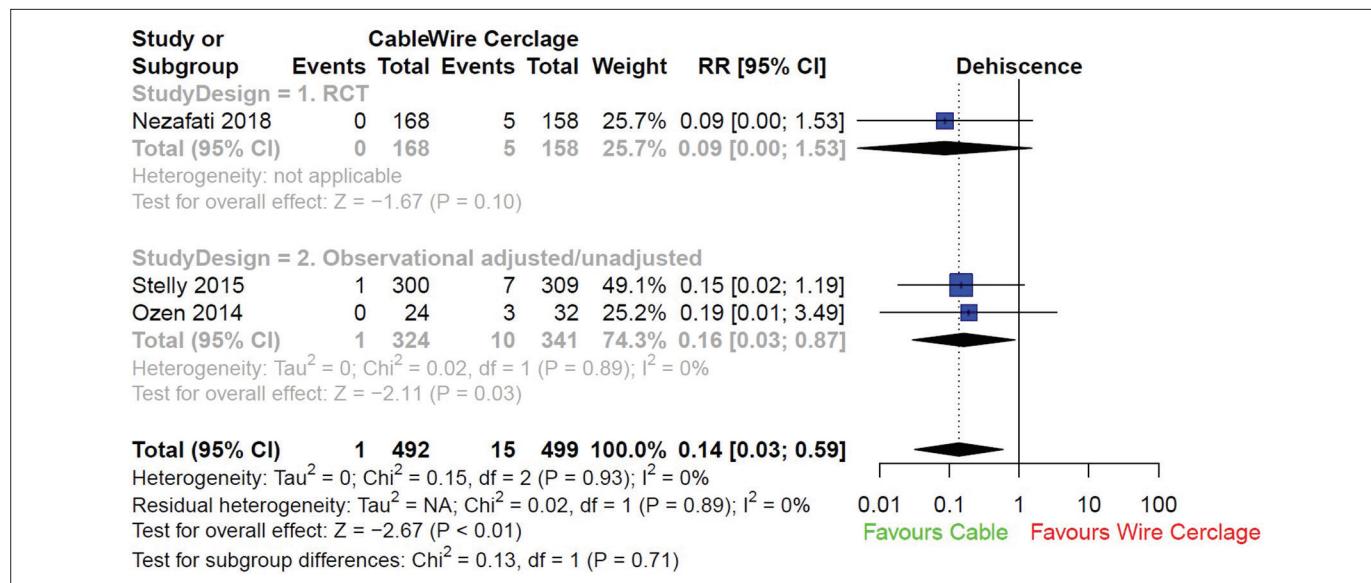


Fig. 2. Forest plot for relative risk of incidence of dehiscence for cable closure versus wire cerclage closure groups, subgrouped according to study design. CI, confidence interval; RR, risk ratio; RCT, randomized controlled trial.

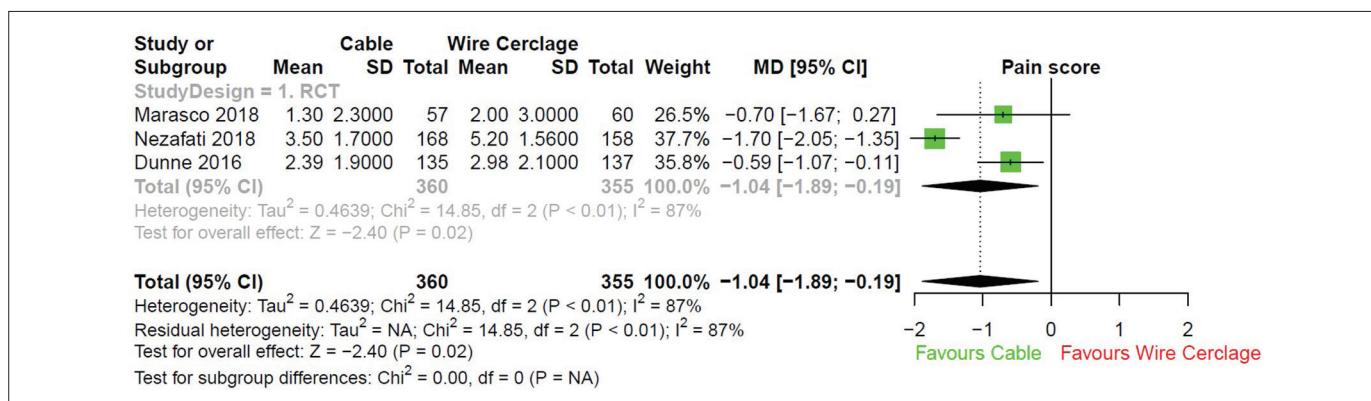


Fig. 3. Forest plot for mean difference in pain score for cable closure versus wire cerclage closure groups, subgrouped according to study design. CI, confidence interval; MD, mean difference; RCT, randomized controlled trial; SD, standard deviation.

ultrasonography (the study's primary outcome) and no significant difference in pain scores.⁹ These discrepant findings may be explained by differences in the statistical analyses of pain score outcomes between the studies and in the blinding of researchers. In both studies, pain scores were lower in the cable closure group though the more recent RCT did not find these differences statistically significant. Unlike the more recent RCT, the earlier study involved the unblinded surgeon assessing sternal dehiscence and postoperative pain. Furthermore, the ultrasonography technique was only used in the more recent RCT to assess sternal closure stability.¹⁶

In this meta-analysis, the 2 cable closure devices that have been used are ZipFix, a polymer-based cable-tie system, and Pioneer, a multifilament metallic cable. Both devices have reportedly lower "fatigue failure" than traditional wires though they are applied in different ways. To account for the variation in both devices, a subgroup analysis was conducted to assess the appropriateness of combining both devices into a single group for analysis. This analysis showed no significant differences between the 2 devices in most outcomes that were assessed. As a result, this suggests that both cable devices have adequate similarity to be combined into 1 class in this meta-analysis.

Sternotomy remains one of the most commonly performed bone osteotomies and most surgeons elect to repair the fracture through WC. In contrast, in all other surgical specialties, some form of rigid fixation is used to help heal bone fractures, following on key principles of bone healing: reapproximation, stabilization, and immobilization. The optimal sternal closure technique has been researched intensely recently. In a

meta-analysis of 7 RCTs by Pinotti et al. that included over 2,138 patients, a reinforced parasternal wiring technique showed no difference when compared to traditional sternal wiring.¹⁷ Another method of sternal wound closure is rigid plate fixation. In a multicenter RCT by Allen et al., this technique was found to significantly improve sternal healing, reduce sternal complications, and reduce pain in patients as compared to WC.^{4,18} Similarly, in a meta-analysis comparing rigid plate fixation to traditional WC, Tam and colleagues found that the incidence of sternal wound infections was reduced in patients at high risk for sternal complications.¹⁹ However, findings of this study were driven largely by observational data and may be confounded by selection bias, which highlights the need for more large-scale RCT evidence in this arena. Though mechanisms such as rigid plate fixation may show promise, cable closure systems are more similar to WC. As a result, the learning curve may be lower and adoption of cable closure technology may be higher as compared to rigid plate fixation.

Study Limitations

Several limitations must also be considered to objectively examine this study. While we performed a comprehensive review of the available literature, only 7 studies matched the inclusion and exclusion criteria, of which only 3 were RCTs. We recognize that the inclusion of retrospective observational studies may raise concerns for treatment allocation bias. While some studies employed extensive statistical adjustments, we acknowledge that there remain unmeasured or unknown confounders, which may still bias the results. Importantly, pooled

Table 5. Continuous Outcomes for Cable Closure Versus Wire Cerclage Analysis.

	Cable mean	WC mean	MD [95% CI]	P-value
Pain score				
RCT/Adjusted ($n = 3$)	2.3	3.3	-1.04 [-1.89, -0.19]	0.02
Pooled ($n = 3$)	2.3	3.3	-1.04 [-1.89, -0.19]	0.02

Abbreviations: CI, confidence interval; MD, mean difference; RCT, randomized controlled trial; WC, wire cerclage.

analysis of baseline characteristics suggests that groups undergoing either treatment were largely similar. Furthermore, while this remains the most comprehensive review of this topic, findings must still be interpreted with caution as some outcomes may be underpowered given the relatively low number of studies that were available. We also found substantial heterogeneity in some of the outcomes such as pain score. We attempted to explore this heterogeneity by performing a subgroup analysis to include the cable closure manufacturer (ZipFix and Pioneer) as there may be differences in cable surface area that may potentially explain this heterogeneity. However, results appeared to be consistent between device manufacturers. We note that a wide variation in the surgical techniques was used in the conventional WC groups (as described in Supplemental Table 2) and that this potentially could explain the heterogeneity in outcomes. Furthermore, there was some variation in how clinical endpoints such as “sternal wound infection” and pain score outcomes were evaluated due to the different standards used for diagnosis or assessment and follow-up time points. This highlights the importance of and need for standardized definitions for these outcomes in future studies.

Conclusions

Overall, in this meta-analysis of RCTs and observational data, cable closure systems were associated with a lower incidence of dehiscence and improved pain scores when compared to WC. Nonetheless, there remains a limited number of studies on this topic and further high-quality studies are required to confirm the results of this meta-analysis. In addition, prospective head-to-head comparisons to other sternal closure devices may be warranted.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: DYT is supported by a CIHR Fellowship. SEF is supported by the Bernard S. Goldman Chair in Cardiovascular Surgery (Toronto, Ontario).

Supplemental Material

Supplemental material for this article is available online.

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A Novel Quantitative Ex Vivo Model of Functional Mitral Regurgitation

Innovations
2020, Vol. 15(4) 328–336
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DOI: [10.1177/1556984520930336](https://doi.org/10.1177/1556984520930336)
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Abstract

Objective: Durability of mitral valve (MV) repair for functional mitral regurgitation (FMR) remains suboptimal. We sought to create a highly reproducible, quantitative ex vivo model of FMR that functions as a platform to test novel repair techniques. **Methods:** Fresh swine hearts ($n = 10$) were pressurized with air to a left ventricular pressure of 120 mmHg. The left atrium was excised and the altered geometry of FMR was created by radially dilating the annulus and displacing the papillary muscle tips apically and radially in a calibrated fashion. This was continued in a graduated fashion until coaptation was exhausted. Imaging of the MV was performed with a 3-dimensional (3D) structured-light scanner, which records 3D structure, texture, and color. The model was validated using transesophageal echocardiography in patients with normal MVs and severe FMR. **Results:** Compared to controls, the anteroposterior diameter in the FMR state increased 32% and the annular area increased 35% ($P < 0.001$). While the anterior annular circumference remained fixed, the posterior circumference increased by 20% ($P = 0.026$). The annulus became more planar and the tenting height increased 56% (9 to 14 mm, $P < 0.001$). The median coaptation depth significantly decreased (anterior leaflet: 5 vs 2 mm; posterior leaflet: 7 vs 3 mm, $P < 0.001$). The ex vivo normal and FMR models had similar characteristics as clinical controls and patients with severe FMR. **Conclusions:** This novel quantitative ex vivo model provides a simple, reproducible, and inexpensive benchtop representation of FMR that mimics the systolic valvular changes of patients with FMR.

Central Message

A novel quantitative ex vivo model was created that is simple, reproducible, inexpensive, and an accurate benchtop representation of FMR. Utilizing this model, new repair techniques can be explored with quantitative 3-dimensional analysis prior to large animal and clinical studies.

Keywords

functional mitral regurgitation, ischemic mitral regurgitation, FMR, ex vivo model

Introduction

Functional mitral regurgitation (FMR) is estimated to affect 1.6 to 3.3 million individuals in the United States alone.^{1,2} It is a consequence of ventricular dilation, papillary muscle displacement, and annular dilation, resulting in tenting of the mitral leaflets and inadequate coaptation. Severity of FMR has a graded association with reduced survival and symptoms, independent of left ventricular function.^{3–5}

The recent Cardiothoracic Surgical Trials Network randomized trial that compared repair with replacement for patients with an ischemic etiology of FMR demonstrated that almost 60% of valve repairs performed with conventional annuloplasty techniques had recurrent moderate or greater MR by 2 years.⁶ In addressing this issue, several novel repair techniques have

been proposed, including papillary muscle approximation, chordal cutting, and patch augmentation of the mitral valve (MV).^{7–10} Thus far, these alternatives have not demonstrated consistent efficacy or durability and there remains an intense

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*Presented at the 44th Annual Meeting of the Western Thoracic Surgical Association in Goleta, CA, USA, June 2018.

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need for novel surgical and catheter-based interventions that result in a durable repair.

An ex vivo FMR model provides an initial platform to test the performance of various new repair techniques. We sought to create a reproducible, quantitative model of FMR that simulates the systolic annular and valvular changes seen in patients with significant FMR.

Methods

Creation of the FMR Model

Mitral annular and ventricular derangements in FMR patients undergoing 3-dimensional (3D) ultrasound assessment were used to create the ex vivo model design, and the vectors of annular dilation and papillary muscle displacement seen in patients who develop FMR were used as a guide to create the model.^{11,12} Specifically, as described by Dudzinski and Hung, there is an outward radial and apical vector of the anterolateral and posteromedial papillary muscle relative to the anterior mitral annulus (closely approximated to the center of the ventricle) with an associated increase in interpapillary muscle distance.¹¹ This outward radial and apical vector reproducibly tethers the MV to create FMR, and was, therefore, utilized when tethering the chordae.

Fresh whole swine hearts (446 [interquartile range {IQR}: 414 to 512] g) and ascending aorta from a commercial abattoir were used for the model. The aorta was clamped and the heart was suspended by an aortic cross clamp (Fig. 1a). The coronary arteries were then ligated. A purse-string suture was placed in the ascending aorta and an 18 Fr arterial cannula was placed through the aorta and aortic valve. The cannula was connected to 38 W linear-drive air-pump (Thomas, Gardner-Denver Medical, Sheboygan, WI, USA) and the left ventricle was pressurized with air to maintain a static pressure of 120 mmHg. Pressurizing the heart did not result in significant expansion of the ventricle, as the swine heart is particularly hypertrophied and in an inanimate state. The left atrium was excised to a level

just above the mitral annulus and the MV was imaged in the closed state. The geometric alterations of FMR were then created by first displacing both the papillary muscle tips radially and laterally, followed by symmetrically and radially dilating the annulus (Fig. 1b). The chordae were displaced by separately placing 4 silk sutures around the base of the chordae tendinae at the tip of the papillary muscle. Separate sutures were placed around: 1) the anterior leaflet chords to the anterolateral papillary muscle, 2) the anterior leaflet chords to the posteromedial papillary muscle, 3) the posterior leaflet chords to the anterolateral papillary muscle, and 4) the posterior leaflet chords to the posteromedial papillary muscle. The sutures were exteriorized through the papillary muscle and left ventricular wall and simultaneously tethered with apical, posterior, and lateral vectors. Symmetric annular dilation was achieved by placing 8 equidistant, horizontal mattress annular sutures (3, 0 braided nylon) through two 0.2 to 0.4 cm width expandable silicon bands, distributing the tension along the bands. One band was placed at the level of the posterior annulus from commissure to commissure (CC), and the other band was placed along the anterior annulus at the base of the anterior leaflet, excluding the fibrous trigones. This process of chordae tethering followed by annular dilation was adjusted in a stepwise fashion to find the threshold of coaptation exhaustion, defined as failure of the left ventricle to remain pressurized due to lack of leaflet coaptation. This threshold revealed the minimal amount of leaflet coaptation necessary to maintain a pressurized left ventricle.

In order to prevent tissue drying and change in tissue quality, the ventricular and, in particular, valvular tissue was kept dampened with water sprayed every 30 to 60 minutes. With the tissue adequately wet, tissue handling was similar to that of live, *in vivo* swine hearts.

Image Acquisition and Data Analysis

Direct imaging of the mitral leaflets and annulus was performed utilizing a 3D structured-light scanner (Artec 3D, Luxembourg),

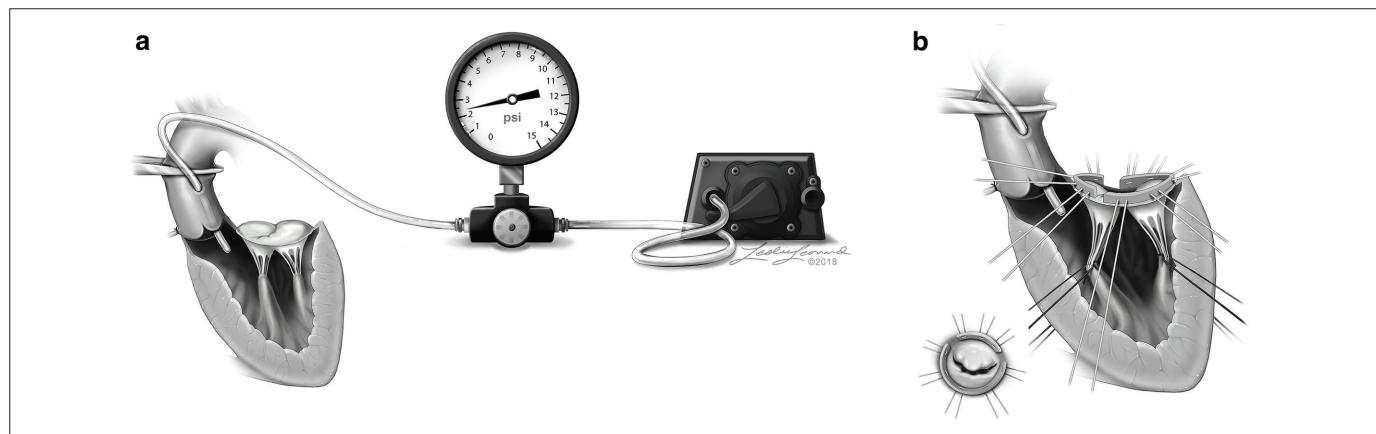


Fig. 1. Setup of the ex vivo model in the (a) control state and (b) functional mitral regurgitation state.

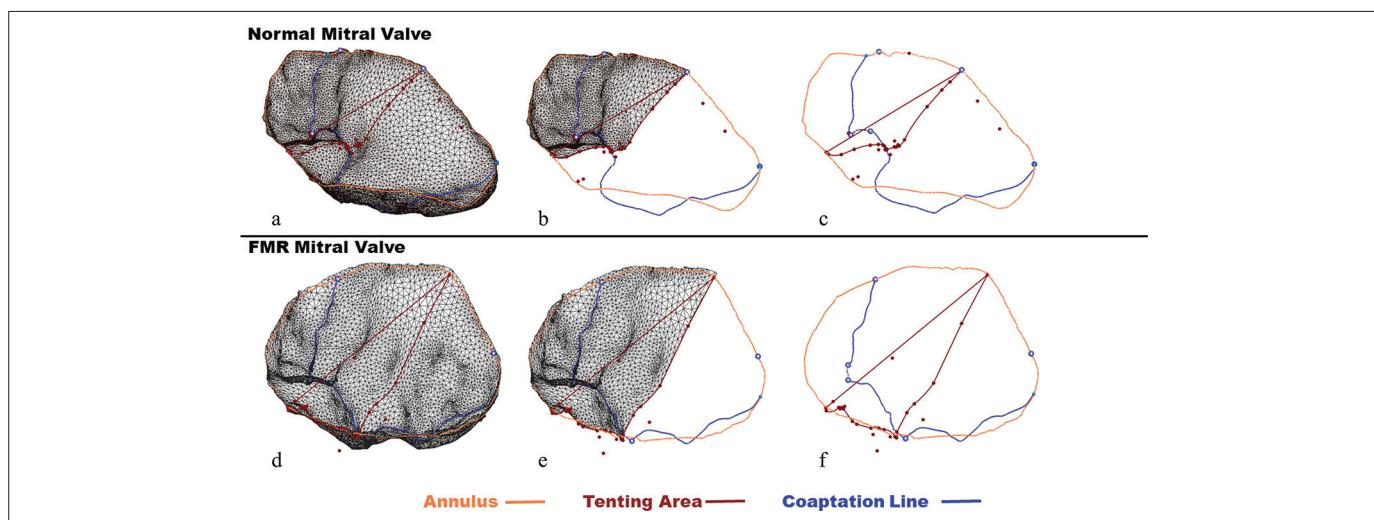


Fig. 2. Postimaging analysis of the mitral valve in the normal (a–c) and functional mitral regurgitation (d–f) state. (a) and (d) represent the points created by the structured light scanner, which are then meshed together to create a representation of the mitral valve. Using this mesh, elements of the valve apparatus can be marked and measured, including the annulus (orange), tenting region (red), and atrial surface of coaptation [blue]. (b) and (e) represent the mesh half cut-away and (c) and (f) represent the valve components without the mesh. This valve frame can then be used to measure components of the valve such as annular area, annular circumference, leaflet angles, and tenting.

which records the 3D structure, texture, and color of the MV with accuracy approaching 0.05 mm. The 3D scanner uses light triangulation and distortion to generate a 3D point cloud. The scanner, with a known position of the light and sensor, shines a textured light pattern onto the object, and the sensor receives the light at a known coordinate. By capturing the distortions of this light onto a nonplanar surface, the scanner can generate 3D surface coordinates.

After generating a 3D point cloud, a finite element mesh is created (Fig. 2) and the color and texture are added to the mesh based on the 3D coordinates. Using this mesh, several components of the valve apparatus, including the annulus, coaptation line, and tenting area, can be marked and measured using scan-to-CAD software (Geomagic Design X 3D Systems, Cary, NC, USA; Supplemental Video). The mesh can then be removed, leaving the valve frame, and valve components can be quantified.

Clinical Validation

To validate the FMR model, the ex vivo control and FMR models were compared to mid-systolic state of 20 patients with normal MVs and 11 patients with severe FMR who underwent 3D transesophageal echocardiograms preoperatively. This clinical dataset has been previously utilized by Bouma et al. with details regarding image acquisition, segmentation, and analysis.¹³ The FMR patients were selected from 37 patients with FMR and represented the subgroup that developed a recurrence (\geq grade 2) of MR within 6 months of annuloplasty ring repair. The subgroup of patients with early recurrence was specifically utilized, as this subset represents the FMR patients at the highest risk of failure by conventional techniques. Institutional Review

Board approval was obtained at the University of Pennsylvania and written informed consent was obtained from all patients. Briefly, full-volume 3D transesophageal echocardiograms of the MV in mid-systole were segmented and Cartesian (x,y,z) coordinates were exported into Matlab (Mathworks, Natick, MA, USA). All geometric analyses were performed in Matlab.

Outcomes

The primary outcomes of the study were change in annular, leaflet, and coaptation characteristics between the ex vivo FMR state and control state. All ex vivo analyses were performed with scan-to-CAD software.

Annular measurements included anteroposterior (AP) distance, CC distance, annular surface area, and annular circumference. Anterior annular circumference was defined as the annular length associated with the anterior leaflet (Supplemental Fig. 1a) and the posterior annular circumference was defined based on the corresponding posterior leaflet (Supplemental Fig. 1b). Annular surface area was defined as a 3D surface with the annulus as boundaries (Supplemental Fig. 1c). Annular height was defined, as previously described, by first creating the least-squares plane of the annulus (Supplemental Fig. 1d).¹⁴ The distance between the 2 maximally displaced markers in the “z-axis,” above and below this plane, was used as the annular height.¹⁵ Nonplanarity angle was defined as the angle subtended between the anterior and posterior horns at the commissural diameter of the mitral annulus (Supplemental Fig. 1e).¹⁶ Circularity index was defined as the AP/CC diameter. All measurements were performed at the midpoint of the anterior and posterior leaflets (A2 and P2). Tenting height was defined as the distance from the atrial surface of coaptation to the annular

plane. Noncoaptation anterior and posterior leaflet area was defined as the exposed atrial surface area of the anterior and posterior leaflet, respectively, in the systolic state.

Cooptation depth was measured by marking the line of cooptation on the atrial surface of the leaflet in the systolic state using different colored dyes (Wilton, Naperville, IL, USA). The perpendicular, 3D distance between the line of cooptation and the edge of the leaflet was measured at 12 evenly spaced points, separately, on the anterior and posterior leaflets using the scan-to-CAD software. Four points each within A1/P1, A2/P2, and A3/P3 were chosen and cooptation was graphically depicted.

Statistical Analysis

Data were analyzed using SAS Software, Version 9.3 (SAS Institute Inc., Cary, NC, USA). Given the sample size and inability to adequately assess normality, continuous variables are presented as median with IQR and were compared using the Wilcoxon rank-sum test. Paired pre- and postdilation measurements were compared with the Wilcoxon signed-rank test. A *P*-value of less than 0.05 was considered statistically significant.

Results

Ex Vivo Model Characteristics

Ten porcine hearts were imaged in both the control and FMR states. Compared to control, AP diameter in the FMR model increased 32% (2.5 [IQR: 2.4 to 2.6] vs 3.3 [IQR: 3.1 to 3.4] cm, *P* < 0.001) while the commissural diameter remained unchanged (3.3 [IQR: 3.1 to 3.4] vs 3.3 [IQR: 3.2 to 3.6] cm, *P* = 0.464). There was a 35% increase in annular area (7.8 [IQR: 7.0 to 8.4] vs 10.5 [IQR: 9.7 to 11.5] cm², *P* < 0.001). While the anterior annular circumference remained fixed, the posterior circumference increased by 20% (7.0 [IQR: 6.6 to 7.3] vs 8.4 [IQR: 7.4 to 8.8], *P* = 0.026).

The annulus became less saddle-shaped, evidenced by a 25% decrease in the annular height (8 [IQR: 6 to 9] vs 6 [IQR: 4 to 7] mm, *P* = 0.009) and 14° increase in the nonplanarity angle from 130° to 144° (*P* = 0.006).

There was a 52% increase in tenting height (9 [IQR: 9 to 10] vs 14 [IQR: 11 to 14] mm, *P* < 0.001) with a corresponding 61% increase in tenting area (133 [IQR: 117 to 153] vs 214 [IQR: 178 to 260] mm², *P* < 0.001). The median cooptation depth of both the anterior and posterior leaflets was substantially less in the FMR state compared to the control state (anterior leaflet: 5 [IQR: 4 to 8] vs 2 [IQR: 1 to 3] mm, *P* < 0.001; posterior leaflet: 7 [IQR: 5 to 9] vs 3 [IQR: 1 to 5] mm, *P* < 0.001). Moreover, cooptation depth at each matched point along the leaflet was significantly decreased in the FMR state (*P* < 0.05 for 10/12 points on anterior leaflet and *P* < 0.05 for 9/12 points on posterior leaflet). In controls, median cooptation depth varied from a range of 4 to 8.5 mm. After changing the geometric configuration to FMR parameters, the median cooptation depth was

substantially decreased to a range of 0.5 to 4 mm (Fig. 3). At all points in both the control and FMR state, the anterior leaflet had less cooptation depth than the posterior leaflet, and, therefore, served as the minimal cooptation reserve along the leaflet.

Validation of the Ex Vivo Model with 3D Echocardiography of Patients with FMR

Compared to control patients without evidence of FMR, the ex vivo baseline geometry had similar annular characteristics, with a comparable annular surface area (*P* = 0.878) and annular circumference (*P* = 0.113; Table 1). Both the clinical and ex vivo controls had saddle-shaped annuli, evidenced by a similar annular height (ex vivo: 8 [IQR: 6 to 9] vs clinical: 7 [IQR: 6 to 8] mm, *P* = 0.468) and nonplanarity angle (ex vivo: 130° [IQR: 123 to 136] vs clinical: 123° [IQR: 113 to 131], *P* = 0.068; Table 2). However, the ex vivo model had greater anterior (ex vivo: 37° [IQR: 32 to 50] vs clinical: 17° [IQR: 15 to 20], *P* < 0.001) and posterior leaflet angle (ex vivo: 46° [IQR: 39 to 54] vs clinical: 31° [IQR: 26 to 35], *P* < 0.001) at baseline.

Compared to the preoperative transesophageal echocardiograms of patients with FMR, the ex vivo FMR model demonstrated similar annular dimensions, including AP diameter (*P* = 0.275), commissural diameter (*P* = 0.971), and annular circumference (*P* = 0.067; Table 1). While there was a statistically significant difference in annular area between the patient and ex vivo FMR model, both demonstrated a similar increase in area from baseline (ex vivo FMR: 10.5 [IQR: 9.7 to 11.5] vs clinical FMR: 9.6 [IQR: 7.3 to 10.1] cm², *P* = 0.038). Moreover, both demonstrated flattening of the annulus, evidenced by a decreased annular height compared to control (ex vivo FMR: 6 [IQR: 6 to 7] vs clinical FMR: 6 [IQR: 6 to 7] mm, *P* = 0.181) and increased nonplanarity angle compared to control (ex vivo FMR: 144° [IQR: 133 to 147] vs clinical FMR: 137° [IQR: 130 to 151], *P* = 0.700).

In both the patient and the ex vivo FMR model, there was a significant increase in tenting height (ex vivo *P* < 0.001, clinical *P* = 0.004) and tenting area (ex vivo *P* < 0.001, clinical *P* < 0.001; Table 3). In the ex vivo FMR state, anterior leaflet angle (ex vivo FMR: 38° [IQR: 33 to 49] vs clinical FMR: 23° [IQR: 19 to 28], *P* < 0.001) and posterior leaflet angle (ex vivo FMR: 53° [IQR: 47 to 61] vs clinical FMR: 41° [IQR: 36 to 47], *P* = 0.001) were greater than the leaflet angles of patients.

Discussion

This study establishes a simple, reproducible, inexpensive, and accurate benchtop representation of the mid-systolic state of FMR that mimics both normal systolic MV configuration and geometric valvular changes that occur in patients with FMR. Geometric attributes of this ex vivo model correlated closely with the mid-systolic state of patients who have normal MVS, as well as those with FMR. Two key unique aspects of this model include the use of air instead of fluid to create a systolic

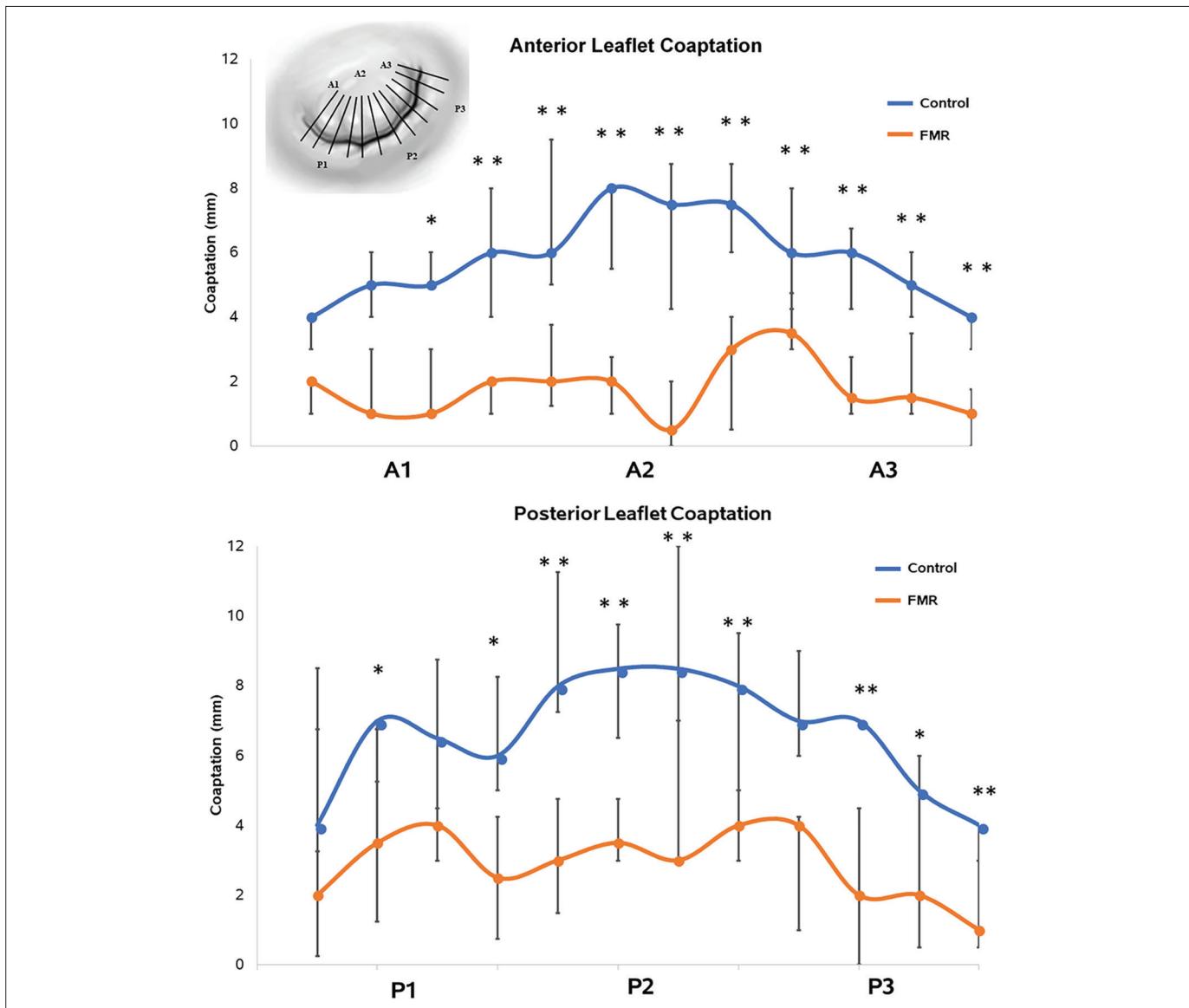


Fig. 3. Amount of coaptation of the (a) anterior leaflet and (b) posterior leaflet in the control (blue) and functional mitral regurgitation (orange) state. * $P < 0.05$, ** $P < 0.01$. FMR, functional mitral regurgitation.

state, and the use of structured light scanning to precisely quantitate the geometry of the mitral apparatus.

Utilizing air as a substrate to fill the ventricle rather than a fluid such as water enabled quantitation of MV geometry with tremendous accuracy. The use of air to simulate closure of the mitral valve has been previously described by Jimenez et al. with the Georgia Tech Left Heart simulator.¹⁷ This group described removing the MV and subvalvular apparatus from the heart and implanting the annulus along with papillary muscles in an *in vitro* gantry. Using this simulator, they demonstrated changes similar to those seen in an *in vivo* ovine model of FMR.¹⁸ Moreover, the use of air as a substrate was also described by Villard et al., who utilized air to fill the normal swine left ventricle and micro-computed tomography to image the heart.^{19,20} In contrast, our air-filled model of FMR leaves

the left ventricle and MV apparatus intact. This allows for a simple, yet reproducible model of clinical FMR without explanting of the annulus or papillary muscles, and preserves the relationships between the leaflets, annulus, and subvalvular apparatus. The use of a portable 3D light scanner to image the MV provides for rapid and precise acquisition of the mitral apparatus, with a scan time of under 1 minute. The 3D light scanner also provides texture and color superimposed onto the scanned image with accuracy approaching 0.05 mm, greater than 3D echocardiography and potentially even 3D computed tomography (0.1, 0.3 mm).^{21,22}

One key advantage of this model is that it allows direct measurement of the depth of coaptation across the entire coaptation surface of the anterior and posterior leaflets. We demonstrated a coaptation reserve of 4 to 8.5 mm in the normal MV model,

Table 1. Annular Characteristics.

		Control	Functional mitral regurgitation	P-value
Anteroposterior diameter (cm)	Ex vivo	2.5 (2.4, 2.6)	3.3 (3.1, 3.4)	<0.001
	Clinical	2.9 (2.7, 3.1)	3.2 (2.6, 3.4)	0.122
	P-value	0.003	0.275	
Commissural diameter (cm)	Ex vivo	3.3 (3.1, 3.4)	3.3 (3.2, 3.6)	0.464
	Clinical	3.2 (2.9, 3.5)	3.4 (3.1, 3.5)	0.374
	P-value	0.391	0.971	
Annular surface area (cm ²)	Ex vivo	7.8 (7.0, 8.4)	10.5 (9.7, 11.5)	<0.001
	Clinical	7.8 (6.7, 9.4)	9.6 (7.3, 10.1)	0.087
	P-value	0.878	0.038	
Annular circumference (cm)	Ex vivo	10.9 (10.3, 11.6)	12.3 (11.4, 12.7)	0.026
	Clinical	10.3 (9.5, 11.3)	11.6 (10.6, 12.0)	0.013
	P-value	0.113	0.067	
Anterior annular circumference (cm)	Ex vivo	3.8 (3.8, 4.3)	4.1 (3.7, 4.2)	0.970
	Clinical	3.9 (3.5, 4.3)	4.9 (4.6, 5.8)	<0.001
	P-value	0.982	0.002	
Posterior annular circumference (cm)	Ex vivo	7.0 (6.6, 7.3)	8.4 (7.4, 8.8)	0.026
	Clinical	6.4 (5.6, 7.0)	6.5 (5.7, 6.6)	0.912
	P-value	0.041	0.001	

P-values in rows represent comparison between control and functional mitral regurgitation. P-values in columns represent comparison between the ex vivo model and clinical patients. Data presented as median (interquartile range).

in sharp contrast to the 0.5 to 4 mm of coaptation reserve in the FMR state. While previous studies have reported varying coaptation depths, coaptation depth assessment has commonly been estimated by subtracting the noncoapted length of the leaflet in systole from the total length of the leaflet in diastole.^{23,24} However, these studies do not consider strain of the leaflet associated with loading from systolic pressure, which is substantial and varies based on ventricular pressure and annular configurations.^{25,26} Moreover, visualization of the leaflet with echocardiography is often imperfect and further limits assessment of coaptation depth. Given the strain of the leaflets under loading, the present study utilized a variation of the intraoperative “ink test” to precisely measure coaptation depth.²⁷

As previously described, this study confirms that the systolic geometry and dimensions of the porcine MV are similar to that of humans.²⁸ Moreover, by tethering the chordae and dilating the

annulus of the swine MV, a model of the mid-systolic state of FMR can be created that mimics the geometric derangements seen during systole in patients with FMR.^{13,29} As previously shown using sonomicrometry analysis of the annulus, annular dilation in FMR predominantly occurs via posterior annulus, as the anterior annulus is largely fixed within the fibrous trigones. Our model similarly showed these findings, with the anterior annulus remaining fixed despite radial dilation of the annulus in this region.^{30,31}

Importantly, this model is not intended to further understand mechanisms underlying FMR, but rather, used as a platform to test novel repair techniques. FMR is a dynamic, complex process with many etiologic factors. However, the systolic configurations of the annulus and valve represent the phase of the cardiac cycle that is of particular significance when determining valvular competence or failure. In testing novel repair techniques, this model

Table 2. Annular Shape.

		Control	Functional mitral regurgitation	P-value
Annular height (mm)	Ex vivo	8 (7, 11)	6 (6, 7)	0.009
	Clinical	7 (6, 8)	6 (6, 7)	0.353
	P-value	0.037	0.181	
Nonplanarity angle (degrees)	Ex vivo	130 (123, 136)	144 (133, 147)	0.006
	Clinical	123 (113, 131)	137 (130, 151)	0.003
	P-value	0.068	0.700	
Circularity index	Ex vivo	0.79 (0.70, 0.87)	1.0 (0.87, 1.06)	0.007
	Clinical	0.91 (0.84, 0.95)	0.93 (0.90, 1.06)	0.445
	P-value	0.005	0.751	

P-values in rows represent comparison between control and functional mitral regurgitation. P-values in columns represent comparison between the ex vivo model and clinical patients. Data presented as median (interquartile range).

Table 3. Valve Dimensions.

		Control	Functional mitral regurgitation	P-value
Tenting height (mm)	Ex vivo	9 (9, 10)	13.7 (11.1, 14.0)	<0.001
	Clinical	5 (5, 7)	8.1 (6.6, 9.6)	0.004
	P-value	<0.001	<0.001	
Tenting area (mm ²)	Ex vivo	133 (117, 153)	214 (178, 260)	<0.001
	Clinical	131 (92, 185)	228 (189, 310)	<0.001
	P-value	0.809	0.379	
Noncoaptation anterior leaflet area (cm ²)	Ex vivo	5.6 (4.9, 6.4)	7.1 (6.4, 8.3)	0.007
	Clinical	4.5 (3.9, 5.1)	5.3 (4.7, 7.2)	0.027
	P-value	0.005	0.010	
Noncoaptation posterior leaflet area (cm ²)	Ex vivo	6.1 (5.1, 7.0)	8.9 (8.0, 9.4)	0.004
	Clinical	4.4 (3.3, 4.8)	4.4 (3.1, 5.8)	0.445
	P-value	<0.001	<0.001	
Anterior leaflet angle (degrees)	Ex vivo	37 (32, 50)	38 (33, 49)	1.000
	Clinical	17 (15, 20)	23 (19, 28)	0.045
	P-value	<0.001	<0.001	
Posterior leaflet angle (degrees)	Ex vivo	46 (39, 54)	53 (47, 61)	0.058
	Clinical	31 (26, 35)	41 (36, 47)	<0.001
	P-value	<0.001	0.001	

P-values in rows represent comparison between control and functional mitral regurgitation. P-values in columns represent comparison between the ex vivo model and clinical patients. Data presented as median (interquartile range).

can be used to assess predictors of repair durability, including leaflet angles, tenting, and coaptation reserve. Examples of repair techniques that have been tested within this model include conventional undersized annuloplasty repair and various patch augmentation repair techniques. With each of these techniques, improvement in coaptation, leaflet angles, and tenting height was seen.

We specifically validated the ex vivo model with data from FMR patients who developed an early recurrence, as these represent the patient population at greatest need for improved repair techniques. While the leaflet angles in the ex vivo model were greater than the FMR patients, posterior leaflet angles >45° and anterior leaflet angles >25° to 39.5° have previously reported in patients with FMR who are at high risk of failure with conventional annuloplasty techniques.^{32–36}

Limitations

A considerable limitation of the ex vivo model is the noncontractile state of the swine heart, in contrast to the contracted systolic state of a normal or FMR heart *in vivo*. Moreover, the cadaveric swine hearts, while fresh, likely do not have the same deformability as *in vivo* tissue. Thus, certain measurements such as tension or strain have limited applicability in an ex vivo setting. Moreover, dynamic changes to the annulus or subvalvular apparatus in response to certain repairs may not be well recognized in an ex vivo setting. Still, both the cadaveric and hypertrophied nature of deceased swine hearts limits the expansion of ventricular chamber ex vivo, and we found that the geometry from this model closely tracked measurements from patients with FMR, validating the measurements from this model. Coaptation of the leaflets

using pressurized air mimics testing the mitral apparatus using saline intraoperatively during cardioplegic arrest, and the predictive ability of a saline test is well appreciated by MV repair surgeons.

The air-filled model allows for unique imaging with a 3D light scanner but represents a vastly different density than blood. Thus, there may be associated differences in the mechanics of valve closure. There may also be other unrecognized differences associated with gas compared to fluid dynamics. Moreover, assessment of regurgitation volume of the FMR valve, or residual regurgitation after repair in the present model configuration is limited. Instead, in its current configuration, predictors of repair durability, including leaflet angles, tenting height, tenting area, and coaptation depth, must be used to assess repair efficacy.

Conclusions

This novel quantitative ex vivo model provides a simple, reproducible, inexpensive, and accurate benchtop representation of FMR that mimics the systolic geometric derangements in patients with FMR. Utilizing this model, new surgical and catheter-based FMR repair techniques, specifically focused on adequately mobilizing tethering leaflets, can be explored and optimized with quantitative 3D analysis prior to large animal and clinical studies.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article:

JSG: Consultant, Edwards Lifesciences; MND: Consultant, Edwards Lifesciences; FVC: Employee, Edwards Lifesciences.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported from divisional funds and grateful patient donations.

Supplemental Material

Supplemental material for this article is available online.

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One-Stage Versus Sequential Hybrid Radiofrequency Ablation: An In Vitro Evaluation

Innovations
2020, Vol. 15(4) 337–344
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DOI: 10.1177/1556984520930070
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Abstract

Objective: To compare lesion size and depth between a 1-step, a sequential, and a delayed radio-frequency ablation in a hybrid setup. **Methods:** Left atrium tissues obtained from fresh porcine hearts were mounted into the ABLABOX simulator. Based on the time differences between the index epicardial (epi) and consequent endocardial (endo) ablation, 3 study groups were compared: a 1-stage (SEQ- 0) group (0-minute delay), an SEQ I group (60-minute delay), and an SEQ 2 group (240-minute delay). During the experiment, a constant epicardial (300 gr) and endocardial (30 gr) force were applied. Per group, 20 samples were studied, and the resulting lesion size and depth were quantified with morphometric evaluation. **Results:** Overall, no transmural lesion was obtained. Lesions in SEQ 0 had better maximum and minimum diameters ($P < 0.001$), a larger total area ($P < 0.001$), and volume ($P < 0.001$) than SEQ I and SEQ 2. There was no statistical difference in morphometric parameters (all, $P > 0.05$) between the delayed procedures (SEQ I and SEQ 2). **Conclusions:** In our in vitro model, different time sequences of combined epi–endo ablation did not result in transmural lesions. However, simultaneous epi–endo ablation produced broader and deeper lesions. Our findings need to be confirmed by further research.

Central Message

Using fresh porcine heart tissue, morphometric results indicated that in hybrid ablation, the lesion transmurality is not dependent on the time frame between the epicardial and the endocardial procedure.

Keywords

ablation, catheter ablation, surgical ablation, hybrid ablation

Introduction

Hybrid ablation of atrial fibrillation (AF) is a treatment approach that combines 2 separate steps: a thoracoscopic epicardial ablation with an endocardial catheter ablation.¹ The early report on hybrid AF ablation showed promising results,² and these initial results have been confirmed in other, more recent reports.^{3,4} Nevertheless, the hybrid approach is based on a mutually reinforcing collaboration between the surgeon and the electrophysiologist and by concept inextricably linked to the continued search for improvements, resulting in a more effective treatment approach.^{5–7}

Potential development is the optimization of the time lapse between the endocardial and epicardial stage, which can vary from minutes to months.^{5,8–10} To date, it is not known whether a 1-stage or a 2-stage procedure translates in better efficacy.¹¹ The objective of this study is to evaluate, in a vitro model, the size and depth of lesions made through simultaneous, sequential, or delayed epi–endocardial approach.

Methods

Samples

The left atrium tissue was obtained from freshly slaughtered porcine hearts, washed with NaCl 0.9% (B. Braun, Melsungen, Hessen, Germany) and put into a transport

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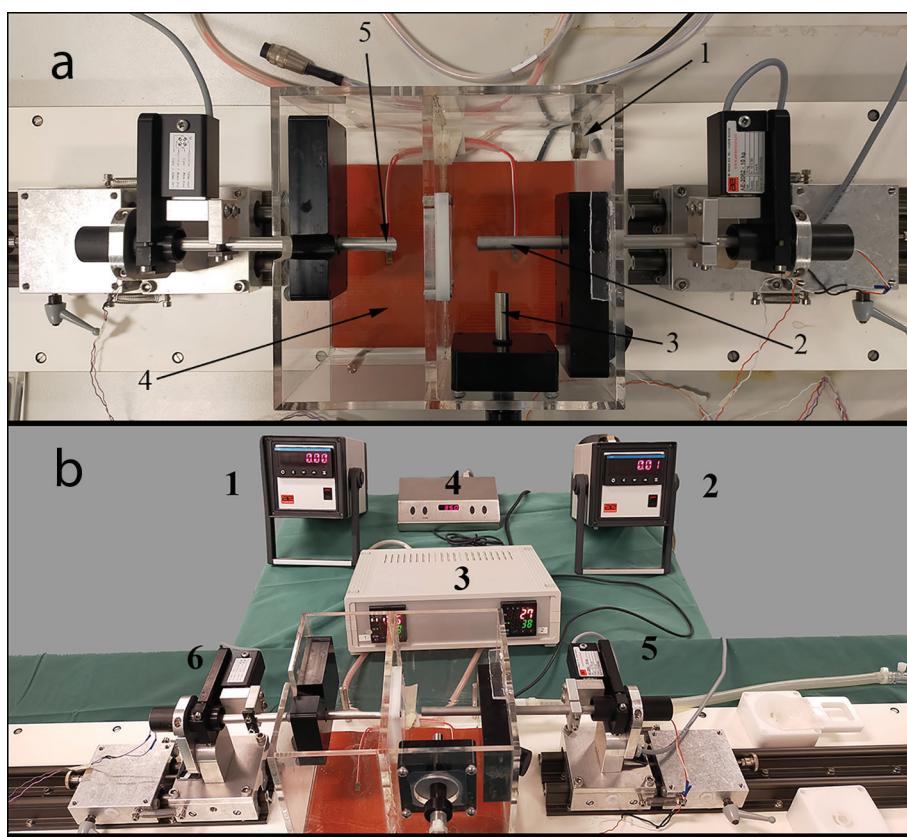


Fig. 1. (a) Ablabox: 1 = pump flow outlet, 2 = endocardial catheter holder, 3 = pump flow inlet, 4 = heating plate, 5 = epicardial catheter holder. (b) Ablabox System: 1,2 = digital screen for catheter force application, 3 = heating plate control console, 4 = magnetic stirrer motor control console, 5,6 = catheter contact force sensors.

medium RPMI 1640 (Sigma-A Samples Aldrich, St Louis, MO, USA). This medium was also used for sample conservation.

The Simulator

The ABLA-BOX simulator (IDEE—Instrument Development Engineering and Evaluation, Maastricht University, The Netherlands) has been previously described.¹² Briefly, the chamber mimicking the internal part of the left atrium has an inlet and outlet access plugged into an external pump (COBE precision blood pump, COBE Cardiovascular Inc, Arvada, CO, USA) for blood circulation (Fig. 1a and b). A heating plate (IDEE—Instrument Development Engineering and Evaluation, Maastricht University, Maastricht, The Netherlands) and a heating exchange device (Bio Cal 370, Medtronic, Minneapolis, MN, USA) are employed to keep the temperature constant throughout the experiments. The stirring motor mimicking AF blood turbulence is connected with its dedicated controller (Cyclone 1Y100, HMCEurope, Tuessling, Germany). Two pressure transducers (AE sensors, Dordrecht, The Netherlands) allow accurate control of the applied forces.

The 2 cm × 2 cm specimens were mounted between 2 plastic plates magnetically held to keep the samples of tissue firmly (Fig. 2).

Catheters

An epicardial pen (Isolator long-pen TT, AtriCure, Cincinnati, OH, USA) and an endocardial catheter (Celsius FLTR, Biosense Webster Inc, Diamond Bar, CA, USA) were employed. The epicardial catheter was plugged in a power console (Ablation Sensing Unit ASU, AtriCure, Cincinnati, OH, USA). In contrast, a Biosense Webster Stockert 70 RF Generator was used to power the endocardial catheter. The energy power was set up at 25 and 30 W (probe temperature, 65°C; impedance 100 Ω impedance; tissue temperature, 38°C) for the epicardial and the endocardial catheters, respectively.¹³

Experimental Setup

Left atrial tissue samples were randomly assigned to 3 groups, based on the time delay between the epicardial and the endocardial ablation application: (1) SEQ 0 (0-minute delay), i.e.,

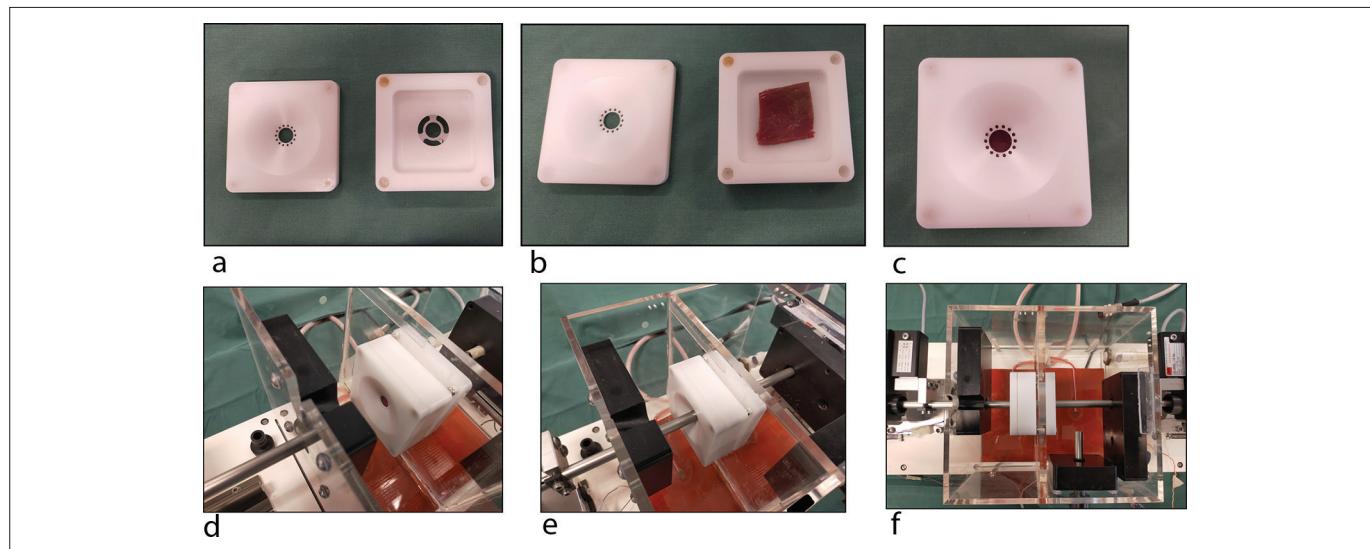


Fig. 2. Specimen holder open and closed with its lid (a, b, c). Placement into the Ablabox (d, e, f).

simultaneous procedure; (2) SEQ 1 (60-minute delay); and (3) SEQ 2 (240-minute delay). A total of 60 samples were analyzed/studied (20 for each group).

The thicknesses of the samples were 4.3 ± 0.2 , 4.2 ± 0.2 , and 4.3 ± 0.2 in SEQ 0, SEQ 1, and SEQ 2, respectively ($P \geq 0.09$).

In the delayed procedures (SEQ 1 and SEQ 2), the epicardial approach was performed first, followed by the endocardial ablation, to mimic the sequence in the clinical setting.¹ In all samples, the epicardial ablation cycle was automatically terminated by the console, whereas the endocardial ablation time was 30 seconds.

Based on our previous experiences,^{12,14} the endocardial contact force was set up at 30 gr. From the epicardial side was chosen a 300 gr force as currently employed in surgery.

Moreover, the flow rate was set up at 5 L/min, the temperature at 38°C, and the stirrer motor at 400 rpm.

Morphometric Evaluation of Myocardial Tissue Ablation

The samples were included in 10% neutral buffered formalin (NBF) for 48 hours, immersed in a sucrose solution (20%), and finally put on a metallic disc and embedded to Tissue-Tek® OCT™ compound. The blocks obtained were put into a cryostat at -20°C and sliced in consecutive sections (100 µm) perpendicular to the direction of the catheter ablation. The slices were laid down on the acetate sheet and covered and dried at room temperature for 1 hour. Afterward, the slices were digitalized at 300 dpi using a flatbed scanner. Later, the images were imported into computer software for image processing (Image J version 1.48 software; National Institutes of Health, Bethesda, MD, USA). In total, we obtained 42.05 ± 4.33 layers from each sample, and for every single slice, total maximum diameter (D_{\max}), total minimum diameter (D_{\min}), and total ablated area (AA) were measured. Besides, for any slice, volume (V) was obtained multiplying the area by the thickness of

a single slice, fixed to 100 µm by the setup of the cryostat. Likewise, maximum and minimum lesion's diameter (D_{epi} and D_{endo} , d_{epi} and d_{endo}), area (a_{epi} and a_{endo}), and volume (v_{epi} and v_{endo}) were measured at both epicardial and endocardial sides (Fig. 3).

Statistical Analysis

The Shapiro-Wilk normality test was performed and variables were expressed as median and interquartile range. Lesion measurements were compared with the Kruskal-Wallis test.

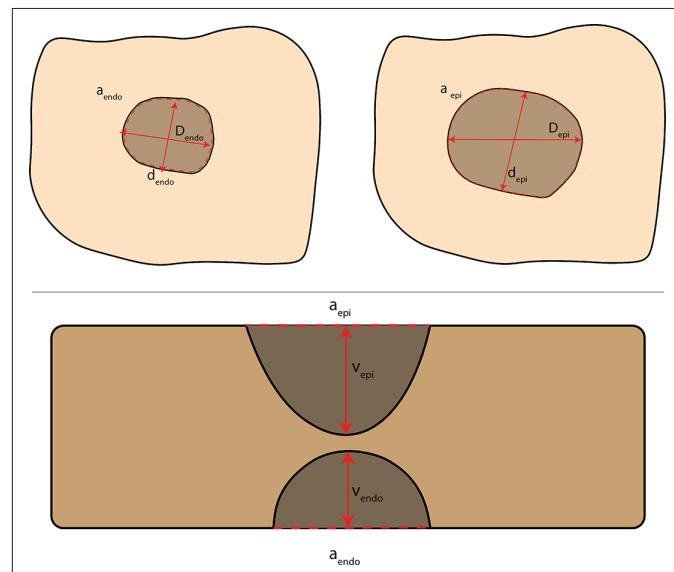


Fig. 3. Scheme of the measurements acquired: maximum endocardial diameter (D_{endo}), maximum epicardial diameter (D_{ephi}), minimum endocardial diameter (d_{endo}), minimum epicardial diameter (d_{ephi}), endocardial area (a_{endo}), epicardial area (a_{ephi}), epicardial penetration volume (v_{ephi}), endocardial penetration volume (v_{endo}).

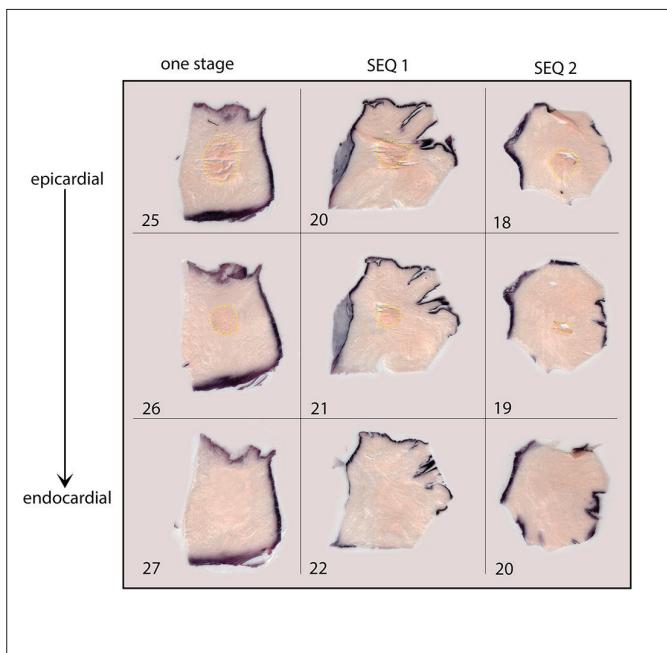


Fig. 4. Progression of lesions within the groups and the number of corresponding slices. There is no transmurality evidence. In the 1-stage sample, the ablation lesion disappears at the 27th slice, whereas in the other 2, the lesion stops before, showing a lower penetration.

Intraobserver and interobserver variabilities were tested on 5 samples randomly chosen, and κ -statistics were used to determine the degree of intraobserver and interobserver agreement after correction for the agreement expected by chance. The variables tested were D_{\max} and AA . A κ -value has a maximum of 1.0 when the agreement is perfect. A value of 0 indicates no agreement better than chance agreement. All statistical analyses were conducted using SPSS Statistics Version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

The intraobserver and interobserver variabilities were D_{\max} ($k = 0.98$), AA ($k = 0.93$), and D_{\max} ($k = 0.88$), AA ($k = 0.86$), respectively. During the experiment, no overheating steam pops occurred. Overall, no transmural lesion was identified (Fig. 4, Fig. 5). Morphometric data are shown in Table 1.

Lesion Size

D_{\max} was comparable between SEQ 1 and SEQ 2 ($P = 0.149$), but it was broader in SEQ 0 ($P < 0.001$). Also, D_{\min} was larger in simultaneous ablated tissue compared to both SEQ 1 and SEQ 2 (both, $P < 0.001$), which did not show any difference between them ($P = 0.118$). Moreover, AA was different between 1-stage and SEQ 1 ($P < 0.001$) and SEQ 2 ($P < 0.001$) that were comparable ($P = 0.706$).

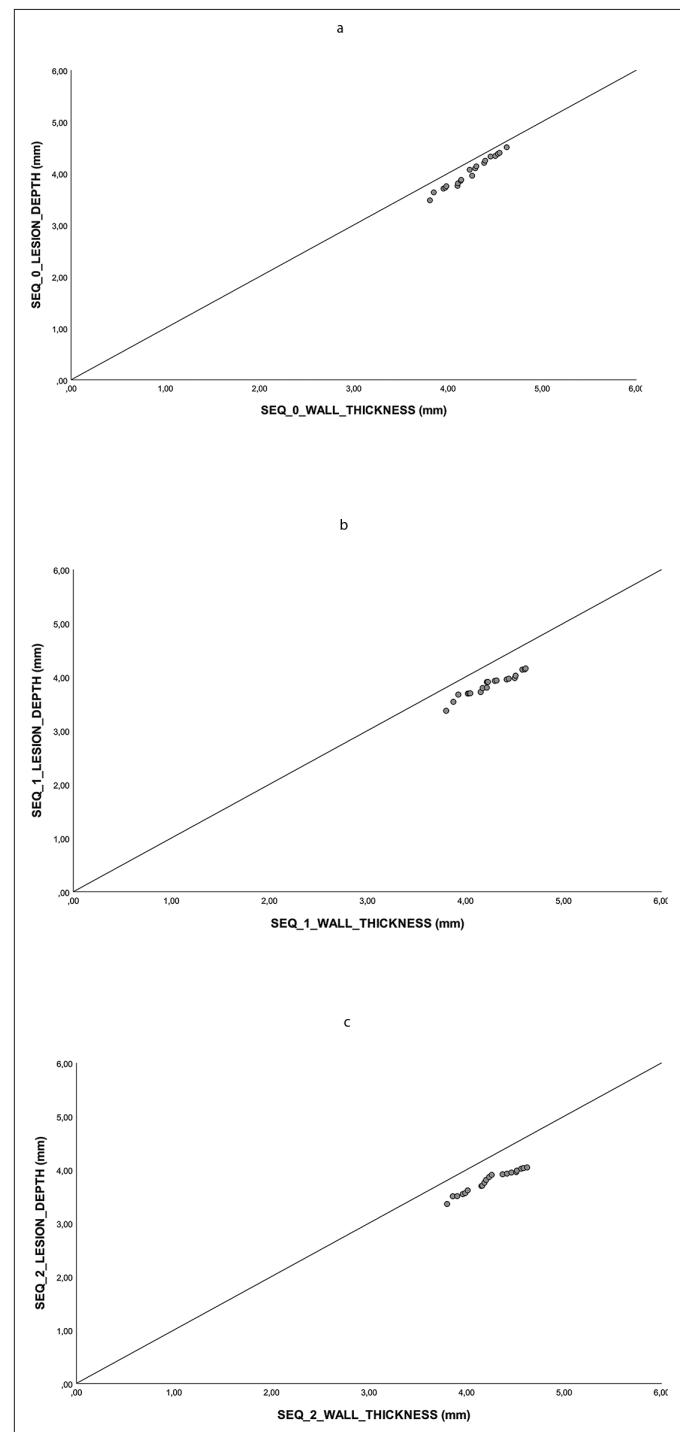


Fig. 5. Lesion depth is plotted against tissue thickness. If the lesion is transmural, its point will fall on the line of identity. (a) SEQ 0 group, (b) SEQ 1 group, (c) SEQ 2 group.

Additionally, D_{epi} did not differ in SEQ 1 and SEQ 2 ($P = 0.121$), while both resulted smaller than in the 1-stage (both, $P < 0.001$). Furthermore, D_{endo} was similar in SEQ 1 and SEQ 2 ($P = 0.842$), but lesions in both were smaller than in the 1-stage ($P = 0.018$ and $P < 0.001$, respectively). Besides, d_{epi}

Table I. Ablation Lesion Results.

Measurements	Time points			P value
	SEQ 0	SEQ 1	SEQ 2	
Transmurality (%)	0	0	0	
D_{\max} (mm)	8.61 [3.25]	7.94 [3.17] ^a	7.80 [2.76] ^b	<0.001
D_{\min} (mm)	7.10 [2.84]	5.91 [2.74] ^a	5.81 [2.30] ^b	<0.001
AA (mm^2)	58.66 [43.23]	47.40 [43.73] ^a	47.30 [36.83] ^b	<0.001
V (mm^3)	5.77 [4.39]	4.66 [4.52] ^a	4.73 [3.68] ^b	<0.001
D_{epi} (mm)	9.12 [3.53]	8.63 [2.77] ^a	8.27 [2.47] ^b	<0.001
D_{endo} (mm)	8.57 [2.40]	7.89 [2.84] ^a	7.99 [2.18] ^b	<0.001
d_{epi} (mm)	7.65 [2.59]	6.70 [2.26] ^a	6.59 [2.16] ^b	<0.001
d_{endo} (mm)	6.96 [2.42]	5.68 [2.40] ^a	5.64 [1.79] ^b	<0.001
a_{epi} (mm^2)	66.72 [47.32]	62.44 [38.33] ^a	61.43 [39.82] ^b	0.014
a_{endo} (mm^2)	57.01 [33.41]	45.43 [39.21] ^a	45.13 [27.50] ^b	<0.001
v_{epi} (mm^3)	6.67 [4.73]	6.24 [3.83] ^a	6.14 [3.98] ^b	0.014
v_{endo} (mm^3)	5.70 [3.34]	4.54 [3.92] ^a	4.51 [2.75]	<0.001

Abbreviations: AA, total area; a_{endo} , endocardial area; a_{epi} , epicardial area; d_{endo} , minimum diameter endocardial side; D_{endo} , maximum diameter endocardial side; d_{epi} , minimum diameter epicardial side; D_{epi} , maximum diameter epicardial side; D_{\max} , total maximum diameter; D_{\min} , total minimum diameter; V, total volume; v_{endo} , endocardial volume; v_{epi} , epicardial volume.

Data are shown as median [interquartile range] or number (percentage).

All morphometric data were referred to single slices.

^asignificant SEQ 1 vs. 1-stage.

^bsignificant SEQ 2 vs. 1-stage.

and d_{endo} were wider in 1-stage (both, $P < 0.001$), but they were comparable in SEQ 1 and SEQ 2 ($P = 0.780$ and $P = 0.161$, respectively).

Likewise, a_{epi} and a_{endo} were larger in 1-stage ($a_{\text{epi}}, P = 0.031$ vs. SEQ1 and $P = 0.045$ vs. SEQ2; $a_{\text{endo}}, P < 0.001$ vs. SEQ 1 and $P < 0.001$ vs. SEQ 2, respectively) but they did not differ between the 2-stage procedures ($P = 0.965$ and $P = 0.295$, respectively).

Lesion Depth

Likewise, V was similar in SEQ 1 and SEQ 2 ($P = 0.997$) but it was larger in 1-stage ($P < 0.001$ vs. both). Finally, v_{epi} and v_{endo} were comparable between SEQ 1 and SEQ 2 ($P = 0.965$ and $P = 0.295$, respectively), while it was bigger in 1-stage ($v_{\text{epi}}, P = 0.031$ vs. SEQ 1, $P = 0.045$ vs. SEQ 2; $v_{\text{endo}}, P < 0.001$ vs. SEQ 1, $P < 0.001$ vs. SEQ 2).

Discussion

Hybrid AF ablation is a treatment approach that combines thoracoscopic epicardial ablation with endocardial transcatheter ablation.^{2,5,7} The epicardial step is performed first because it allows long-lasting isolation of the pulmonary veins and the creation of additional lines in the left atrium, resulting in a so-called box lesion.⁴ The second part, carried out by the electrophysiologist, consists of mapping-guided demonstration of entry/exit block and offers the possibility of additional tailored substrate modification.

Although hybrid AF ablation is well defined as a concept, the time frame between both steps is not so clearly specified

yet, and varies from a few hours up to 6 months.^{8,10,15} For example, Mahapatra et al. performed the endocardial procedure 4 days after the surgical ablation,^{16,17} and the other clinicians 30 to 45 days after the surgical procedure.^{15,18} Bulava et al. completed the second step 6 to 8 weeks after surgery,¹⁰ and Gaita and co-workers carried out the catheter ablation after a blanking period of 3 months.¹⁹ Other clinicians performed either 1-stage or 2-stage procedures.^{20–22} Supporters of the delayed approach claim that a catheter ablation performed in a second stage significantly increases the likelihood of identifying conduction gaps in the surgical lesions, which potentially translates in a higher mid-term success rate.^{15,18} Advocators of a contemporary approach argue that it strengthens the cooperation and mutual understanding between the surgeon and the electrophysiologist. Nonetheless, results were comparable in series using both approaches.²²

However, the superiority of one technique over the others is still debated.²³ As far as we know, no study has specifically addressed this issue. Furthermore, no evidence exists on simultaneous ablation, performed in 1 step with the atrial tissue interposed between the catheters.

In this study, we tested whether simultaneous ablation results in deeper transmural lesions compared to 1-stage ablation (SEQ 1, after 60 minutes) or sequential ablation (SEQ 2, after 240 minutes). The tests were performed on the ABLA-BOX that allows to control contact force, blood temperature, and flow to mimic physiological conditions.¹⁴

In our observations, we checked diameter maximum, diameter minimum, ablated area, ablated volume, as well as

maximum and minimum diameters and volumes measured at epicardial and endocardial sides.

We observed smaller ablation diameters on the endocardial surface compared to the epicardial one ($P < 0.001$). This finding is not surprising because of the different sizes and shapes and differences in the applied force of the 2 catheters. Nonetheless, noteworthy is that all the lesions measured were larger in the 1-stage samples.

D_{\max} and D_{\min} , and consequently AA and V , were significantly larger in the 1-stage group. First, this might be the result of a deeper penetration during simultaneous ablation, as a result of higher forces, and thus better contact. Nonetheless, we failed to find transmurality in the samples. We might postulate that the pressure applied from both sides reduces the extracellular space of tissue, increasing its impedance,²⁴ leading to lateral irradiation of the radiofrequency. This lateral irradiation could lead to energy loss that may be responsible for the lack of transmularity. Importantly, we could expect that the tissue compression negatively affects the penetration of RF, but, in contrast, we found that the penetration into the tissue, expressed as volume v_{endo} and v_{epi} , was higher in the 1-stage group ($P < 0.001$). In contrast, we failed to find any difference between the 60- and 240-minute delay ($P = 0.29$). This difference could be attributed to the higher contact force of the epicardial catheter. Nonetheless, despite the contact, the force applied was the same in the 3 groups, and v_{epi} and v_{endo} were higher in the 1-stage samples, so this is more likely related to RF physics properties. Indeed, it is known that approximately 90% of the RF energy delivered is adsorbed in the first 1 mm of tissue, and the remainder of tissue heating occurs for indirect conduction. The heating transmission inside the tissue is slower than the RF, and, for this reason, the heating continues rising for several seconds after RF delivery interruption (thermal latency phenomenon).²⁵

In our previous experience,¹⁴ we obtained transmural lesions using a different setup. In the experiments reported here, we tried to mimic clinical settings. For instance, the endocardial contact force was set up to 300 gr and the epicardial force at 30 gr and endocardial impedance close to ideal 120 Ω .²⁶ Therefore, we might postulate that the lower impedance, employed in our previous experiments, as well as the difference in tip temperature, could explain the different outcomes.

However, it can be concluded from our findings that the lack of transmularity was not related to different time frames between the endocardial and the epicardial step, and this is a call for specifically improved catheters with optimized design for hybrid AF ablation.

To address the lateral dispersion and enhance more penetration by the RF energy, after some preliminary tests, we are developing a specific “true-bipolar” catheter with the atrial tissue compressed between the 2 ablation poles. This prototype will be the object of an upcoming study. The aim is to obtain fully linear transmural ablations in 1 step and to get a complete, effective left atrium isolation, which is a key feature of AF ablation.^{27,28}

Also, the lack of postablation edema that, *in vivo*, may reduce the lesion effectiveness^{10,23} prevents us from drawing conclusions. Hence, further *in vivo* studies to compare 1-step, sequential, and delayed approaches, including electromapping and pathophysiologic changes, are needed.

Finally, the findings from the study add to the voluminous experimental and clinical evidence that unipolar RF does not reliably produce linear, transmural lesions.

However, our findings must be read with caution. Indeed, the real application of simultaneous epi–endocardial ablation is far from being applied to the hybrid clinical arena. Further research is necessary to explore the reliability and feasibility of this technique and whether the challenges entailed in the implementation of this technique can be overcome.

Limitations

Our study suffers from some limitations that should be highlighted. First, we did not make histological evaluations to demonstrate the necrosis induced by the RF. The “TUNEL” (Terminal deoxynucleotidyl transferase [TdT] dUTP Nick-End Labeling) assay might have been the best method for indicating the necrosis but, in our setup, it was impossible due to the number of layers from each sample. This technique is mainly in use, and it has been designed to detect apoptotic cells undergoing extensive DNA degradation during the late stages of apoptosis. It is based on the ability of TdT to mark the blunt ends of double-stranded DNA breaks following apoptosis as well as other forms of cellular necrosis.^{29–31} Second, we employed tools that were not designed to be used simultaneously. Therefore, the lack of transmularity may be due to the *in vitro* setup and the characteristics of the catheters used, and this must be taken into account when reading our results.

Third, dead tissue was used, thus excluding all pathophysiological mechanisms occurring *in vivo*. In addition, the absence of microvascularization that performs as a heat sink decreases the penetration of RF in alive tissue.²⁵ Fourth, we did not test other devices. This was beyond the aims of our paper, but it will be the object of further research.

Fifth, the delay from the first ablation not being longer than 240 minutes related to tissue conservation issues. Furthermore, we did not perform multiple ablations. This issue might have led to improved depth of penetration. Sixth, the tissue employed was not viable, and as a consequence, either microcirculation or intrinsic electrophysiological properties were absent, thus excluding all pathophysiologic mechanisms occurring *in vivo* in response to heating stress. In addition, the absence of microvascularization that performs as a heat sink decreases the penetration of RF in alive tissue.²⁵ These aspects may limit the applicability to the clinical settings, and thus data have to be confirmed in further studies with a different setup.

Finally, porcine tissue came from young, healthy, 7-month-to 1-year-old animals bred for human consumption. It is likely that the heart tissue did not show any pathologic event typical of AF, like fibrosis development.

Conclusions

In this ex vivo evaluation of different hybrid procedure techniques, 1-stage, sequential, and delayed, transmurality was not reached by any procedure. Nonetheless, the 1-stage approach showed deeper and broader lesions. Our findings need to be confirmed by further research.

Authors' Contributions

All authors actively contributed to the paper in the following domains: conception or design of the work, data collection, data analysis, and interpretation, drafting the article, critical revision of the article, final approval of the version to be published.

The last two authors equally contributed to the paper.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Five-Year Experience with VATS Versus Thoracotomy Segmentectomy for Lung Tumor Resection

Innovations
2020, Vol. 15(4) 345–353
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DOI: 10.1177/1556984520938186
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Abstract

Objective: Segmentectomy for lung tumors has been performed with either video-assisted thoracoscopic surgery (VATS) or thoracotomy; however, there is a lack of contemporary, multicenter study that compares both approaches. The aim of this study was to compare the 30-day surgical outcomes of VATS versus thoracotomy for segmentectomy using a large national database. **Methods:** We performed a retrospective analysis of prospectively maintained American College of Surgeons National Surgical Quality Improvement Program database. Patients who underwent segmentectomy for benign or malignant tumors between 2013 and 2017 were included and divided into 2 groups based on whether they received a thoracotomy or VATS approach. All VATS patients were then into 2 subgroups: early (2013 to 2015) and late (2016 to 2017). Propensity-matched analysis was conducted, and the perioperative variables and outcomes were compared. **Results:** A total of 1,785 patients met the inclusion criteria. VATS segmentectomy was associated with shorter hospital stays (3.9 vs 5.8 days, $P < 0.001$) and higher rates of home discharge (94% vs 89%, $P = 0.002$) compared to thoracotomy segmentectomy. VATS was also associated with less postoperative pneumonia (2.8% vs 5.8%, $P = 0.007$), unplanned intubation (1.5% vs 3.5%, $P = 0.016$), prolonged intubation (0.6% vs 2.7%, $P = 0.001$), transfusion requirement (1.7% vs 5.8%, $P < 0.001$), and deep venous thrombosis (0.1% vs 1.1%, $P = 0.03$). Compared to the earlier VATS group, the late group was associated with less cardiac arrests (0% vs 0.8%, $P = 0.025$) and shorter hospital stays (3.3 vs 4.2 days, $P < 0.001$). **Conclusions:** When compared with thoracotomy, VATS segmentectomy is associated with less postoperative complications and shorter hospital length of stay. VATS segmentectomy has been used more frequently and with improved outcomes.

Central Message

When compared with thoracotomy, video-assisted thoracoscopic surgery (VATS) segmentectomy is associated with fewer postoperative complications and shorter hospital length of stay. Surgeons in the United States are increasingly utilizing VATS for segmentectomy instead of thoracotomy. This trend was associated with fewer complications and shorter hospital lengths of stay.

Keywords

segmentectomy, NSQIP, VATS, thoracotomy, surgical outcomes

Introduction

With the introduction of low-dose computed tomography screening for lung cancer, more patients are diagnosed at an earlier stage,^{1,2} and the number of patients requiring surgical resection has increased. Lobectomy for lung cancer is the most common approach to oncologic resection of lung cancer since the publication of Ginsberg's report in 1996³; however, there has been an increased interest in sublobar pulmonary resection for stage I lung cancer.⁴ Anatomic segmentectomy is a lung-sparing resection that has survival rates comparable to

lobectomy.^{5,6} It is superior to nonanatomical wedge resection⁶ and is particularly suitable for elderly patients who have a limited cardiopulmonary reserve.⁷

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Segmentectomy has been performed through either a thoracotomy approach or a video-assisted thoracoscopic surgery (VATS) approach. There are several single-center studies in the literature that compared VATS and thoracotomy for segmentectomy.^{8–10} However, these studies were based on single-institution experiences and therefore included relatively small numbers of enrolled patients. Also, there is a single multicenter study that compared both surgical approaches based on the Surveillance Epidemiology and End Results database; however, patients in that study were over 65 years of age and underwent segmentectomy between the years 1994 and 2007.¹¹ Therefore, we believe that there is a need for a multi-institutional study of the contemporary practice of VATS segmentectomy compared to open thoracotomy.

The aim of this study was to evaluate the 30-day postoperative surgical outcome of VATS versus thoracotomy segmentectomy for lung cancer in the United States in the period between 2013 and 2017. We used the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP®) database, which is a large and multicenter national database. We also observed a trend in VATS segmentectomy practice over the course of the study and reported it as a separate subanalysis.

Methods

We conducted a retrospective cohort study comparing the postoperative outcomes of thoracotomy and VATS segmentectomy with trending the outcome of VATS over time. We queried the ACS NSQIP database for patients who underwent VATS and thoracotomy segmentectomy for benign or malignant lung tumors between 2013 and 2017. The ACS NSQIP contains over 135 variables captured from surgical cases performed in participating hospitals. These variables include preoperative characteristics, intraoperative events, and postoperative outcomes within 30 days of the operation. The database is provided in the form of research-friendly files called the Participant Use Data Files (PUF). These PUF files have de-identified data captured as part of the national quality improvement program and are available to researchers at participating sites.

We used the Current Procedural Terminology (CPT) code (32484) to identify patients who underwent thoracotomy segmentectomy and the CPT code (32669) to identify patients who underwent VATS segmentectomy. We then used the International Classification of Diseases version (ICD) 9 and 10 codes to identify patients with benign and malignant lung tumors. The following ICD 9 codes were used for patient identification: 162, 162.3, 162.4, 162.5, 162.8, and 162.9 for patients with malignant neoplasms of the bronchus or lung; 197.0 for secondary malignant neoplasms; 209.7 for neuroendocrine tumors; 212.3 for benign neoplasms of bronchus and lung; 231.2 for carcinoma in situ; 235.7 for neoplasms of uncertain behavior of trachea, bronchus, and lung; and 239.1 for neoplasms of unspecified nature of the respiratory system. We used the ICD10 C34 codes to identify patients with malignant

neoplasms of the bronchus and the lung, C78 for secondary malignant neoplasms, D02.21 and D02.22 for carcinoma in situ, D14.30 for benign neoplasms, D38.1 for neoplasms of uncertain behavior, D3A.090 for carcinoid tumors, D49.1 for other neoplasms of unspecified behavior of the respiratory system, and, finally, R91.1 for solitary pulmonary nodules. We excluded the patients who underwent segmentectomy secondary to sarcoidosis and infectious diseases including pulmonary abscess, mycobacterial infection, coccidioidomycosis, and mycoses.

We divided the patients into 2 groups based on whether they received a thoracotomy or a VATS approach. Propensity-matched analysis was conducted between the VATS and the thoracotomy groups based on preoperative variables that were significant in the bivariate analysis (patient age, weight, gender, functional status, American Society of Anesthesiologists [ASA] classification, and the year of operation), which created 2 comparable groups with similar preoperative demographics and risk factors. Based on our sample sizes, we chose a 2:1 matching to include as many as possible of the patients who underwent VATS to increase the precision of our analyses.¹² The matched groups were then compared for postoperative outcomes. All VATS patients were then divided arbitrarily based on the date of the operation into 2 roughly equal groups: early (2013, 2015) and late (2016, 2017), and the perioperative variables were compared. The early and later VATS patient groups had comparable preoperative characteristics apart from a statistically significant higher incidence of severe chronic obstructive pulmonary disease (COPD) in the early patient group. Propensity matching was thus conducted ensuring equivalent preoperative patient characteristics between the 2 subgroups.

We used bivariate analysis to compare the variables. Descriptive summaries were frequencies and percentages for categorical variables and means and standard deviations for numeric variables. Comparisons among groups were done using Pearson's χ^2 test for categorical data and Wilcoxon rank-sum tests for continuous data. The level of significance was set at 5%. Analyses were done using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Thoracotomy Versus VATS Segmentectomy

A total of 1,785 patients met the inclusion criteria; 1,333 patients underwent VATS and 452 had thoracotomy. The distribution of etiologies of the resected pulmonary lesions was statistically no different between the 2 surgical approaches with the majority of the patients undergoing segmentectomy for primary malignant lesions (Table 1). The thoracotomy group had higher male-to-female ratio (46%:54% vs 36%:64%, $P < 0.001$), slightly younger patients (66.2 ± 10 vs 67.6 ± 10 , $P = 0.018$), and slightly higher patient weight mean (78.5 ± 19 vs 76.5 ± 18 , $P = 0.037$) with comparable body mass index. Preoperative creatinine was statistically but not clinically

Table 1. Distribution of Etiologies of the Resected Pulmonary Lesions in Both Surgical Approaches.

Surgical approach	Primary benign	Primary malignant	Metastatic disease	Carcinoid tumors	Tumor of uncertain behavior	P-value
Thoracotomy	4.90%	80.65%	8.86%	3.03%	1.86%	0.1
VATS segmentectomy	6.35%	80.16%	6.11%	2.46%	2.22%	

Abbreviation: VATS, video-assisted thoracoscopic surgery.

significantly higher in the open group. Racial representation was comparable. Preoperative risk factors, including diabetes mellitus, hypertension, history of active smoking, congestive heart failure, and end-stage renal disease along with preoperative hematocrit, were similar in both groups. There were no significant differences in preoperative serum albumin or weight

loss. The thoracotomy segmentectomy patients were more likely to be functionally dependent (1.78%, 0.60%, $P = 0.02$) and had statistically significant higher comorbid physical status based on the ASA score. The majority of patients had ASA 3 classification with a higher rate of ASA 4 in the thoracotomy patients (7.96%, 4.96%, $P = 0.018$; Table 2).

Table 2. Preoperative Comorbidities, Risk Factors, and Characteristics of Thoracotomy and VATS Segmentectomy Groups

	Thoracotomy segmentectomy n = 452	VATS segmentectomy n = 1,333	P-value
Gender			
Female	242 (53.5%)	847 (63.5%)	<0.001
Male	210 (46.5%)	486 (36.5%)	
Race			
Black	25 (6.0%)	76 (6.2%)	0.52
Other	18 (4.3%)	70 (5.7%)	
White	375 (89.7%)	1,074 (88.0%)	
Age	66.2 ± 10.7	67.7 ± 10.2	0.02
BMI	28.2 ± 6.1	27.9 ± 5.9	0.31
Preoperative serum creatinine	0.9 ± 0.5	0.9 ± 0.5	0.03
Preoperative serum albumin	4.1 ± 0.4	4.1 ± 0.4	0.55
Preoperative hematocrit	40.3 ± 4.5	40.3 ± 4.2	0.89
Surgical specialty			
Cardiothoracic	418 (92.5%)	1,254 (94.1%)	0.23
General	34 (7.5%)	79 (5.9%)	
Diabetes mellitus			
Insulin	22 (4.9%)	61 (4.6%)	0.30
No	375 (83.0%)	1,143 (85.7%)	
Non-insulin	55 (12.2%)	129 (9.7%)	
Current smoker within 1 year	143 (31.6%)	401 (30.1%)	0.53
Functional health status			
Dependent	8 (1.8%)	8 (0.6%)	0.02
Independent	441 (98.2%)	1,322 (99.4%)	
History of severe COPD	125 (27.6%)	353 (26.5%)	0.63
CHF within 30 days before surgery	0 (0.0%)	8 (0.6%)	0.10
Hypertension requiring medication	254 (56.2%)	805 (60.4%)	0.12
Currently on dialysis (preop)	3 (0.7%)	6 (0.45%)	0.58
>10% body weight loss in last 6 months	6 (1.3%)	13 (1.0%)	0.53
ASA classification			
1	1 (0.2%)	4 (0.3%)	0.02
2	74 (16.4%)	286 (21.5%)	
3	341 (75.4%)	975 (73.3%)	
4	36 (7.9%)	66 (4.9%)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; VATS, video-assisted thoracoscopic surgery.

Bold values indicate statistical significance.

Table 3. Bivariate Analysis of Postoperative Outcomes of Thoracotomy Versus VATS Segmentectomy After Propensity Matching Creating Equally Comparable Groups with Similar Preoperative Characteristics.

	Thoracotomy segmentectomy n = 452	VATS segmentectomy n = 868	P-value
Pneumonia	26 (5.8%)	24 (2.8%)	0.007
Unplanned intubation	16 (3.5%)	13 (1.5%)	0.016
Pulmonary embolism	6 (1.3%)	5 (0.6%)	0.15
On ventilator >48 hours	12 (2.7%)	5 (0.6%)	0.001
Acute renal failure	3 (0.7%)	1 (0.1%)	0.09
Urinary tract infection	8 (1.8%)	15 (1.7%)	0.96
Stroke	2 (0.4%)	3 (0.4%)	0.79
Cardiac arrest requiring CPR	3 (0.7%)	5 (0.6%)	0.85
Myocardial infarction	1 (0.2%)	5 (0.6%)	0.36
Transfusions	26 (5.8%)	15 (1.7%)	<0.001
Deep venous thrombosis	5 (1.1%)	1 (0.1%)	0.03
Sepsis	8 (1.8%)	9 (1.0%)	0.26
Return to OR	23 (5.1%)	22 (2.5%)	0.015
Prolonged admission >30 days	5 (1.1%)	2 (0.2%)	0.04
Readmission	36 (8.0%)	65 (7.5%)	0.74
Superficial surgical site infection	6 (1.3%)	3 (0.4%)	0.04
Deep surgical site infection	1 (0.2%)	0 (0.0%)	0.17
Organ site infection	1 (0.2%)	3 (0.4%)	0.70
Total operation time	161.3 ± 87.4	139.8 ± 78.5	<0.001
Days from operation to discharge	5.8 ± 5.3	3.9 ± 4.0	<0.001
Discharge destination			0.003
Home	402 (88.9%)	813 (93.8%)	
Facility	44 (9.7%)	51 (5.9%)	
Mortality	6 (1.3%)	10 (1.2%)	0.78

Abbreviations: CPR, cardiopulmonary resuscitation; OR, operating room; VATS, video-assisted thoracoscopic surgery.

Bold values indicate statistical significance.

After propensity matching on all the statistically significant preoperative characteristics, comparable patient groups were created with 1,320 patients. Compared to thoracotomy, VATS was found to be associated with less postoperative complications including pneumonia (2.76%, 5.75%, $P = 0.007$), unplanned intubation (1.50%, 3.54%, $P = 0.016$), and prolonged intubation for greater than 48 hours (0.58%, 2.65%, $P = 0.001$). The VATS group was less likely to have postoperative bleeding requiring transfusion (1.73%, 5.75%, $P < 0.001$), to develop deep venous thrombosis (DVT; 0.12%, 1.11%, $P = 0.03$), and had lower rates of superficial surgical site infection (0.35%, 1.33%, $P = 0.03$). Other reported postoperative complications were comparable between the groups and there was no difference in the mortality rates. VATS segmentectomy was associated with shorter operative time (139 ± 78 vs 161 ± 87 minutes, $P < 0.001$) and fewer chances of postoperative complications requiring a return to the operating room (OR; 2.53%, 5.09%, $P = 0.015$). Postoperatively, the VATS patients had fewer inpatient days from the operation date to discharge (3.9 ± 3.9 vs 5.8 ± 5.2 days, $P < 0.001$), and were more likely to be discharged home (94%, 89%, $P = 0.003$; Table 3).

Early Versus Late VATS Segmentectomy

There were 623 patients included in the early (2013, 2015) VATS patient group and 710 in the late (2016, 2017) group. Both were comparable with respect to patient demographics of age, gender, race, and preoperative comorbidities including diabetes, hypertension, heart failure, dialysis dependence, and smoking history. There was a statistically significant higher rate of severe COPD in the early group (30.66%, 22.82%, $P = 0.001$). There were no differences in the functional status or ASA classifications between the subgroups (Table 4).

Prior to propensity matching, the early group patients were found to have higher rates of pneumonia (3.37%, 1.83%, $P = 0.07$). However, that difference was noted to vanish after the patient characteristics were matched to history of severe COPD creating 2 groups with 594 patients each with similar preoperative factors. Compared to the earlier VATS group, the late group was associated with fewer cardiac arrests requiring CPR (0.84%, 0%, $P = 0.02$) and statistically significant fewer hospital stays with days from operation to discharge (3.3 ± 3 vs 4.2 ± 4, $P < 0.001$). Postoperative bleeding trended toward statistical significance with fewer transfusion requirements in the late group (0.84%,

Table 4. Preoperative Comorbidities and Characteristics of the Early Versus Late VATS Groups.

	Early VATS segmentectomy n = 623	Late VATS segmentectomy n = 710	P-value
Gender			
Female	391 (62.8%)	456 (64.2%)	0.61
Male	232 (37.2%)	254 (35.8%)	
Race			
Black	30 (5.1%)	46 (7.3%)	0.14
Other	29 (4.9%)	41 (6.5%)	
White	528 (89.9%)	546 (86.3%)	
Age	67.7 ± 10.2	67.6 ± 10.2	0.97
BMI	27.9 ± 6.2	27.9 ± 5.7	0.60
Preoperative serum creatinine	0.9 ± 0.6	0.9 ± 0.4	0.62
Preoperative serum albumin	4.1 ± 0.4	4.0 ± 0.4	0.15
Preoperative hematocrit	40.3 ± 4.2	40.4 ± 4.1	0.92
Surgical specialty			
Cardiothoracic	578 (92.9%)	676 (95.2%)	0.06
General	45 (7.2%)	34 (4.8%)	
Diabetes mellitus			
Insulin	24 (3.9%)	37 (5.2%)	0.18
No	546 (87.6%)	597 (84.1%)	
Non-insulin	53 (8.5%)	76 (10.7%)	
Current smoker within 1 year	191 (47.6%)	210 (52.4%)	0.67
Functional health status			
Dependent	4 (0.6%)	4 (0.6%)	0.85
Independent	617 (99.4%)	705 (99.4%)	
History of severe COPD	191 (30.7%)	162 (22.8%)	0.001
CHF within 30 days before surgery	5 (0.8%)	3 (0.4%)	0.37
Hypertension requiring medication	389 (48.3%)	416 (51.7%)	0.15
Currently on dialysis (preop)	5 (0.8%)	1 (0.1%)	0.07
>10% body weight loss in last 6 months	7 (1.1%)	6 (0.9%)	0.61
ASA classification			
1	0 (0.0%)	4 (0.6%)	0.20
2	138 (22.2%)	148 (20.9%)	
3	456 (73.4%)	519 (73.1%)	
4	27 (4.4%)	39 (5.5%)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; VATS, video-assisted thoracoscopic surgery.

Bold values indicate statistical significance.

2.19%, $P = 0.057$). None of the postoperative complications increased over time. There was no difference in mortality rates (Table 5).

Over the years of the study, it was noted that the ratio of VATS-to-thoracotomy segmentectomy increased over time from being in 65%:35% range to >80%:20% suggesting trends toward more minimally invasive approach use (Fig. 1). The length of stay was noted to decrease significantly throughout the years of the study (Fig. 2).

Discussion

The minimally invasive nature of VATS, in theory, should minimize the burden of the operation and lower the rates of postoperative complications of lung resection. This assumption has its

basis in the well-established favorable outcome of VATS over open lobectomy in national and international studies.^{13–17} However, in the case of technically demanding operations like segmentectomy, one might question whether VATS is associated with procedural adverse events, which may eventually mitigate the benefits of the minimally invasive nature of the operation. Our study showed that despite being more technically demanding compared to other VATS operation,¹⁸ VATS segmentectomy is associated with lower rates of postoperative complications when compared to thoracotomy segmentectomy.

In our study, the rate of pneumonia with VATS segmentectomy was almost half of that observed in patients who had thoracotomy. VATS segmentectomy also was associated with lower rates of respiratory failure as evidenced by the reduced need for subsequent intubation and the ability to wean patients

Table 5. Postoperative Outcomes and Complications of Early Versus Late VATS After Propensity Matching.

	Early VATS segmentectomy n = 594	Late VATS segmentectomy n = 594	P-value
Pneumonia	20 (3.4%)	13 (2.2%)	0.22
Unplanned intubation	10 (1.7%)	7 (1.2%)	0.46
Pulmonary embolism	3 (0.5%)	3 (0.5%)	1.00
On ventilator >48 hours	2 (0.3%)	5 (0.8%)	0.26
Acute renal failure	0 (0.0%)	1 (0.2%)	0.32
Urinary tract infection	12 (2.0%)	11 (1.9%)	0.83
Stroke	2 (0.3%)	2 (0.3%)	1.00
Cardiac arrest requiring CPR	5 (0.8%)	0 (0.0%)	0.025
Myocardial infarction	2 (0.3%)	4 (0.7%)	0.41
Transfusions	13 (2.2%)	5 (0.8%)	0.06
Deep venous thrombosis	1 (0.1%)	1 (0.1%)	0.60
Sepsis	5 (0.8%)	4 (0.7%)	0.73
Return to OR	14 (2.4%)	17 (2.9%)	0.59
Prolonged admission >30 days	1 (0.2%)	1 (0.2%)	1.00
Readmission	43 (7.2%)	45 (7.6%)	0.82
Superficial surgical site infection	4 (0.7%)	2 (0.3%)	0.41
Organ site infection	1 (0.2%)	4 (0.7%)	0.18
Total operation time	140.2 ± 76.6	142.5 ± 73.8	0.38
Days from operation to discharge	4.2 ± 4.0	3.30 ± 3.1	<0.001
Discharge destination			
Home	559 (94.3%)	563 (94.9%)	0.45
Other facility	33 (5.6%)	27 (4.6%)	
Mortality	7 (1.2%)	2 (0.3%)	0.10

Abbreviations: CPR, cardiopulmonary resuscitation; OR, operating room; VATS, video-assisted thoracoscopic surgery.

Bold values indicate statistical significance.

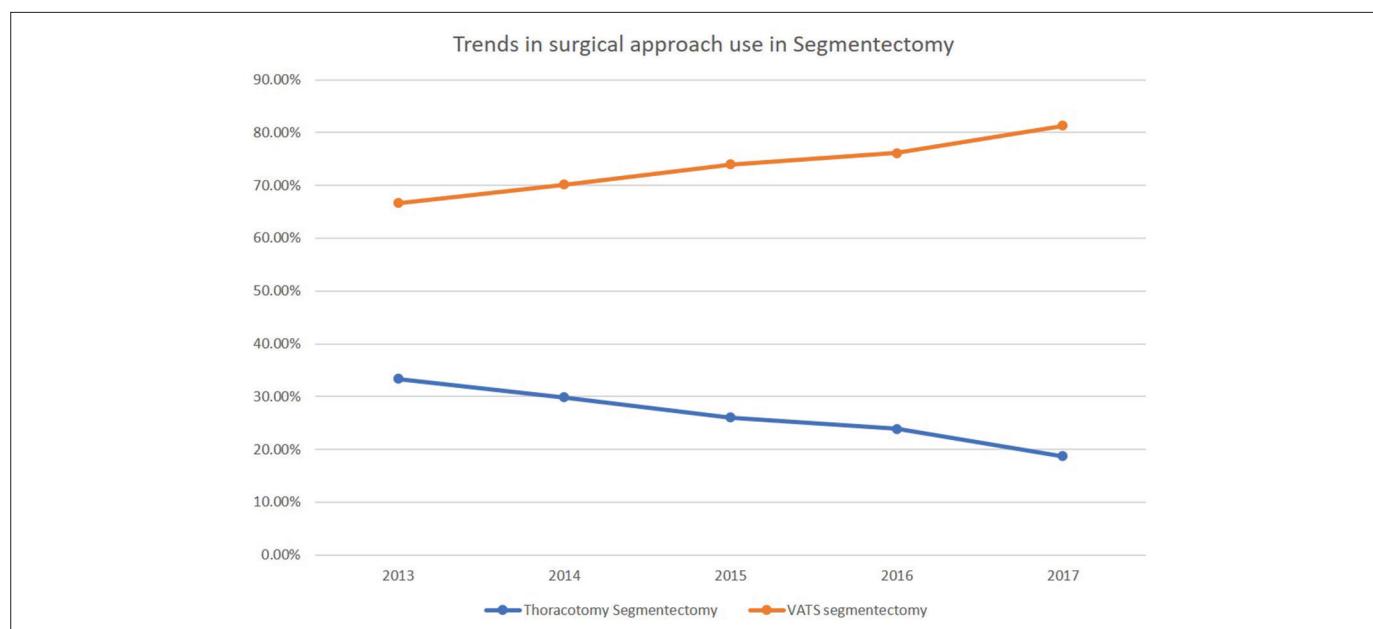


Fig. 1. Trends in utilizing thoracotomy and VATS approaches for segmentectomy between 2013 and 2017. VATS, video-assisted thoracoscopic surgery.

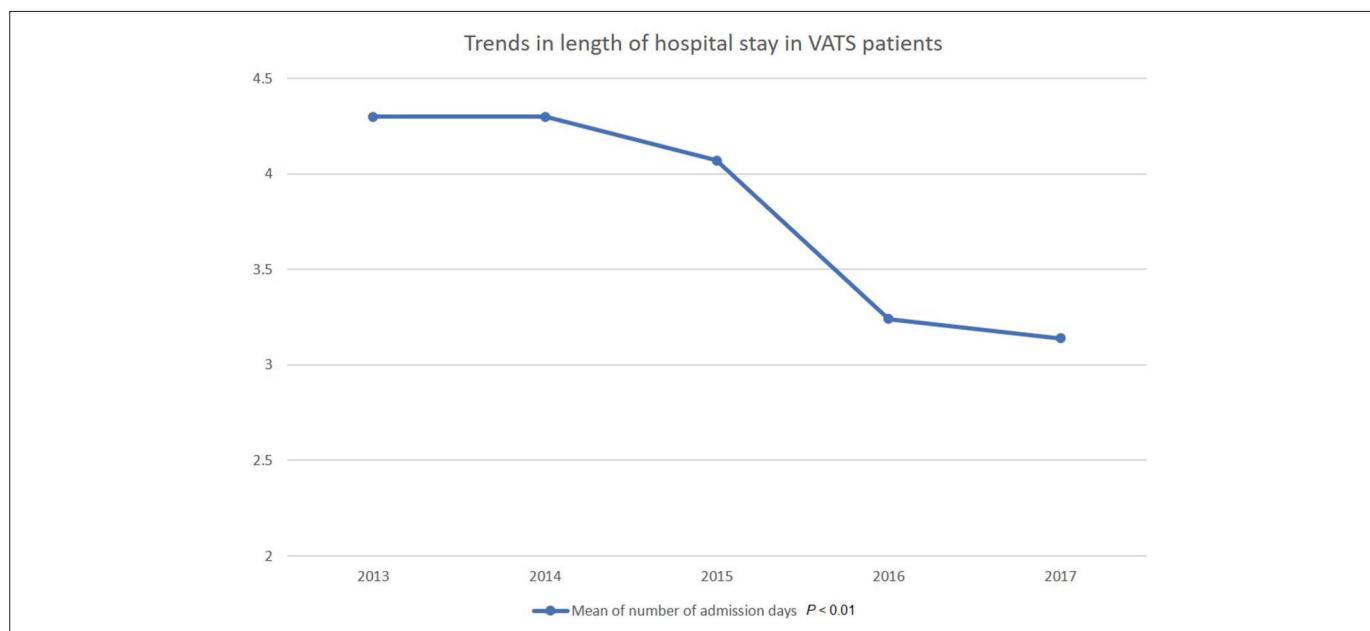


Fig. 2. Trend in the hospital length of stay for patients who underwent VATS segmentectomy between 2013 and 2017. VATS, video-assisted thoracoscopic surgery.

off mechanical ventilation faster. These findings are important as postoperative atelectasis, pneumonia, and respiratory failure are common reasons for morbidity and mortality in thoracic surgeries, and cause an increase in the hospital length of stay, intensive care stay, and utilization of health-care resources.¹⁹ Konstantinidis et al., in a study to identify risk factors for 90-day hospital readmission after VATS lobectomy or segmentectomy, using 481 patients, found that pneumonia is the most frequent reason for readmission (17 patients with pneumonia out of the 59 readmitted patients).²⁰ Furthermore, we found that the rate of DVT was significantly lower with VATS when compared to thoracotomy. These observations are probably due to the reduced postoperative pain, the ability to ambulate easier, and participate more efficiently in postoperative pulmonary physiotherapy.^{21,22}

We also found that surgical site infections were reduced with the VATS segmentectomy group. According to the ACS-NSQIP, the surgical wound in segmentectomy for lung cancer (VATS or thoracotomy) is classified as a clean-contaminated wound since the respiratory tract was entered in a controlled fashion and there is no prior contamination.²³ There is support in the literature of lower incidence of surgical site infections with minimally invasive approach compared to thoracotomy. Recently, Cvijanović et al. published a 12-year retrospective study comparing risk factors and incidence of surgical site infections (SSI) in thoracic surgical procedures including wedge resection, lobectomy, and pneumonectomy²⁴ with reported cumulative SSI rates of 2.2% in the VATS surgical group compared to 3.5% after open thoracotomy. However, no segmentectomy group was reported in the study.

Atkins et al. from Duke in North Carolina, in a single-institution study between 2000 and 2006, demonstrated that VATS segmentectomy is associated with reduced hospital length of stay when compared to thoracotomy (4.3, 6.8 days).⁸ In our study, the hospital length of stay was reduced on average by a day and a half with VATS, and interestingly, fewer patients were admitted for a prolonged period (over 30 days) after VATS compared to thoracotomy. Furthermore, patients who had VATS were more likely to be discharged home and not to another facility like rehab or nursing home. These favorable outcomes certainly are reflections of the reduced VATS postoperative morbidity. The shorter hospital stay, increased likelihood of going home, and potentially reduced rate of readmission after VATS segmentectomy are significant factors as they reduce the overall cost of health care and, more importantly, ensure patient satisfaction and overall well-being.^{25,26}

Perhaps the most interesting finding of our study was the trend of segmentectomy practice over the 5-year period. We found that US surgeons are increasingly using VATS over thoracotomy, and that the rate of utilizing VATS increased in a linear fashion over the 5-year period of the study. This increase was associated with a significant decline in the need for blood transfusions during the patient hospitalizations. This American trend of utilizing VATS more frequently compared to thoracotomy for segmentectomy is mirrored internationally as well. Lopez-Pastorini et al. reported their experience in Cologne, Germany, with only 9 out of 78 segmentectomies being done by VATS in 2009, but 76 out of 98 segmentectomies being done by VATS in 2015.¹⁰ However, their experience did not show a convincing improvement in

the rates of complications between VATS and a thoracotomy. Our study also showed that the hospital length of stay for patients undergoing VATS decreased significantly and continuously over the study period. We live in an era where there is tremendous pressure on surgeons to be economically sound and efficient. In the world of thoracic surgery, fast-tracking and enhanced recovery pathways have been employed long before other specialties, like colorectal surgery.²⁷⁻²⁹ Regardless of whether our observed decrease in the length of stay was in fact due to a change in the practice or a result of being safer and more efficient in the OR, it is a welcome trend that further validates VATS technique.

Our study had limitations that were inherent to the nature of our database and the variables collected in it. NSQIP is not an oncology-oriented database; therefore, information regarding tumor stage, extent of lymph nodes dissection, tumor location, or the lung segment resected were not collected. Furthermore, perioperative factors unique to thoracic surgery like pulmonary function test, duration of chest tubes placement and air leak, and postoperative pain were not collected in NSQIP. All these variables may have influenced the surgeon's decision to use thoracotomy over VATS and may have contributed to the higher complication rates in thoracotomy. Also, the CPT code 32669 that we used may have included robotic cases, which we were not able to identify. Finally, this study highlighted the 30-day surgical outcome differences between the 2 approaches and did not provide answers regarding the long-term outcomes. However, we elected to use NSQIP database because it is a large national database and derived from multiple centers throughout the United States. This database is collected directly from patient charts, and it is risk-adjusted (to account for differences in risk factors between patients), and case-mix-adjusted (to account for difference between hospitals).³⁰ These qualities made NSQIP database particularly suitable to answer our questions regarding the 30-day postoperative surgical, nononcologic, outcomes of segmentectomy.

Conclusions

Even though VATS segmentectomy for lung tumors is a technically demanding operation, it has fewer 30-day postoperative complications when compared to thoracotomy. The rates of pneumonia, unplanned intubation, prolonged ventilation, transfusion, DVT, SSI, return to OR, and length of stay are lower in VATS segmentectomy. However, there is no difference in 30-day mortality between both surgical approaches.

Author Contributions

Mr Wolfe was responsible for data collection and statistical analysis. Drs Sabra, Alwatari, Bierema, and Shah were responsible for data collection, study design, and writing the manuscript. Drs Shah and Cassano were responsible for the manuscript revision and approval. Dr Shah supervised the project.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Routine Placement of Temporary Epicardial Pacing Leads Is Not Required After Minimally Invasive Aortic Valve Replacement

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Abstract

Objective: Our objective is to identify the incidence of urgent transvenous (TV) pacing wire placement following minimally invasive aortic valve replacement (mini-AVR). **Methods:** This is a single-center, retrospective, observational study including 359 individuals who underwent isolated mini-AVR through right anterior mini-thoracotomy between January 2015 and September 2019. Patients were grouped according to avoidance or insertion of epicardial pacing wires, and further subdivided based on the requirement for postoperative emergent temporary TV pacing or permanent pacemaker (PPM) placement during the index admission. **Results:** Two hundred forty-two (67.4%) had acceptable rate and no high-degree atrioventricular (AV) block prior to chest closure and did not have insertion of epicardial pacing wires. Of those patients, only 3 (1.2%) required emergent TV pacing and 6 (2.5%) required nonemergent TV pacing with or without PPM placement during the index admission. Sixty-two (17.3%) patients received only atrial epicardial pacing leads secondary to sinus bradycardia or junctional rhythm and 3 (4.8%) of those patients required PPM placement due to sick sinus syndrome and 1 (1.6%) patient required nonemergent TV pacing and PPM due to high-grade AV heart block. Fifty-five (15.3%) patients received ventricular leads due to high-grade AV heart block and 7 (12.7%) of those patients required PPM placement during the index admission. **Conclusions:** Temporary epicardial lead insertion is not routinely required in mini-AVR in patients with normal rate and acceptable AV conduction prior to chest closure. In the absence of epicardial ventricular lead insertion, the chance of requiring urgent TV pacing wire placement during the index admission is 0.99%.

Central Message

In the absence of epicardial ventricular lead insertion, the chance of requiring urgent transvenous pacing is less than 1%. Routine placement of temporary epicardial leads following minimally invasive aortic valve replacement is not required in patients with normal rate and acceptable atrioventricular conduction prior to chest closure.

Keywords

aortic valve replacement, minimally invasive surgery, temporary epicardial pacing wire, permanent pacemaker

Introduction

Temporary epicardial leads or pacing wires (PWs) were routinely placed following all cardiac surgical procedures since 1960s for diagnostic and therapeutic interventions.¹ Temporary epicardial PW placement is still a standard at many cardiac surgical departments and specifically inserted following almost all valve and congenital heart surgical procedures.^{2,3} Temporary leads are removed 24 hours to several days postoperatively after a stable cardiac rhythm is established.⁴ Although the use of temporary epicardial PW is helpful in management of some patients, it is associated with infrequent but life-threatening complications

including serious arrhythmias, hemorrhage and tamponade from atrial and ventricular lacerations, and death.⁵ Also, retained

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Table 1. Population Demographics and Preoperative Data in 359 Patients Undergoing Isolated Mini-AVR.

Variable	Value n (%) or mean ± SD
Age, years	68 ± 11
Gender	
Male	225 (62.7)
Female	134 (37.3)
Hypertension	282 (78.6)
PAD	43 (12.0)
CAD	221 (61.6)
Prior MI	44 (12.3)
Arrhythmia	42 (11.8)
Diabetes	97 (27.0)
Dyslipidemia	227 (63.2)
History of smoking	201 (56.0)
Obesity (BMI > 30 kg/m ²)	177 (49.3)
Heart failure	59 (16.4)
Stroke	22 (6.1)
Renal dialysis	2 (0.6)
COPD	54 (15.0)
NYHA Class III-IV	11 (3.1)
LVEF < 40%	13 (3.6)
STS risk score	1.7 ± 1.3

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; MI, myocardial infarction; mini-AVR, minimally invasive aortic valve replacement; NYHA, New York Heart Association; PAD, peripheral arterial disease; SD, standard deviation; STS, Society of Thoracic Surgeons.

epicardial PW after cardiac surgery may cause serious complications including deep mediastinal infections.⁶

The aim of this study is to identify the incidence of urgent temporary PW placement and to demonstrate that routine placement of temporary epicardial PW is not necessary following minimally invasive aortic valve replacement (mini-AVR).

Methods

Patients

This study is an observational, retrospective review of the clinical, operative, and outcome data from patients who underwent mini-AVR at our institution between January 2015 and September 2019. The Institutional Review Board of the hospital approved this study and waived the requirement for written informed consent. A total of 359 patients were included in the study who underwent isolated mini-AVR. Exclusion criteria include an existing permanent pacemaker (PPM), conversion to full median sternotomy, and concomitant procedure at the time of index operation. The Society of Thoracic Surgeons database and our institutional electronic medical records were used to retrospectively collect preoperative, intraoperative, and postoperative data for the variables listed in the tables.

Table 2. Preoperative Electrocardiographic Findings.

Rhythm	Number of patients (N = 363) n (%)
Sinus rhythm	268 (73.8)
Atrial fibrillation/flutter	17 (4.7)
Pre-existing PPM	4 (1.1)
Conduction abnormality	
First-degree AV block	29 (8.0)
Left anterior hemiblock	10 (2.8)
RBBB	23 (6.3)
LBBB	12 (3.3)

Abbreviations: AV, atrioventricular; LBBB, left bundle branch block; PPM, permanent pacemaker; RBBB, right bundle branch block.

Surgical Technique

Our approach for aortic valve replacement via right anterior mini-thoracotomy has been previously described.⁷ We employ a camera for enhanced visualization. A 4 to 5-cm incision in the right second intercostal space is made with a camera port placed lateral to the incision. Cardiopulmonary bypass is established via central aortic and peripheral venous cannulation, and patients are cooled to 30°C. An aortic cross-clamp is placed through a 5-mm incision in the third interspace anterior to mid-axillary line, and anterograde Histidine Tryptophan Ketoglutarate cardioplegia is administered. After aortic leaflet removal and annular decalcification, annular and prosthetic sutures are placed. The valve is then seated, and the sutures secured using the COR-KNOT® device and titanium fasteners (LSI SOLUTIONS®, Victor, NY, USA). Cardiopulmonary bypass is discontinued, and the wound is then closed in layers.

Statistical Analysis

Statistical analysis was performed using the data analysis in Microsoft Excel 2016 and consisted mainly of descriptive statistics. Categorical variables are presented as counts and percentages. Continuous variables are presented as means ± standard deviation or medians.

Results

A total of 359 patients underwent isolated mini-AVR with ages ranging from 57 to 79 years with mean age of 68 years. The

Table 3. Intraoperative Data.

Variable	Value mean ± SD
CPB time (minutes)	125 ± 42
Aorta cross-clamp time (minutes)	93 ± 25

Abbreviations: CPB, cardiopulmonary bypass; SD, standard deviation.

main demographic characteristics, preoperative data including electrocardiogram (ECG) rhythm findings, and intraoperative data are summarized in Table 1, Table 2, and Table 3.

According to the insertion or avoidance of temporary epicardial PW, 3 groups of patients were identified: group 1 had only atrial temporary epicardial PW inserted secondary to sinus bradycardia or junctional rhythm; group 2 had either ventricular or atrial and ventricular temporary epicardial PW inserted secondary to high-grade atrioventricular (AV) block; and group 3 had normal rate and acceptable AV conduction prior to chest closure and did not have any temporary epicardial PW inserted (Fig. 1).

The prevalence of postoperative urgent TV pacing and PPM implantation is summarized in Table 4. Group 1 consisted of 62 (17.3%) patients and no patient requiring urgent TV pacing. Only 1 (1.6%) patient required nonurgent TV pacing due to high-grade AV block and 3 (4.8%) patients needed PPM placement secondary to sick sinus syndrome during the index admission. Group 2 consisted of 55 (15.3%) patients with 7 (12.7%) patients requiring PPM placement during the index admission secondary to persistent high-grade AV block. Group 3 consisted of 242 (67.4%) patients with 3 (1.2%) patients requiring urgent TV pacing postoperatively secondary to high-grade AV block with hemodynamic compromise. Six (2.5%) patients needed nonurgent TV pacing and 5 (2.1%) patients required PPM placement due to persistent high-grade AV block without hemodynamic compromise during the index admission. Groups 1 and 3 consisted of 304 (84.7%) patients who had no ventricular epicardial PW inserted with only 3 (0.99%) requiring urgent TV pacing wire placement during the index admission.

Table 4. Prevalence of Postprocedure Urgent Transvenous Pacing Wire Placement and Permanent Pacemaker Implantation During Index Admission.

Variable	Number of patients (N = 359) n (%)
Group 1 (A pacing wires only)	62 (17.3)
Urgent TV pacing	0
Nonurgent TV pacing	1 (1.6)
PPM	3 (4.8)
Group 2 (V or A+V pacing wires)	55 (15.3)
PPM	7 (12.7)
Group 3 (no pacing wires)	242 (67.4)
Urgent TV pacing	3 (1.2)
Nonurgent TV pacing	6 (2.5)
PPM	5 (2.1)
Groups 1 and 3	304 (84.7)
Urgent TV pacing	3 (0.99)
Nonurgent TV pacing	7 (2.3)
PPM	8 (2.6)

Abbreviations: A, atrial; PPM, permanent pacemaker; TV, transvenous; V, ventricular.

Group 1: placement of A pacing wires secondary to sinus bradycardia or junctional rhythm.

Group 2: placement of V or A + V pacing wires secondary to high-grade AV block.

Group 3: no pacing wires due to normal rate and acceptable AV conduction intraoperatively.

In Table 5, the prevalence of PPM implantation during index admission is shown for each year from 2015 to 2019. For the first 194 patients, 14 patients required PPM during index admission.

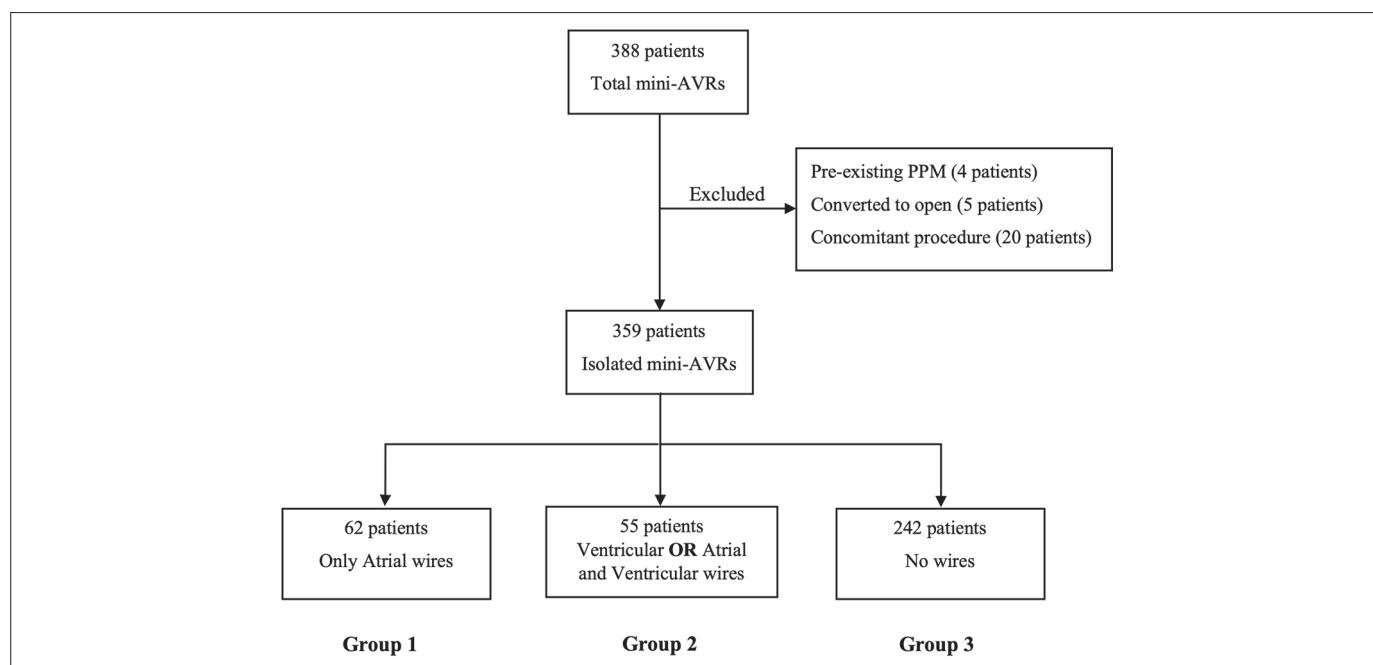


Fig. 1. Study workflow, patients grouped according to avoidance or insertion of epicardial pacing wires intraoperatively. AVR, aortic valve replacement; PPM, permanent pacemaker.

Table 5. Annual Prevalence of PPM Implantation During Index Admission.

Year	Number of isolated mini-AVR (N = 359)	PPM n (%)
2015	13	1 (7.7)
2016	92	5 (5.4)
2017	89	8 (8.9)
2018	107	1 (0.9)
2019 (Jan-Sep)	58	0

Abbreviations: AVR, aortic valve replacement; mini-AVR, minimally invasive aortic valve replacement; PPM, permanent pacemaker.

For the last 165 patients, only 1 patient required PPM implantation. Table 6 summarizes the incidence of postoperative outcomes during the index admission. Early postoperative mortality occurred in 6 (1.7%) patients secondary to major bleeding and subsequent shock with multiple organ failure. There was no mortality due to complete heart block in the presence or absence of temporary epicardial PW. Prior studies report a 30-day mortality rate of 2.2% to 5.2% following conventional full sternotomy AVR and mortality rate of 1.5% to 2.1% following mini-AVR.⁸⁻¹¹ Our 30-day mortality of 1.7% is in line with prior reports. The rate of re-exploration for bleeding following mini-AVR is reported 4.9% in a meta-analysis done by Shehada et al. that included 2,279 mini-AVR patients,¹¹ which is also consistent with our 4.5% rate of re-exploration for bleeding.

Discussion

Temporary epicardial pacing leads are routinely placed following cardiac surgery, which can be due to their simple and efficient method for optimizing cardiac function and for treating severe or mild conduction disorders that may occur postoperatively.¹² However, the use of temporary epicardial PW is not benign and can lead to infrequent but lethal complications. These complications could arise during placement, removal, or if leads are retained in the body. In the literature, the incidence of major

complications following temporary epicardial PW insertion or removal is reported anywhere from 0.04% to 0.8%.^{12,13} These complications can range from simply a failure of sensing or capturing to more serious complications including tamponade, hemothorax, disruption of coronary anastomoses, and migration of retained wires.¹⁴⁻¹⁶ There is a higher risk of complications in anticoagulated and redo cardiac surgery patients.

Retention of epicardial PW is not necessarily benign and can result in local infection potentially leading to more serious complications including deep mediastinal infection or migration and erosion to adjacent mediastinal structure.¹⁷ Although this is a rare complication, a few cases of mediastinal abscess cavity have been reported many years following cardiac surgery associated with retained epicardial PW.^{17,18}

Selective placement of temporary epicardial PW is an appealing strategy. Some centers have restricted their use only for patients complicated by intraoperative bradycardia, AV conduction block, and nodal or junctional arrhythmia. A retrospective study performed by Alwaqfi et al.,¹⁹ which included 400 valve surgery patients, found 170 had no temporary epicardial PW and none required postoperative pacing, and 230 had temporary epicardial PW with 23.9% requiring pacing after surgery.¹⁹ It has been reported that older age, higher New York Heart Association class (III/IV), prolonged aortic cross-clamp time, preoperative digoxin, high pulmonary artery pressure (>50 mmHg), multiple valve procedures, and heavy annular calcification were predictors of the need for pacing after valve surgery.^{19,20} We limited temporary epicardial PW placement in patients easily coming off cardiopulmonary bypass with acceptable rate and no high-degree AV block prior to chest closure. As reported in Table 4, we found 304 (84.7%) patients had no ventricular epicardial PW inserted with 7 (2.3%) requiring nonurgent TV pacing secondary to transient high-degree AV block without hemodynamic compromise and only 3 (0.99%) requiring urgent TV pacing wire placement during the same hospitalization. All 3 patients requiring urgent TV pacing in the cohort with no ventricular epicardial PW had no evidence of conduction abnormalities on the preoperative ECG. In addition, all 3 had acceptable rate with no high-degree AV block intraoperatively. Of those 3 patients, 1 required PPM placement due to complete heart block on postoperative day 4 and the other 2 patients recovered with no need for PPM placement. Most patients will never require temporary pacing postoperatively and the chance of requiring urgent TV pacing is less than 1% in the absence of epicardial PW. Moreover, those who do require TV pacing typically recover their underlying rhythm soon after surgery. Therefore, routine placement of temporary epicardial PW is not required in patients with acceptable rate with no high-degree AV block intraoperatively.

Baseline conduction disturbances have been reported as a risk factor for new PPM following surgical AVR.²¹ Prevalence of new PPM implantation after surgical AVR is 3% to 6%, varying by the decade.^{22,23} In a retrospective study conducted at Cleveland Clinic that included 5,807 patients undergoing elective surgical AVR, 151 (2.6%) of patients required new PPM

Table 6. Postoperative Outcomes During the Index Admission.

Event	Number of patients (N = 359) n (%)
RTOR due to bleeding	16 (4.5)
PPM	15 (4.2)
Atrial fibrillation	26 (7.2)
Requiring cardioversion	6 (1.7)
Stroke	2 (0.6)
Acute renal failure	2 (0.6)
Requiring HD	1 (0.3)
Mortality	6 (1.7)

Abbreviations: HD, hemodialysis; PPM, permanent pacemaker; RTOR, return to operating room.

implantation following surgical AVR.²⁴ Our data summarized in Table 5 corroborate this finding. In the first 194 patients from 2015 to 2017, we found the rate of new PPM implantation to be 5% to 8% when we started minimally invasive AVR. However, in the last 165 patients, the rate of new PPM significantly dropped to less than 1% in 2018 and none with new PPM placement in 2019. The only patient in 2018 who required a new PPM secondary to complete heart block had a right bundle branch block preoperatively and required temporary epicardial ventricular PW intraoperatively due to AV block. Reflecting on the first group of 194 patients from 2015 to 2017, the rate of new PPM implantation appeared high and deliberate effort was made to minimize risk of conduction disturbances by placing sutures close to aortic side of the annulus. This resulted in significant reduction of new PPM in the second group of 165 patients in 2018 and 2019.

Limitations of this study include that it is a single-center study reflecting the practice of a single surgeon. It is also non-randomized and there may be bias regarding the placement of temporary epicardial PW. However, the study provides new information relative to use of temporary epicardial PW following isolated minimally invasive AVRs.

Conclusions

Temporary epicardial PW carry a small but significant safety risk, and complications should not be understated. Most patients will never require pacing and those who do typically recover their underlying rhythm soon after surgery. In the absence of epicardial ventricular lead insertion, the chance of requiring urgent TV pacing is less than 1%. Routine placement of temporary epicardial leads following mini-AVR is not required in patients with normal rate and acceptable AV conduction prior to chest closure.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Hossein Amirjamshidi, MD is a research fellow in the Peter A. Knight Fellowship Program at URMC, which is funded, in part, by LSI SOLUTIONS®. Courtney Vidovich, BSc is a medical student at University of Rochester with no financial disclosures. Peter A. Knight, MD is a professor of cardiac surgery at URMC with no financial disclosures for this work.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Outcomes of Florida Sleeve Procedure in Patients with Bicuspid Versus Tricuspid Aortic Valve

Innovations
2020, Vol. 15(4) 360–367
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DOI: [10.1177/1556984520938470](https://doi.org/10.1177/1556984520938470)
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Abstract

Objective: Outcomes of the Florida Sleeve (FS) procedure in patients with bicuspid aortic valve (BAV) have not been reported before. We compared outcomes of the FS procedure between patients with BAV and those with tricuspid aortic valve (TAV). **Methods:** From May 1, 2002 to January 1, 2016, 177 patients including 18 BAV and 159 TAV underwent the FS procedure. Baseline characteristics, perioperative outcomes, and echocardiographic measurements were compared between the 2 groups. Kaplan-Meier and life-table analyses were used to evaluate survival and freedom from reintervention rates. **Results:** Mean ± standard deviation age and aortic root diameter were comparable in BAV and TAV groups, 47.83 ± 11.19 versus 49.59 ± 15.79 years ($P = 0.55$) and 56.57 ± 6.18 versus 55.17 ± 8.84 mm ($P = 0.46$), respectively. The 30-day mortality and stroke rates were zero in the BAV group and 1.88% ($n = 3$) in the TAV group ($P = 1.00$). One patient (5.55%) in the BAV group and 8 (5.03%) patients in the TAV group needed permanent pacemaker implantation ($P = 0.62$). Freedom from reoperation was 93% in the BAV group and 99% in the TAV group at 8 years ($P = 0.041$). Patient survival rate was 100% in the BAV group and 91% in the TAV group at 8 years ($P = 0.42$). Freedom from aortic insufficiency greater than mild was 93% in the BAV group and 96.5% in the TAV group at 5 years ($P = 0.61$). **Conclusions:** This is the first study reporting outcomes of the FS procedure in patients with BAV. This technique is feasible, and the results appear to be durable when compared to patients with TAV.

Central Message

The Florida Sleeve procedure for valve-sparing aortic root replacement is safe and appears durable for management of aortic insufficiency secondary to aortic root dilation in both patients with bicuspid and tricuspid aortic valve.

Keywords

Florida Sleeve, bicuspid aortic valve, tricuspid aortic valve, valve-sparing technique

Introduction

Bicuspid aortic valve (BAV) is the most common congenital cardiac disease affecting 1% to 2% of general population.¹ It has been reported that 50% of these patients have aortic root, ascending aorta, or aortic arch aneurysm, which can lead to aortic insufficiency (AI) in young ages.² The Bentall aortic root and valve replacement is the gold standard approach for treatment of aortic root aneurysm associated with AI.³ However, aortic valve replacement (AVR) using a mechanical valve increases risk of anticoagulant-related hemorrhage, and AVR with bioprosthetic valve may require reoperation.⁴ Aortic valve-sparing (AVS) approaches (David and Yacoub) were suggested as appropriate alternatives for AVR that can preserve the patient's native valve and eliminate lifelong anticoagulant therapy.^{5,6} Mid-term

outcomes of patients with BAV who underwent the valve-sparing root reimplantation are equivalent to outcomes of those who

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*Presented at the Annual Scientific Meeting of the International Society for Minimally Invasive Cardiothoracic Surgery, May 29 to June 1, 2019, New York City, NY, USA.

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underwent AVR.⁷ However, a majority of centers still consider AVR as the first-line treatment option due to complexity of the AVS approaches.^{3,8} Adoption of the David and Yacoub procedures has been estimated as 15% in most centers.⁹ The UF Health (University of Florida, Gainesville, FL, USA) introduced the Florida Sleeve (FS) technique as a simplified approach that preserves the native aortic valve and improves valve function in patients with AI secondary to aortic root dilation.^{10,11}

Richardt et al. reported increased degree of AI following David procedure in patients with BAV.¹² On the other hand, Kari et al. found significant improvement of aortic valve function after the David procedure.¹³ However, there is no report regarding outcomes of the FS procedure in patients with BAV. In an earlier FS study by Hess et al., only 2 out of 18 patients had BAV.¹¹ Further, there are no data comparing outcomes of the FS procedure between patients with BAV and those with tricuspid aortic valve (TAV). To fill these gaps of knowledge, we compared early and long-term outcomes of the FS procedure between BAV and TAV patients.

Methods

Study Population

In this single-center retrospective cohort study, all patients with AI secondary to aortic root aneurysms who underwent the FS procedure were retrospectively reviewed. From May 1, 2002 to January 1, 2016, 177 patients underwent the FS procedure, of which 18 patients had BAV and 159 patients had TAV. The Institutional Review Board approved the study protocol and waived patient informed consent. However, we consented all patients who had the procedure after March 2006, which allowed us to gather patient survival status and clinical outcomes via primary care providers (PCPs) and cardiologists. Patients who met the following inclusion criteria were included: patients with type I AI secondary to aortic root aneurysm and those with normal or slightly abnormal leaflets. We excluded patients from the study and considered them for AVR if they had any of the following: previous aortic surgery, type II AI, and severely damaged, prolapsed, or nonfunctional aortic valve leaflets. Also, patients with very eccentric jets underwent a Bentall procedure.

Procedural Technique

Hess et al. have previously described details of the FS procedure.^{10,11} We used transesophageal echocardiography prior to cardiopulmonary bypass (CPB) to evaluate morphology of the aortic valve leaflets, presence of aortic valve prolapse, and dimensions of the aortic annulus and sinotubular junction. The ascending aorta was transected immediately above the sinotubular junction. We place 4 to 6 subannular mattress sutures in a similar horizontal level 2 to 3 mm below cusp insertion site. For patients with TAV, 3 sutures are placed at the nadir of each commissure, with additional sutures placed at the nadir of

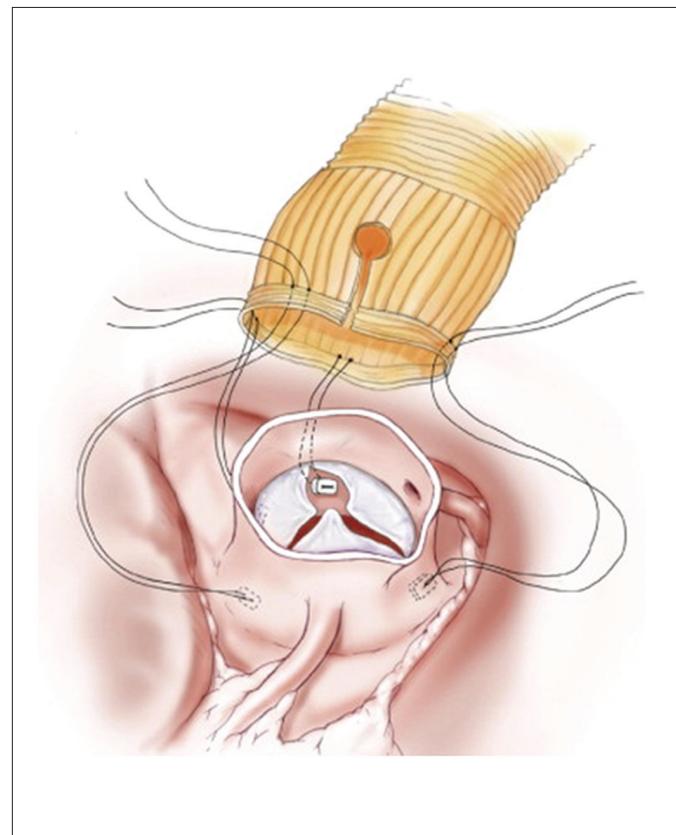


Fig. 1. The 4 subannular anchoring sutures are placed in the same horizontal plane, 2 to 3 mm below the lowest point of the center of the leaflets; 3 are in line with the commissures, and the fourth is placed under the noncoronary cusp. The left coronary artery keyhole is cut after the sleeve is temporarily seated. The slits in the graft below the coronary keyholes are repaired after the sleeve is seated. Figure reprinted from Aalaei-Andabili et al. in *Aorta* under a CC BY 4.0 license.²⁰

noncoronary cusp if additional annular reduction is desired for patients with a markedly dilated annulus in excess of 30 mm (Fig. 1). Patients with Sievers 0 BAV had 2 mattress sutures placed under each of the commissures and 2 other mattress sutures in opposite sides of each other in an equidistant position from the commissures. For patients with Sievers type 1 BAV, 3 mattress sutures are placed under each commissure, including under the region of the leaflet fusion. We used Hegar dilators (Jarit Instruments, Hawthorne, NY, USA) or valve sizers intraoperatively for annular sizing. Hegar dilators were used to directly measure the size of the annulus, with estimation that Valsalva graft would reduce the annulus approximately 5 to 7 mm from Valsalva graft size given 3 annular sutures. The target annulus diameter was 22 to 24 mm for women and 24 to 26 mm for men, with 32 or 34 mm Valsalva grafts most commonly chosen. Adequate leaflet coaptation and valve competence were considered as our clinical goal for sizing. The mattress sutures were delivered through the sleeve graft and tied down, while a presized Hegar dilator was placed through the graft into

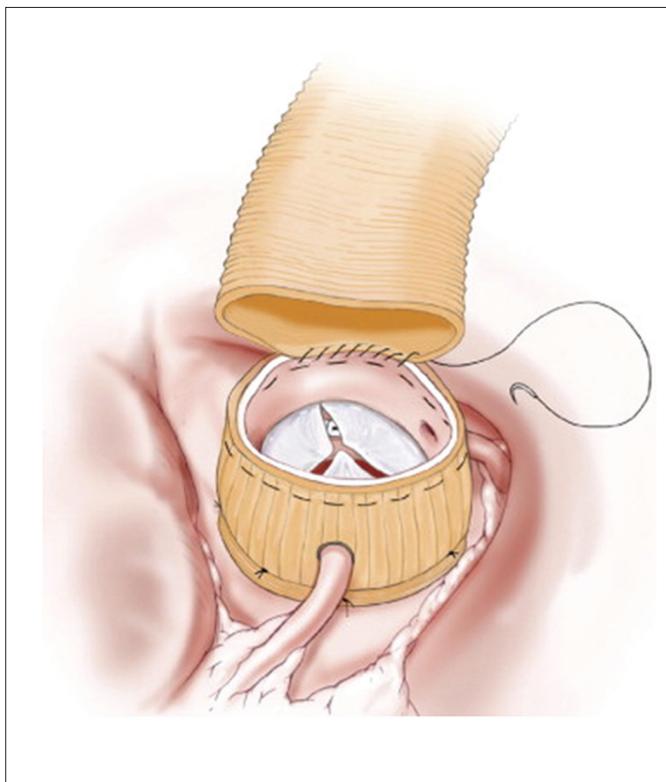


Fig. 2. The running horizontal mattress suture both suspends the aorta and orients the posts of the commissures. Redundant aortic wall at the sinotubular junction should be imbricated with small pleats using multiple, closely spaced bites of the running anastomotic suture. Figure reprinted from Aalaei-Andabili et al. in *Aorta* under a CC BY 4.0 license.²⁰

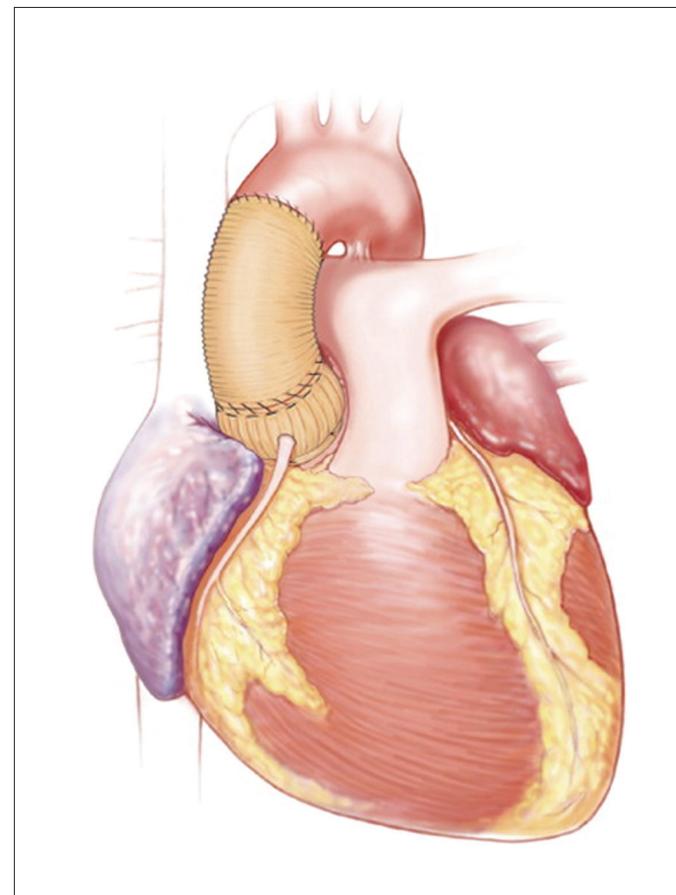


Fig. 3. Completed repair. Figure reprinted from Aalaei-Andabili et al. in *Aorta* under a CC BY 4.0 license.²⁰

the left ventricular outflow tract (LVOT) to prevent excessive narrowing of the annulus during suture tying. Following temporary placement of the sleeve graft, we marked coronary artery locations and made vertical slits to create coronary keyholes. When the sleeve graft was appropriately seated over the aortic root, we repaired the slits by simple sutures below the coronary arteries. Paying careful attention to the keyholes during the FS procedure is required to prevent coronary artery impingement. Intraoperative transthoracic echocardiography is also imperative to monitor ventricular function following the CPB. We sewed the sleeve graft at the sinotubular junction with a running horizontal mattress (Fig. 2). Finally, a smaller graft was used distal to the sleeve graft to reduce the sinotubular junction incorporating the aorta and the sleeve graft by a hemostatic running suture (Fig. 3).

Patient Outcomes

We defined our primary endpoints as procedural safety (early mortality and operation-related complications), freedom from reoperation, and long-term durability. The secondary endpoints chosen were improvement of aortic valve sufficiency and left ventricular dimensions compared to preoperative measurements.

Preoperative and postoperative echocardiography were used for this assessment. To compare perioperative and postoperative aortic valve and left ventricular functions, the following echocardiography measurements were used: left ventricular end-systolic diameter (LVEDD), left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), and AI that was graded as 0 = none, 1 = trace/minimal, 2 = mild, 3 = moderate, and 4 = severe. As a tertiary center, we did not have follow-up echocardiography measurements for all patients, because many of them had postoperative follow-up echocardiography at outside centers. However, we were able to call and send a fax to the PCPs and local cardiologists to gather additional follow-up data of patients who provided an informed consent (after March 2006). We collected patient survival status and need for reoperation using social security death index and our electronic medical record database (EPIC), respectively, and verified the data with patient PCPs or cardiologists to validate our findings.

Statistical Analysis

We present continuous variables as mean \pm standard deviation (SD) and categorical data as frequency and percentage. We used Student's *t*-test and Mann-Whitney *U*-test for parametric

and nonparametric comparison of the echocardiography measurements before and after the FS procedure. Categorical data were compared using χ^2 or Fisher's exact tests, as applicable. Kaplan-Meier method and life-table were employed to determine survival rates, freedom from reoperation, and freedom from significant AI. Differences in these rates between BAV and TAV groups were evaluated by the log-rank test. A P -value <0.05 (2-tailed) was considered statistically significant. All statistics were performed by SPSS Statistics, Version 24.0 (IBM Corp., Armonk, NY, USA).

Results

Patient Demographics

One hundred and seventy-seven patients, including 18 (10.16%) patients with BAV and 159 (89.83%) patients with TAV, were included. Patients in BAV and TAV groups underwent the FS procedure in a simultaneous timeframe. Thirteen (72.22%) patients in the BAV group and 115 (72.33%) patients in the TAV group were male ($P = 1.0$). Mean \pm SD age and aortic root diameter were comparable in the BAV and TAV groups, 47.83 ± 11.19 versus 49.59 ± 15.79 ($P = 0.55$) and 56.57 ± 6.18 versus 55.17 ± 8.84 ($P = 0.46$), respectively. All patients had their first aortic operation. Six patients in the BAV group had type 1 Sievers BAV and 1 patient had type 0. The Sievers classification was not available in 11 other patients. Nine (50%) patients in the BAV group and 114 (71.69%) patients in the TAV group had concomitant cardiac surgery with the FS procedure ($P = 0.1$). Hemi- or total aortic arch replacement was the most common simultaneous procedure in the BAV ($n = 7$, 38.88%) and the TAV ($n = 72$, 45.28%) groups ($P = 0.80$). The most common risk factor was hypertension in both groups, BAV = 10 (55.55%) and TAV = 83 (52.20%; $P = 0.80$). Preoperative LVEDD and LVESD were not significantly different between 2 groups, while the TAV group had higher mean \pm SD AI grade than the BAV group, 2.27 ± 1.25 versus 1.38 ± 1.38 ($P = 0.044$). There was no other significant difference in baseline characteristics between 2 groups (Table 1).

Early Outcome

Mean \pm SD CPB time was 163.31 ± 38.99 minutes in the BAV group and 182.63 ± 55.93 minutes in the TAV group ($P = 0.09$). Intensive care unit admission time was shorter in patients with BAV than those with TAV, 67.28 ± 52.23 versus 105.66 ± 109.88 hours ($P = 0.08$). Patients had similar length of hospital stay in both groups, 8.94 ± 5.36 days in the BAV group and 8.74 ± 5.71 days in the TAV group ($P = 0.88$). No patient died during hospitalization in the BAV group, but 3 (1.88%) patients died in the TAV group ($P = 1.0$). The 30-day mortality rate remained the same for both groups ($P = 1.0$). No patient developed stroke in the BAV group, whereas 3 (1.88%) patients had stroke in the TAV group ($P = 1.0$). No

Table 1. Patient Characteristics in Bicuspid and Tricuspid Groups.

Variable	Bicuspid group (n = 18)	Tricuspid group (n = 159)	P-value
Age (years)	47.83 ± 11.19	49.59 ± 15.79	0.55
Male	13 (72.22)	115 (72.33)	>0.99
Female	5 (27.77)	44 (27.67)	>0.99
Aortic diameter (mm)	56.57 ± 6.18	55.17 ± 8.84	0.46
LVESD (mm)	35.25 ± 3.30	36.89 ± 8.21	0.86
LVEDD (mm)	49.25 ± 2.21	53.73 ± 6.73	0.65
Ejection fraction (%)	55.20 ± 7.94	57.37 ± 7.15	0.83
Hypertension	10 (55.55)	83 (52.20)	0.80
Diabetes	1 (5.55)	11 (6.91)	>0.99
Prior stroke	2 (11.11)	7 (4.40)	0.22
Prior MI	0	1 (0.62)	>0.99
Prior CABG	0	3 (1.88)	>0.99
Type A dissection	1 (5.55)	15 (9.43)	>0.99

Abbreviations: CABG, coronary artery bypass graft; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; MI, myocardial infarction.

Data presented as mean \pm standard deviation or n (%).

postoperative endocarditis or myocardial infarction was detected in either groups. One (5.55%) patient in the BAV group and 2 (1.25%) patients in the TAV group needed reoperation secondary to bleeding ($P = 0.27$). One (5.55%) patient in the BAV group and 8 (5.03%) patients in the TAV group required permanent pacemaker implantation ($P = 0.62$). Three (16.66%) patients in the BAV group and 12 (7.54%) patients in the TAV group were readmitted within 30 days from the FS procedure due to upper respiratory infection symptoms ($n = 4$), atypical chest pain ($n = 4$), bacterial pneumonia ($n = 2$), atrial fibrillation with rapid ventricular repose ($n = 2$), wound infection/mediastinitis ($n = 1$), minor bleeding ($n = 1$), or mild pleural effusion ($n = 1$), but no intervention was required in either group ($P = 0.18$; Table 2).

At 30 days, 18 patients in the BAV group and 122 patients in the TAV group had follow-up echocardiography measurements. AI grade improved in both groups comparing to the baseline 1.24 ± 0.88 versus 2.29 ± 1.14 ($P < 0.001$) in the TAV group and 0.2 ± 0.42 versus 0.9 ± 1.1 ($P = 0.08$) in the BAV group. Interestingly, the BAV group had significantly lower AI grade comparing to the TAV group, 0.2 ± 0.42 versus 1.24 ± 0.88 ($P = 0.001$; Supplemental Fig. 1). However, the BAV group had lower preprocedural AI grade as well.

Improvement in LVESD was not significant at 30 days in the BAV group, 36.87 ± 8.27 versus 34.37 ± 8.48 ($P = 0.35$). Mean \pm SD LVEDD decreased from 49.25 ± 2.21 at baseline to 46.50 ± 5.45 at 30 days in the BAV patients ($P = 0.79$). No significant change in mean \pm SD ejection fraction was found from baseline to 30 days among patients with BAV, 56.50 ± 6.30 versus 53.50 ± 11.37 ($P = 0.27$). In the TAV group, improvement of LVESD was not significant at 30 days, 34.14 ± 8.49 versus 34.82 ± 9.07 ($P = 0.67$). Although improvement of LVEDD was significant at 30 days (52.58 ± 6.81 versus 46.93 ± 9.44 , $P = 0.001$), no

Table 2. Comparison of Outcomes Between Bicuspid and Tricuspid Aortic Valve Patients After the Florida Sleeve Procedure.

Variable	Bicuspid (n = 18)	Tricuspid (n = 159)	P-value
Concomitant cardiac surgery	9 (50)	114 (71.69)	0.10
Cardiopulmonary bypass time (minutes)	163.31 ± 38.99	182.63 ± 55.93	0.09
ICU hours	67.28 ± 52.23	105.66 ± 109.88	0.08
In-hospital MI	0	0	—
Postoperative endocarditis	0	0	—
In-hospital stroke/TIA	0	3 (1.88)	>0.99
Reintervention due to bleeding	1 (5.55)	2 (12.57)	0.27
Length of stay (days)	8.94 ± 5.36	8.74 ± 5.71	0.88
In-hospital death	0	3 (1.88)	>0.99
Readmission within 30 days	3 (16.66)	12 (7.54)	0.18
Reintervention in readmission	0	0	—
30-day mortality (after discharge)	0	0	—

Abbreviations: ICU, intensive care unit; MI, myocardial infarction; TIA, transient ischemic attack.

Data presented as mean ± standard deviation or n (%).

change in mean ± SD EF was found at 30 days (57.13 ± 6.52 versus 56.89 ± 9.46 , $P = 0.92$) in this group.

Long-Term Follow-Up

Mean ± SD follow-up time was 35 ± 35.73 months. One patient in the BAV group developed progressive eccentric AI with prolapse into the left ventricle and underwent AVR at 8 months, and 2 patients needed reoperation in the TAV group; one due to AI in the setting of degeneration of the aorta who needed transcatheter AVR at 30 months because of comorbidities and being very high risk for AVR, and another one secondary to pseudoaneurysm at 112 months ($P = 0.27$). Patients with BAV had slightly lower rate of freedom from reoperation versus patients with TAV at 8 years, 93% versus 99% ($P = 0.041$; Fig. 4). Patient survival rate was not significantly different between 2 groups at 8 years, 100% in the BAV group and 91% in the TAV group ($P = 0.42$; Fig. 5).

At 5 years, 3 patients had echocardiography follow-up in the BAV group and 28 patients in the TAV group. No patient had severe AI in either group and only 1 patient had moderate AI in the TAV group. Freedom from AI greater than mild was 93% in the BAV group and 96.5% in the TAV group at 5 years ($P = 0.61$). However, the number of patients in the BAV group was insufficient to draw a clinical conclusion. Two patients in the BAV group and 9 patients in the TAV group had 10 years echocardiography follow-up. Severe AI was not detected in either group and only 1 patient had moderate AI in the TAV group.

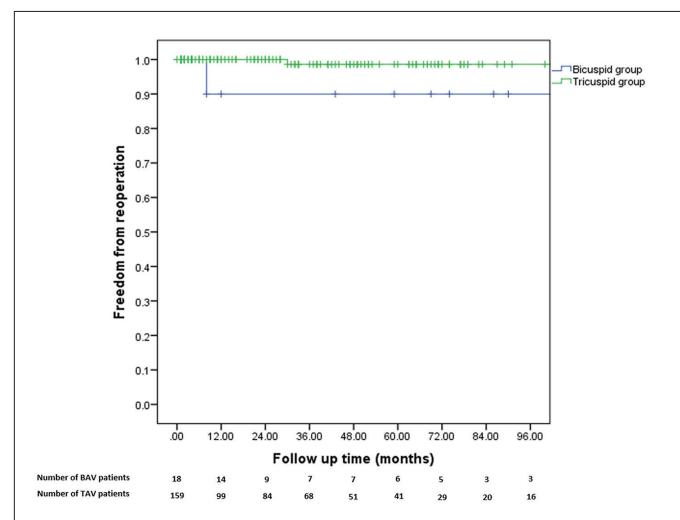


Fig. 4. Freedom from reoperation after the Florida Sleeve procedure in patients with BAV and TAV. BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

However, we did not have adequate number of patients to perform statistical analysis.

Discussion

This retrospective cohort study is the first study that compares outcomes of the FS procedure in patients with BAV and TAV. In-hospital and 30-day mortality rates were zero in the BAV group and less than 2% in the TAV group. We found that long-term survival rate is excellent following the FS procedure in both BAV and TAV groups. Both groups had acceptable long-term freedom from reoperation. Despite meaningful loss to

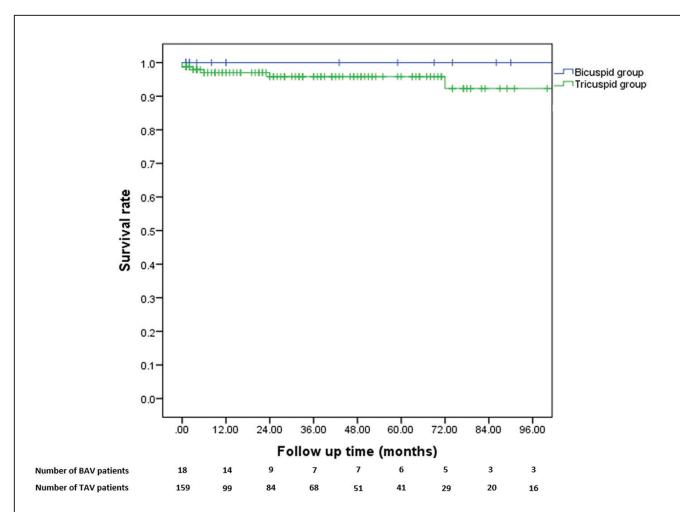


Fig. 5. Survival rate of patients with bicuspid and tricuspid aortic valve after the Florida Sleeve procedure. BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

follow-up of echocardiography measurements, we believe that our results are encouraging and conclude that the FS procedure is safe, effective, and appears to be durable for patients with BAV and TAV.

Schäfers and colleagues reported the first BAV repair with root remodeling technique and found no in-hospital mortality.¹⁴ In another study by Schäfers and coworkers, in-hospital mortality was estimated as 0.7% after AVS root replacement in patients with BAV.¹⁵ Later, the same group compared outcomes of AVS approaches between BAV and TAV patients; in-hospital mortality rate was estimated as zero in the BAV group and 6.2% in the TAV group.¹⁶ Similarly, early mortality rate was zero in our study among patients with BAV; however, we found 1.8% in-hospital mortality rate in our patients with TAV. Consistent with our study, Vallabhajosyula et al. also found zero mortality rate during hospitalization and at 30 days in patients with BAV following valve-sparing root reimplantation.⁷ Another study by Richardt and colleagues also reported zero early and late mortality rates after the David procedure.¹² Long-term survival rate of our patients with BAV was excellent (100%), which was slightly higher than the rate in patients with TAV at 8 years (91%). The Stanford group also reported comparable survival rate between BAV and TAV groups at 5 and 10 years.¹⁷ In contrast, in the study by Aicher and associates, BAV patient survival rate was significantly higher than the survival rate of those with TAV following previous AVS approaches at 5 years, 100% versus 82% ($P = 0.004$).¹⁶ In another study by Aicher and colleagues, 10-year survival rate was reported as 89%.¹⁸ Kari et al. employed the David reimplantation technique and found 99% survival rate at 6 years in patients with BAV.¹³ Similarly, 6-year survival was estimated at 98% following reimplantation technique in a report by Kerchove et al.¹⁹ These findings suggest that AVS approaches are feasible for patients with BAV, and we observed that outcomes for FS procedure in patients with BAV are not inferior to outcomes of patients with other AVS techniques or outcomes of those patients with TAV.

In this study, freedom from AVR was 93% in the BAV group and 99% in the TAV group at 8 years ($P = 0.04$). The patient in the BAV group who needed AVR had Sievers type 1 BAV with left-right fusion and redundant fused leaflet tissue requiring leaflet plication at the time of FS procedure. It would not be possible to prevent leaflet prolapse by orientation of FS placement. Appropriate graft sizing is important to achieve adequate annular reduction. Furthermore, tying subannular sutures down over an appropriate-sized Hegar dilator is important to avoid overly narrowing left ventricular outflow tract, and possibly inducing leaflet prolapse. This patient had no stenosis and trace insufficiency at time of FS procedure, but was performed early in FS experience and had recurrent valvular insufficiency due to leaflet degeneration. The patient in the TAV group who underwent AVR due to pseudoaneurysm had Marfan syndrome and had undergone FS aortic root reconstruction with ascending aorta replacement 9 years previously. He required reoperation for distal arch aneurysm to 7 cm as the main indication for reoperative surgery. He

was found at that time to have incidental small LV pseudoaneurysm from what appeared to be a subannular suture that had torn through the LVOT, requiring direct repair. This was performed leaving the FS repair intact, as this patient had excellent aortic valve function 9 years post FS procedure without insufficiency or stenosis. Although the difference in freedom from reoperation is statistically significant between the BAV and the TAV groups in our study, we cannot draw major conclusions due to the relatively small number of BAV patients, and a significant drop in freedom from reoperation can be accounted for by 1 patient requiring valve replacement early in our experience. Kvitting et al. compared outcomes of David procedure between BAV and TAV groups and did not find any significant difference in freedom from reoperation between 2 groups ($P = 0.17$).¹⁷ Similarly, Aicher and colleagues also compared freedom from reoperation between patients with BAV and TAV following AVS technique and found 98% freedom from reoperation at 5 years in both groups.¹⁶ Schäfers et al. included 16 patients with BAV in their first study and no patient required reoperation during follow-up.¹⁴ In another study by this group, freedom from AVR was reported to be 97% at 5 and 10 years after valve-preserving root replacement in patients with BAV.¹⁵ Vallabhajosyula et al. reported 100% freedom from aortic reoperation at 5 years.⁷ Consistently, Kerchove and associates also reported 100% freedom from aortic valve reoperation at 6 years following reimplantation technique. On the other hand, Kari et al. found 90% freedom from reoperation in patients with BAV 2.8 years after the David procedure.¹³ This rate was shown to be 89% at 10 years following root remodeling in a study by Aicher and associates.¹⁸ These findings suggest that reoperation rate after AVS techniques is not higher in BAV patients compared to patients with TAV. We only had 1 AVR among our patients with BAV and believe that the FS outcome is not inferior to previous AVS techniques. However, a larger study is warranted to confirm this speculation.

We did not find any severe AI at 5 and 10 years in either group. In a study by Schäfers and colleagues using remodeling (Yacoub) technique for patients with BAV, AI decreased after the procedure and no patient had AI greater than minimal at 1 year.¹⁴ Similar to our study, the degree of AI decreased in both BAV and TAV groups after the initial AVS approaches in the study by Aicher et al. However, they found higher rate of freedom from significant AI in the BAV group comparing to the TAV group, 96% versus 83% ($P = 0.07$).¹⁶ Interestingly, Kerchove et al. and Kari and coworkers found 100% freedom from AI greater than 2+ at 6 years in patients with BAV who had undergone AVS (reimplantation/David) procedure.^{13,19} In addition, Kerchove et al. found 95% freedom from AI greater than 1+ at 6 years among these patients.¹⁹ However, to conclude efficacy of the FS on improvement of aortic valve function in patients with BAV, a larger study with complete echocardiography follow-up is required.

In the present study, no postprocedural stroke was detected in the BAV group, though 3 (1.88%) patients developed stroke after the FS procedure in the TAV group. At least 2 other studies by Kari et al. and Vallabhajosyula et al. also found zero stroke rate

following root reimplantation in patients with BAV^{7,13}, whereas Kerchove and colleagues reported 4% stroke after the same AVS technique.¹⁹ No endocarditis was detected in our study, while Kvitting and coworkers found endocarditis in both BAV (1.58%) and TAV (0.6%) groups after the David procedure.¹⁷ Kari et al. also found late endocarditis in 1 patient who needed AVR at 8 months.¹³ However, Kerchove and coworkers and Schäfers et al. found no endocarditis following the AVS procedure.^{15,19} It was suggested that AVS techniques can minimize risk of postoperative endocarditis, and the results above are consistent with this suggestion.¹⁶ We also believe that the operative complications following the FS procedure are not higher than other AVS techniques in patients with BAV or in those with TAV.

As patients with BAV are more prone to accelerated rates of leaflet or annular calcification when compared to trileaflet valves, so long as there is annular or leaflet calcification there are no additional technical considerations for late transcatheter options beyond the usual considerations that apply to TAVR in BAV patients such as coronary height, aortic root dimensions, significant, bulky calcification, and concern for paravalvular leak. The presence of an FS in the past should not preclude performance of TAVR intervention to the valve if there is appropriate calcification and the usual anatomic considerations are deemed suitable. If, on the other hand, the valve fails with insufficiency in the absence of any calcification, transcatheter options would not be recommended with commercially available devices although with evolution of technology this may be applicable in the future. The presence of the Dacron material at the level of the annulus would theoretically provide similar level of annular support as that seen in a David valve-sparing root replacement.

Study Limitations

We acknowledge the following limitations in our study: 1) a retrospective study design, 2) small number of patients in the BAV group, 3) losses to follow-up of echocardiography measurements, 4) missed data regarding the Sievers classification and not being able to obtain computed tomography images because some operations were performed before initiation of electronic medical record system.

Conclusions

The FS procedure is safe and appears to be durable for management of AI secondary to aortic root dilation in both patients with BAV and TAV. Although aortic valve function meaningfully improved following the FS procedure in the TAV and BAV groups, a larger number of patients will be necessary to definitively conclude efficacy of the FS procedure in patients with BAV.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Supplemental Material

Supplemental material for this article is available online.

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Simple Technique for Central Venous Cannulation with Cannula-Free Wound in Minimally Invasive Aortic Valve Surgery

Innovations
2020, Vol. 15(4) 368–370
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DOI: [10.1177/1556984520925549](https://doi.org/10.1177/1556984520925549)
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Abstract

There are several approaches to venous cannulation in minimally invasive aortic valve surgery. Frequently used options include central dual-stage right atrial cannulation, or peripheral femoral venous cannulation. During minimally invasive aortic surgery via an upper hemisternotomy, central venous cannulas may obstruct the surgeon's visualization of the aortic valve and root, or require extension of the skin incision, while femoral venous cannulation requires an additional incision, time and resources. Here we describe a technique for central venous cannulation during minimally invasive aortic surgery, utilizing a novel device, to facilitate simple, convenient, and expedient central cannulation with a cannula-free surgical working space.

Keywords

minimally invasive cardiac surgery, central venous cannulation

Central Message

Our novel device provides simple, convenient, and fast central venous cannulation in minimally invasive aortic surgery with excellent exposure of the aortic root.

Introduction

We present the use of an original medical device to perform central venous cannulation and achieve a cannula-free surgical wound during minimally invasive aortic surgery via an upper hemisternotomy.

completed in routine fashion, and after decannulation, this fifth or sixth intercostal incision site is used for chest tube placement.

Discussion

Current options for venous cannulation during minimally invasive aortic surgery include central right atrial and peripheral

Surgical Technique

Upper partial sternotomy is performed as usual. The pericardium is opened and secured with stay sutures to the skin. Central aortic cannulation is performed in standard fashion. A polypropylene purse-string suture is applied to the right auricle and a dual-stage venous cannula with a 3/8" connection site (Medtronic Inc., Minneapolis, MN, USA) is inserted to the right atrium and inferior vena cava. Hereafter, our novel device (Fig. 1, PTO Medtechnika Ltd., Kazan, Russia, Patent No. RU185713U1) is connected to the back end of the venous cannula (Fig. 2), and a strong (ex: 2–0 silk) suture is sewn through the eyelet on the distal tip of the device. A 1 to 2 cm incision is performed in the fifth or sixth intercostal space. Using a clamp, the previous suture, novel cannulation device, and venous cannula are collectively guided through this incision, and externalized from the chest (Fig. 3, Supplemental Video). The remainder of the planned operation is

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*Presented at the 2019 ISMICS Annual Scientific Meeting, 29 May–1 June 2019, New York, NY, USA.

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Fig. 1. Ex vivo high-resolution image depicting the novel cannulation adjunct, with a distal suture eyelet, curved taper configuration, and proximal portion configured to fit within a conventional 3/8" venous drainage cannula.

femoral venous cannulation, each with unique limitations. Central venous cannulation during an upper hemisternotomy may require a wider skin incision, and is less convenient for the surgeon if the relatively large venous cannula in any way obscures visualization through a minimal-access incision with reduced working space. On the other hand, peripheral venous cannulation requires additional incisions, time, and resources, and may be accompanied by unique risks including cardiac injury during cannula advancement, as well as local access site complications in up to 6.6% to 10.8% of cases.^{1,2} Peripheral (open or percutaneous) femoral venous cannulation may also require additional cannulation of the right atrium or superior vena cava due to inadequate venous return in some patients.³ Additionally, both open and percutaneous femoral venous cannulations require skilled transesophageal echocardiographic guidance during cannula advancement which may not be routinely available in some centers.

While other surgeons have reported tunneling of the central venous cannula in order to make the surgical wound cannula-free, a reproducible method of cannula tunneling has not been described in the detail.⁴ In our early experience using other described techniques for subcutaneous cannula tunneling, hematoma formation along the subcutaneous tunnel has proved a common limiting factor. In addition, passing the cannula through the subcutaneous tissue leads to contamination of the inner surface of the cannula with fat, so it has to be cleaned prior to circuit connection. Moreover, the exposure of the aortic root may be suboptimal due to a relatively

anterior course of cannula tunneling. These factors led us to conceive and introduce an adjunct medical device to guide the cannula through an intercostal space. With our technique the cannula and right atrial appendage take a more caudal course, which improves the exposure of the aortic root dramatically. Other methods for caudally directed venous tunneling, using a combination of tubes for cannula guidance, have been described,⁵ though we would surmise that our presented technique represents the most simplified and reproducible method to date.

Conclusions

Our presented technique utilizing a novel device during central venous cannulation provides simple, convenient, and fast central venous cannulation in minimally invasive aortic surgery with excellent exposure of the aortic root.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: VIK – Inventor of the device presented, but holds no financial relationship with the manufacturer. The device presented is under patent (Patent No. RU185713U1, 2018). APN, AVM, IAA, SYB – Nothing to disclose. TCN – Abbott – Consultant, Edwards LifeSciences – Consultant, LivaNova – Consultant.

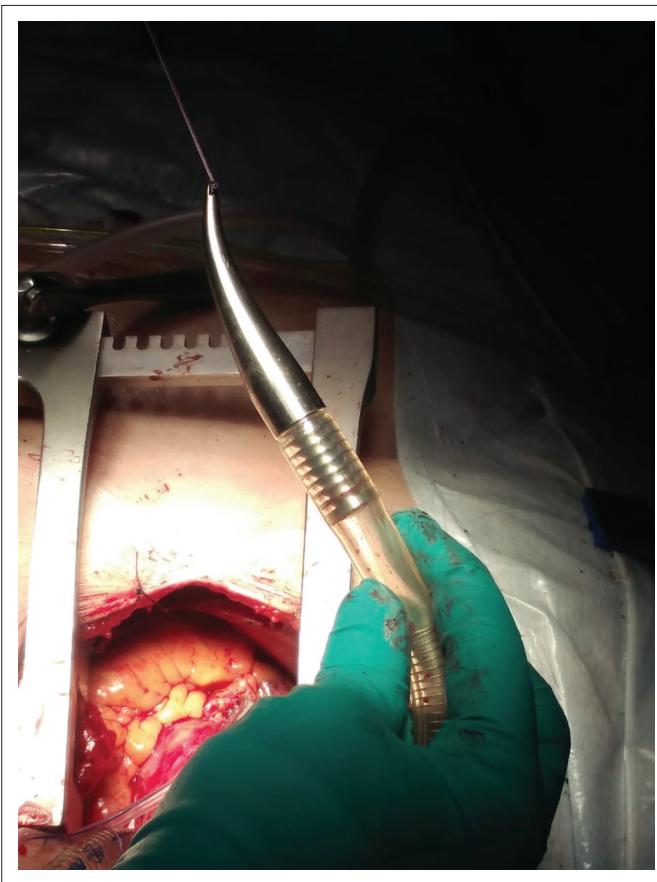


Fig. 2. Novel cannulation adjunct with proximal end secured into 3/8" venous drainage cannula, and suture secured through distal eyelet. Ready for creation of separate incision and cannula passage.

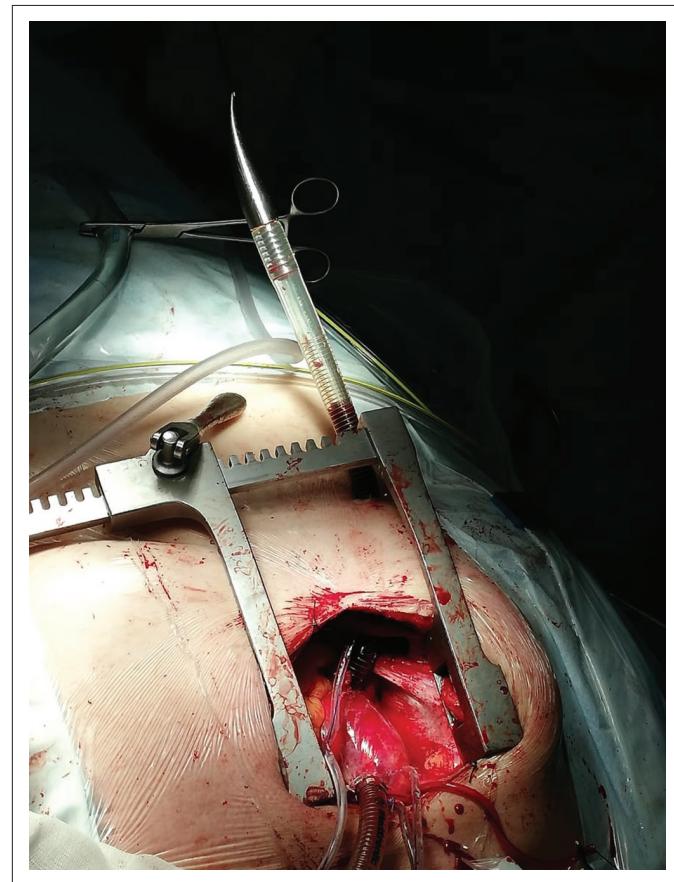


Fig. 3. The venous cannula, using the novel device, has been safely passed through a separate sixth intercostal space incision, which will later be used for chest tube placement at case conclusion.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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Adult Ventricular Septal Defect Repair Using a Robotic Totally Endoscopic Approach: A Case Report

Innovations
2020, Vol. 15(4) 371–374
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DOI: 10.1177/1556984520922978
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Abstract

The growth and advancement of minimally invasive cardiac surgery in recent years has allowed robotic and totally endoscopic procedures to become safe and effective options for the treatment of patients with various diseases of the heart. However, despite these advances, outcome data for robotic correction of congenital cardiac anomalies are scarce. This is particularly true for robotic ventricular septal defect (VSD) repair with initial experiences only recently having been published by a single group. Here, we present the case of a 29-year-old female who underwent robotic totally endoscopic VSD repair due to persistent symptoms with resolution of preoperative shunting and severe tricuspid regurgitation following surgery. This unique case adds to the limited data currently available in the literature on robotic VSD repair to show that it is a safe procedure when performed by a dedicated surgical team experienced in minimally invasive robotic cardiac surgery. We feel that, in this setting, the benefits of a robotic surgical approach can be afforded to more patients with excellent results.

Keywords

ventricular septal defect, congenital cardiac surgery, repair, endoscopic, robotic surgery

Introduction

In recent years, advances in robotic instrumentation and dedication of select surgeons and institutions have allowed for significant leaps to be made in the field of minimally invasive robotic cardiac surgery. These advancements have extended into the treatment of cardiac congenital anomalies as well, allowing for procedures such as endoscopic robotic atrial septal defect (ASD) closure, endoscopic removal of dislocated Amplatzer devices, closure of patent ductus arteriosus, and division of vascular rings.¹ Despite these advances, outcome data for robotic correction of congenital cardiac anomalies are scarce.¹ This is particularly true for robotic ventricular septal defect (VSD) repair, with initial experiences only recently having been published by a single group.^{2,3} Here, we present the case of a 29-year-old female who underwent robotic totally endoscopic VSD repair due to persistent symptoms with resolution of preoperative shunting and severe tricuspid regurgitation (TR) following surgery.

Case Report

A 29-year-old female with a past medical history significant for sickle cell trait and gastroesophageal reflux disease presented

for robotic closure of a restrictive membranous VSD diagnosed and monitored since birth. She had been mostly asymptomatic aside from maternal pulmonary hypertension during her 4 term pregnancies, and had ignored prior recommendations to have a VSD repair. She reported worsening fatigue, lightheadedness, and syncope for the past 2 years with intermittent midsternal chest pain and palpitations at rest or with activity for several months. Physical examination was positive for a 3/6 murmur. Of note, recent transthoracic echocardiography had also shown severe TR.

Transesophageal echocardiography (TEE) was obtained, showing myxomatous degeneration of the tricuspid valve with severe regurgitation (Fig. 1a). The VSD was measured at 0.52 cm in its largest dimension and severe left-to-right

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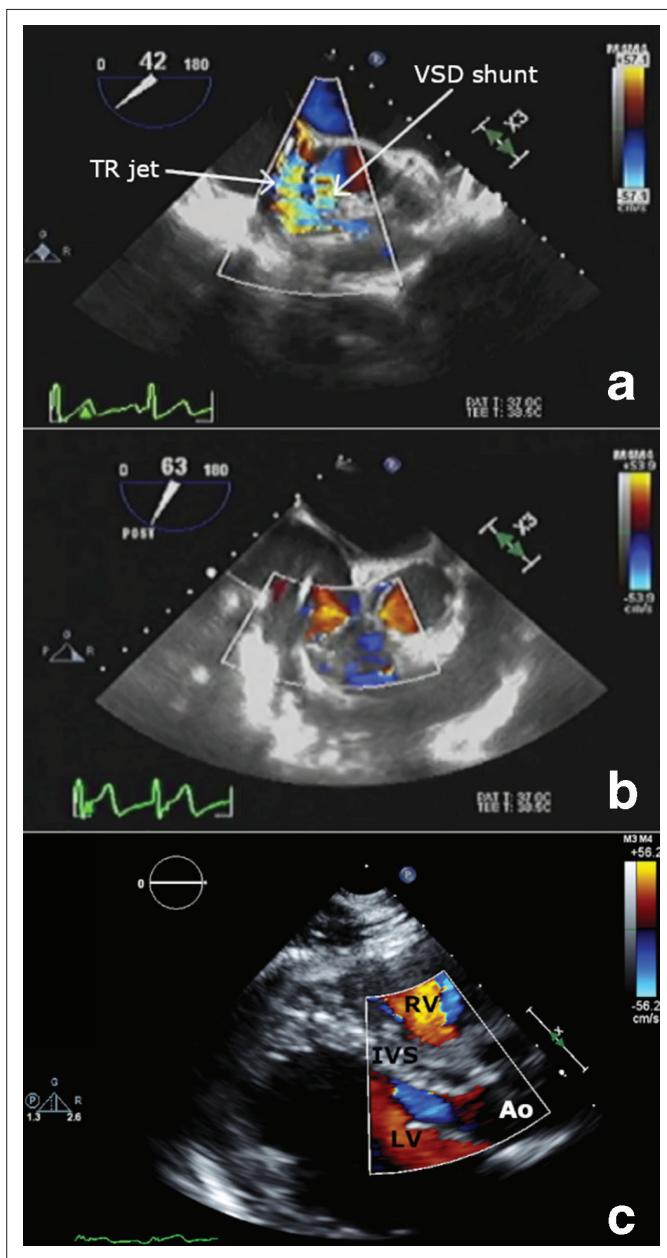


Fig. 1. Resolution of ventriculoseptal shunt and TR was seen on comparison of preoperative (a) to postoperative (b) transesophageal echocardiography. Predischarge transthoracic echocardiography further confirmed complete resolution of the shunt with no residual TR (c) Ao, aorta; IVS, interventricular septum; LV, left ventricle; RV, right ventricle; TR, tricuspid regurgitation; VSD, ventricular septal defect.

shunting was seen with a maximal velocity of 502.3 cm/s across, consistent with a systolic pressure gradient of 101 mmHg. Right ventricular size and function were normal. Right heart catheterization showed no pulmonary hypertension but a significant left-to-right shunt was further confirmed with Qp/Qs of 1.7. Coronary angiography revealed normal coronary arteries. Based on the diagnostic findings and patient symptomatology, she was considered for elective

totally endoscopic robotic-assisted VSD closure and tricuspid valve repair.

The patient tolerated the procedure well with resolution of the VSD shunt and TR on postoperative echocardiography (Fig. 1b, Fig. 1c). The resolution of TR and the lack of tricuspid valve annulus dilation indicated leaflet/chordae scarring and VSD shunting as the likely cause of TR prior to the repair. Before discharge, the patient had an episode of fainting and was found to be bradycardic. Electrophysiology (EP) studies showed paroxysmal infra-Hisian heart block (unrelated to the atrioventricular node or site of surgery), and a permanent pacemaker was implanted. The patient was discharged on postoperative day 7 following normal pacemaker interrogation with stable parameters. One- and 3-month postoperative visits showed minimal ventricular pacing with normal sinus rhythm (NSR). She reported resolution of her preoperative symptoms.

Surgical Technique

The procedure was performed using the da Vinci Si robotic system (Intuitive Surgical Inc., Sunnyvale, CA, United States) with right femoral-femoral cannulation and the endo-aortic occlusion balloon (IntraClude, Edwards Lifesciences, Irvine, CA, United States) for cardiac arrest. Robotic ports were placed in the right chest using a 20-mm nonrib spreading working port in the fourth intercostal space (Fig. 2). The patient was fully heparinized and cannulated, bicaval drainage was established (with a superior vena cava cannula via the right internal jugular vein), and the endo-balloon was positioned with the tip in the ascending aorta. Cardiopulmonary bypass was instituted and the da Vinci robot was docked. After the lungs were deflated, the pericardium was opened and stay sutures were applied. The inferior and superior vena cavae were encircled with silastic snares for right atrial isolation. The endo-balloon was inflated and carefully positioned in the middle of the ascending aorta and the heart was arrested with 1L of del Nido cardioplegia solution.

A right atriotomy was performed and the dynamic atrial retractor was inserted. Using the 30° down scope, the septal leaflet of the tricuspid valve was visualized and detached. There was significant scarring in the area of the VSD with involvement of the leaflet and chordae on the anterior half of the septal leaflet. Following detachment of the base of the anterior portion of the tricuspid septal leaflet, entrance of the VSD toward the left ventricle was nicely visualized underneath the aortic valve with a 30° down scope positioned in the right ventricle (Fig. 3a). The edges of the defect were of good quality such that primary repair was felt to be appropriate. Thus, it was repaired primarily through the detached tricuspid valve using 4-0 Prolene sutures immediately underneath the aortic valve, taking care not to disrupt the aortic valve anatomy (Fig. 3b). The atrioventricular junction was then repaired with 3 interrupted figure-of-eight 4-0 Prolene sutures. The tricuspid valve leaflet was then reattached to the annulus with interrupted Prolene sutures (Supplemental Video). After this was completed, the tricuspid valve was tested and felt to be competent using the water test.

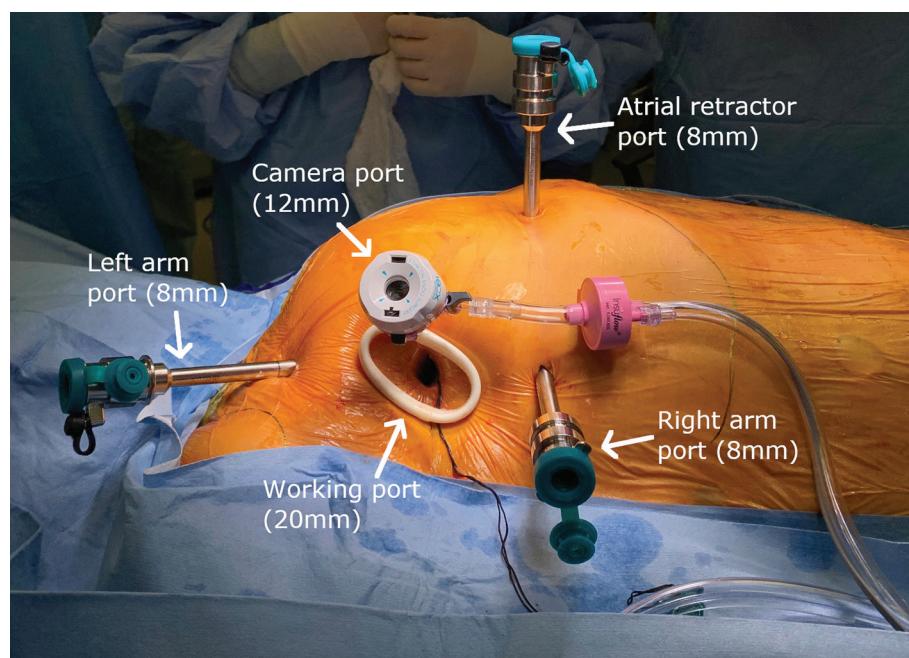


Fig. 2. Robotic port position in the right chest.

The patient was rewarmed and the right atriotomy was closed with a running 4-0 Prolene suture. The endo-balloon was deflated, temporary pacing wires were placed on the right ventricle and the right atrium, and ventricular pacing was commenced. Sinus rhythm eventually resumed. A drain was advanced into the pericardial space and the pericardium was loosely closed. The chest was irrigated, robotic instruments were removed, and lung ventilation was resumed. The patient came off of pump readily on no inotropic support and in sinus rhythm. The postprocedure TEE revealed complete resolution of the ventriculoseptal shunt with no residual TR (Fig. 1b).³

Discussion

Ventricular septal defect is a common congenital heart defect at birth, often associated with other heart defects or conditions. Congenital VSDs are less common in adults due to spontaneous closure in most cases, however, VSDs can also be acquired from acute myocardial infarction or following surgical or interventional procedures in the heart.^{4–6} Clinical presentation of VSDs is dependent upon their size and shunt severity. Indications for VSD closure include hemodynamically significant shunt, significant or worsening aortic regurgitation, and history of endocarditis.⁷

Median sternotomy is the traditional approach for VSD closure. However, despite its excellent results, patients tend to be reluctant to undergo the surgery due to its invasiveness, including a large scar, risks of bleeding and infection, and longer recovery time.³ This was evident in our patient who had refused prior recommendations to have surgery. In recent years, the increasing prevalence of minimally invasive cardiac surgery has provided new options for the treatment of

both acquired and congenital cardiac conditions. Additionally, the development of the da Vinci robotic system has helped overcome many limitations of videoscopic surgery with reports showing totally endoscopic procedures to be a safe and effective method with fewer blood transfusions, shorter hospital stays, faster recovery, and improved quality of life compared to those undergoing a sternotomy.^{8,9}

Although robotic ASD closure in adults has already been established, totally endoscopic robotic VSD repair has only been reported by Gao et al. in 2010 and 2012 where they performed successful VSD closure in 3 and 20 patients, respectively, with no conversions or major complications.^{2,3} As highlighted in their report, complete exposure of the VSD in the surgical field is a critical part of this operation.³ A unique and technically challenging aspect of the operation in our case was the need to visualize the defect from the left ventricle due to significant scarring of the chordae on the anterior half of the septal tricuspid valve leaflet. Once optimal exposure is ensured, closure of the defect can be achieved via direct suture for smaller defects, as in our case, and a patch for larger defects.³ In regard to the arrhythmia we encountered, injury to the conduction system is a widely recognized complication of VSD repair, leading to early complete heart block in 0.7% to 3% of patients.¹⁰ In our patient, however, EP studies showed that the origin of her heart block was in the infra-Hisian area, and given that she came off of pump in sinus rhythm and had minimal ventricular pacing with NSR on follow-up visits, we conclude that this was a transient heart block unrelated to her surgery.

The robotic approach is a natural progression for minimally invasive cardiac surgery to further reduce collateral

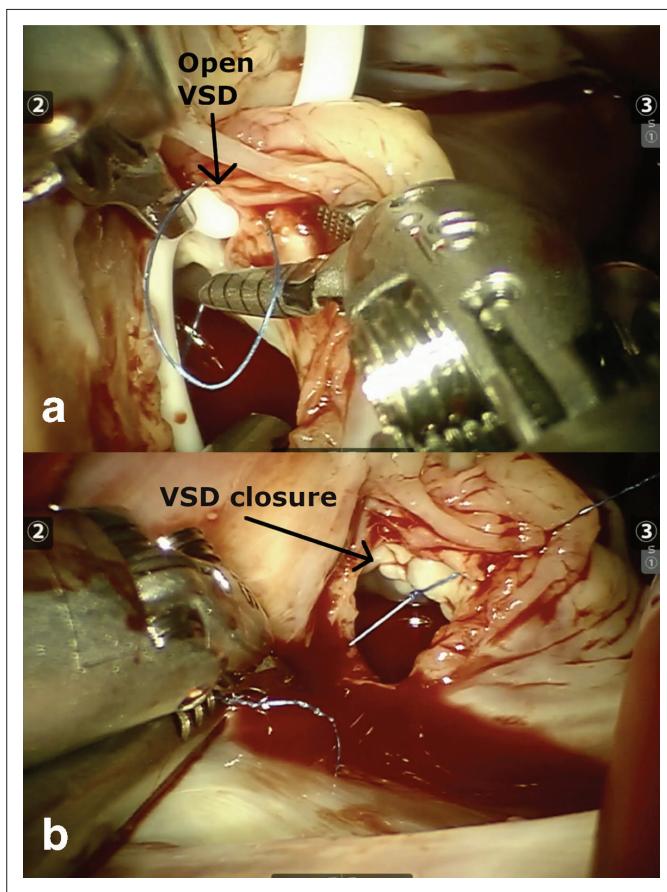


Fig. 3. Following detachment of the base of the anterior portion of the tricuspid septal leaflet, entrance was inadvertently gained into the left ventricle. Using a 30° down scope positioned in the right ventricle, the membranous VSD was visualized immediately underneath the aortic valve (white probe is seen traversing the VSD) (a). The defect was repaired primarily using 4-0 Prolene sutures (b). VSD, ventricular septal defect.

surgical trauma while maintaining excellent outcomes.⁸ With robotic mitral valve surgery and total endoscopic coronary artery bypass surgery having become standardized procedures at our center, we have expanded our indications to other cardiac procedures in various stages of evolution, including robotic aortic valve surgery and pericardectomy.^{11,12} Our unique case adds to the limited data currently available in the literature on totally endoscopic robotic VSD repair to show that it is a safe procedure when performed by a dedicated surgical team experienced in minimally invasive robotic cardiac surgery. We feel that, in this setting, the benefits of a robotic surgical approach can be afforded to more patients with excellent results.

Acknowledgments

We thank Ilya Karagodin, MD (Section of Cardiology, Department of Medicine, University of Chicago Medicine, Chicago, IL, USA) for assistance in obtaining and preparing echocardiographic images.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Balkhy discloses that he is a proctor for Intuitive Surgical, which is the manufacturer of the da Vinci robot.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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Two-Stage Redo Aortic Arch Repair in a Patient With an Isolated Left Vertebral Artery

Innovations
2020, Vol. 15(4) 375–377
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DOI: 10.1177/1556984520922985
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Hidetake Kawajiri¹, MD, Mohammad A. Khasawneh², MBBS, Thomas C. Bower², MD, and Gabor Bagameri¹, MD

Abstract

A 47-year-old male presented with an enlarging distal aortic arch false lumen 6 months status post ascending and hemiarch replacement with antegrade endograft insertion for acute type A aortic dissection complicated by lower body malperfusion. Preoperative computed tomographic angiography showed an isolated but dominant left vertebral artery. A 2-stage open surgical repair was performed. First, the left subclavian artery was transposed on the common carotid and vertebral onto the subclavian. At the second stage, a redo total arch reconstruction was done with bypass grafts taken to the innominate and left common carotid arteries. The patient did well postoperatively.

Keywords

isolated vertebral artery, total arch replacement, staged repair

Introduction

Direct origin of the left vertebral artery (LVA) from the aortic arch is the second most common arch vessel anomaly, with a prevalence of $\leq 6\%$ in patients with thoracic aortic disease, as described by Dumfarth et al.¹ Reconstruction of the left subclavian artery (LSA) and the left anomalous vertebral artery is a challenge with aortic arch surgery, particularly a redo reconstruction. Herein, we present a case of a 2-stage aortic arch repair that was simplified by performing LSA and LVA transpositions before redo sternotomy and total arch reconstruction.

Case Report

A 47-year-old male underwent ascending and hemiarch replacement with antegrade endograft insertion for acute type A aortic dissection which had caused lower body malperfusion. Follow-up computed tomography (CT) at 6 months showed aneurysmal false lumen enlargement of the distal arch caused by a type 1a endoleak. Figure 1a shows the image 1 week after the procedure. Figure 1b and Figure 1c show the sagittal and 3D CT images at 6 months. The LVA originated directly from the aortic arch. None of the supra-aortic trunks exhibited dissection. Head and neck computed tomographic angiography (CTA) showed the LVA to be dominant. There was communication between the posterior cerebral and middle cerebral arteries. A 2-stage repair was planned to ensure revascularization of

the left subclavian vertebral arteries and to simplify the redo aortic arch reconstruction.

First Stage: LVA and LSA Transposition to the Left Common Carotid Artery (LCCA)

Electroencephalographic monitoring (EEG) was utilized. A 6-cm left supraclavicular incision was made between the heads of the sternocleidomastoid muscle. The left carotid artery was dissected free taking care to protect the vagus nerve. The subclavian artery was freed from beneath the sternum to the origin of the left internal mammary artery. The LVA was dissected free from beneath the sternum to the longus colli muscle. The systolic blood pressure was lowered to 90 to 95 mmHg. After systemic heparinization, the subclavian artery was clamped proximal to the left internal mammary artery origin. The proximal subclavian artery was transected and oversewn with a double layer of 4-0 Prolene suture buttressed with felt strips. The mean arterial blood pressure was

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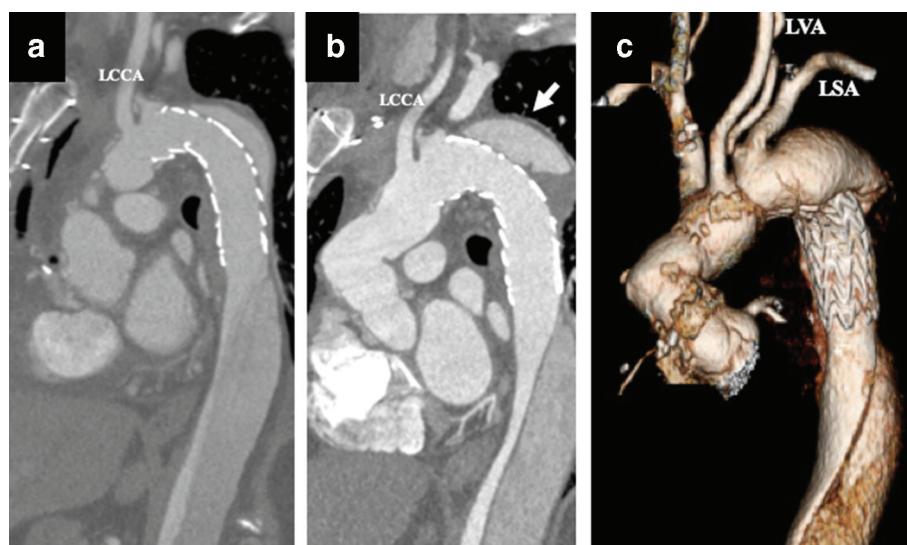


Fig. 1. (a) CT image, 1 week after the procedure (false lumen is patent, diameter at the distal arch is 40 mm). (b) and (c) Sagittal and three-dimensional reconstruction of the aortic arch showing false lumen enlargement of the distal arch (arrow, 7 mm increase over 6 months), which was caused by a type Ia endoleak. CT, computed tomography; LCCA, left common carotid artery; LSA, left subclavian artery; LVA, left vertebral artery.

increased to 90 to 100 mmHg. The carotid artery was clamped and an arteriotomy made on the posterolateral wall. The subclavian artery was transposed onto the carotid end-to-side using 6-0 polypropylene sutures. Subsequently, the LVA was transected and sewn onto the proximal, superior LSA in a similar fashion. There were no EEG changes during the procedure, an intraoperative duplex ultrasound scan showed the transposed LSA and LVA to be widely patent.

Second Stage: Aortic Arch Repair With 2-Vessel Debranching

Redo arch reconstruction was performed the following day. After adhesiolysis, the patient was put on cardiopulmonary bypass and cooled down. The aorta was opened and trimmed under hypothermic circulatory arrest once the EEG flattened, with a bladder temperature of 19°C. Selective antegrade cerebral perfusion catheters were inserted into the innominate artery and left common carotid artery (LCCA). Then, a 26-mm Sienna multicollared graft (Vascutek, Inchinnan, United Kingdom) was brought to the field. The collar was cut to the appropriate diameter, and a 5-cm elephant trunk portion was invaginated into the previous endograft. End-to-end anastomosis with running 3-0 Prolene sutures was performed between the collar of the Dacron graft and proximal end of the aorta to terminate the type 1a endoleak chamber. Branches of the Sienna graft were used to reconstruct the innominate artery and LCCA. During the rewarming period, the right internal thoracic artery was connected in situ to the previous saphenous vein graft to the right coronary artery. The patient recovered without any complications. Postoperative CT revealed a fixed proximal edge of the endograft and patent left vertebral and subclavian arteries (Fig. 2a, Fig. 2b).

Discussion

Ascending and hemiarch reconstruction with antegrade thoracic endovascular aortic repair (TEVAR) for acute type A aortic dissection is used to manage lower body malperfusion, and early outcomes have been acceptable.² Compared to total arch repair with a frozen elephant trunk, late reintervention may be required because the proximal endograft edge is not completely sewn circumferentially to the aorta, which leads to an endoleak and aneurysmal enlargement of the false lumen. Such was the problem in this case aneurysm 6 months after the initial repair. Moreover, the redo repair was complicated by direct origin of the LVA from the aneurysmal aortic arch.

Several hybrid and endovascular approaches have been described to avoid redo sternotomy in these circumstances. Options include extension of the stent graft into zone 1 combined with cervical debranching, or 1 or 2 branched aortic arch endovascular devices together with cervical bypass. Chimney techniques can also be considered. However, we did not feel that any of these were good alternative in the present case because the patient was relatively young, the LVA was dominant and originated from the arch, and there was not a good landing zone for a stent graft into the short ascending aortic graft with kink in the anastomotic site (as shown in Fig. 1b).

Regarding open repair, distal arch and descending aortic repair through a posterolateral thoracotomy seems promising. Although, proximal aortic anastomosis has to be performed right distally to the innominate artery, which requires the management of 3 arch vessels (LVA, left carotid artery, and LSA reconstruction) and can be extremely challenging. Thus, a 2-stage approach was felt best to preserve the left vertebral,

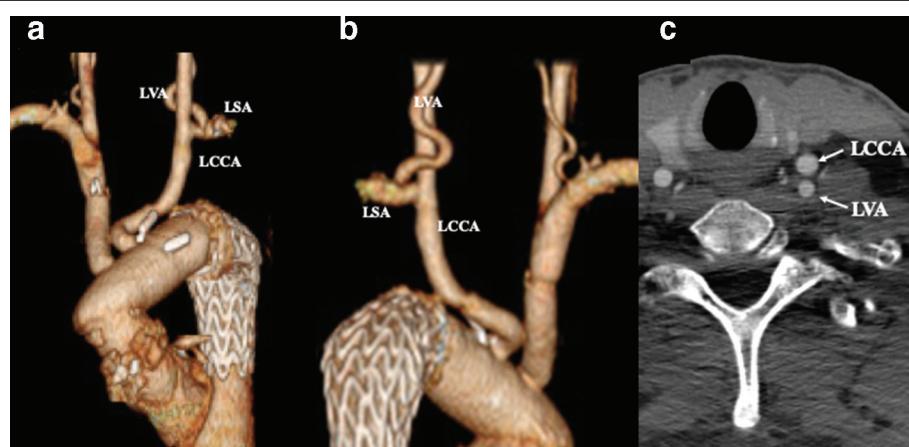


Fig. 2. (a) Postoperative CT image. (b) The proximal edge of the endograft was fixed and arch branches were patent. (c) CT image of the neck vessels showing the large LVA passing posterior to the LCCA. CT, computed tomography; LCCA, left common carotid artery; LSA, left subclavian artery; LVA, left vertebral artery.

simplify a redo total arch reconstruction, and provide a durable repair.

The vertebral arteries join to form the basilar artery and supply blood to the cerebellum and brain stem. We believe that it is important to obtain a CTA of the head and neck prior to aortic arch repair when the left vertebral arises directly from the aortic arch. The CTA will show if one vertebral artery is dominant, if the vertebral arteries join to form the basilar artery or end in a posterior inferior cerebellar artery (PICA; Fig. 2c). We favor preservation of the dominant vertebral, and any vertebral that ends in a PICA to avoid posterior circulation ischemia.³ Our preference for left subclavian reconstruction in cases such as this one is transposition of the artery onto the carotid. This technique preserves the vertebral artery in patients with normal anatomy, has outstanding mid-long-term patency,⁴ and avoids the prosthetic of a carotid to subclavian artery bypass. In the present case, the left vertebral was transposed onto the proximal subclavian, which simplified the subsequent arch and supra-aortic trunk repair.

Several studies have reported total arch replacement in patients with an isolated vertebral artery,^{5–7} where the vertebral artery was reimplanted onto the aortic graft or the LSA graft limb. Cerebral protection during circulatory arrest is critical, particularly the posterior circulation when a dominant vertebral arises directly from the aortic arch. Suzuki et al. described a perfusion technique to protect the dominant vertebral artery that utilizes an 8-Fr catheter.⁵ However, in redo total arch reconstructions, identification, mobilization, and reconstruction of the LSA, or the rare situation in which the left vertebral arises from the arch, is technically challenging. Protection of the anterior and posterior cerebral circulations was facilitated in this case by transposition of the left subclavian vertebral arteries, which then allowed brain perfusion via the innominate artery and LCCA during the arch reconstruction.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Management of Type A Aortic Dissection with Malperfusion Syndrome: A Case Report

Innovations
2020, Vol. 15(4) 378–380
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DOI: 10.1177/1556984520927490
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Abstract

Acute type A aortic dissection (TAAD) with malperfusion syndrome remains a challenging diagnosis and optimal surgical management remains unsettled. We present a case and surgical approach employed for a patient with TAAD and malperfusion syndrome who presented with pulseless bilaterally extremities. Satisfactory outcomes can be achieved with early multidisciplinary collaboration and urgent repair of the aorta and simultaneous efforts to restore blood flow to ischemic tissue.

Keywords

type A, aortic dissection, malperfusion

Introduction

Malperfusion syndrome is a complication of aortic dissection and occurs in 16% to 34% of patients diagnosed with acute type A aortic dissection (TAAD).¹ It is characterized by end-organ ischemia caused by branch-vessel occlusion secondary to increased pressure in the false lumen causing compression of the septum against the ostium of a branch artery (dynamic occlusion) or obstruction by an intimal tear, dissection, or hematoma (static occlusion).

Classically with TAAD, prompt open surgical repair prevents aortic rupture and death from hemorrhagic shock or tamponade. However, with concurrent malperfusion syndrome, the impending risk of end-organ damage from tissue ischemia may be an immediate life-threatening concern. Open aortic repair typically achieves visceral reperfusion for dynamic occlusions but static occlusions may not resolve. Additionally, the physiologic stress of cardiopulmonary bypass prior to correction of malperfusion syndrome may increase morbidity and mortality. In some instances, early endovascular reperfusion followed by delayed aortic repair in hemodynamically stable patients has been successful.^{2,3} Furthermore, cannulation techniques may vary and novel cannulation approaches have been reported.⁴

Herein, we present a case of acute TAAD with malperfusion syndrome and the surgical approach employed.

Case Report

A 63-year-old man with a history of hypertension, left ventricular hypertrophy, and known abdominal aortic aneurysm presented following an episode of tearing chest pain and syncope

while driving. After initially presenting at an outside hospital, the patient arrived in extremis with signs of pericardial tamponade including profound pulsus paradoxus. He was hypotensive with pulseless bilateral lower extremities. Initial laboratory studies revealed lactic acidosis and elevated troponins. Computed tomography scanning from the outside hospital displayed a large TAAD complicated by hemopericardium and decreased blood flow below the level of the superior mesenteric artery (Fig. 1).

The anesthesia and vascular surgery teams were emergently consulted and the patient was taken to the operating room. A subxiphoid window was performed under local anesthesia for evacuation of pericardial hematoma, relief of pericardial tamponade, and stabilization of blood pressure prior to induction of anesthesia. Following intubation, transesophageal echocardiography revealed severe biventricular hypertrophy, mild aortic regurgitation, and intramural hematoma in the proximal

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*Presented at the Eastern Cardiothoracic Surgical Society Annual Meeting, Naples, FL, October 16-19, 2019.

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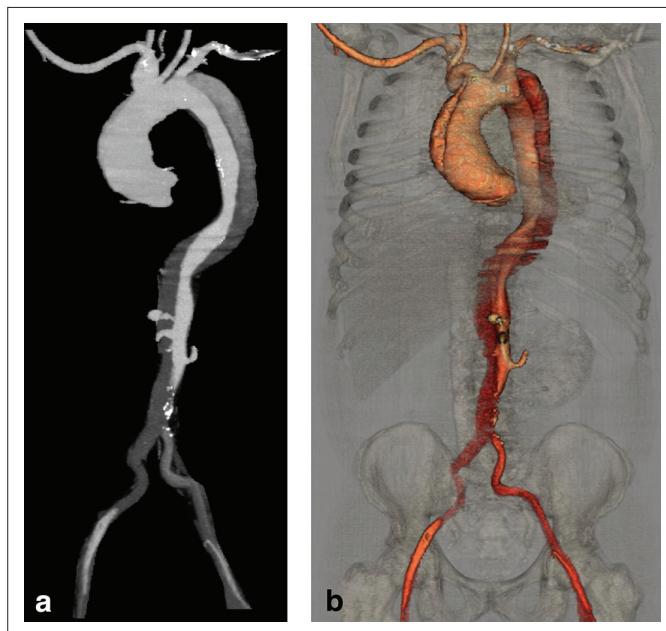


Fig. 1. Preoperative plain (a) and 3-dimensional reconstruction (b) computed tomographic images detailing type A aortic dissection extending from the ascending aortic arch past the aortic bifurcation.

ascending aorta with no identifiable intimal flap. The decision was made to proceed with repair of the TAAD. Cardiopulmonary bypass was initiated through cannulation of the right axillary artery for upper body perfusion and a femoral-femoral bypass graft was utilized for lower body perfusion.

A right axillary cutdown was initiated, while the vascular surgery team achieved exposure of both groins. A beveled 8-mm Hemashield Dacron tube graft (Maquet, Rastatt, Germany) was sewn to the right axillary artery. A 20 French Fem-Flex II arterial cannula (Edwards Lifesciences, Irvine, CA, USA) was secured into this conduit for connection to a Y-limb of the cardiopulmonary bypass arterial line to restore upper body perfusion. The other limb was connected to the side arm of a 9-mm polytetrafluoroethylene axillo bifemoral graft for lower body perfusion using another 20 French Fem-Flex II arterial cannula.

A median sternotomy was performed and the pericardium was opened. A standard dual-stage venous cannula was placed, and cardiopulmonary bypass was initiated with arterial return accomplished via the bifurcated arterial supply as above flowing 5.5 L/min. A pH-stat strategy was utilized for acid-base management while deep hypothermic circulatory arrest at 18 °C was initiated. The aorta was incised and a large tear was present above the sinotubular junction near the noncoronary cusp. The integrity of the aortic root was satisfactory and the aortic valve was intact. To provide cerebral perfusion, umbilical tapes were snared around the head and neck vessels and anterograde perfusion was delivered at 500 mL/min. The distal ascending aorta was trimmed to the base of the head and neck vessels for a hemiarch repair. A 34-mm Valsalva Gelweave graft (Vascutek, Scotland, UK) was anastomosed to the beveled hemiarch. The proximal ascending aortic anastomosis at the



Fig. 2. Postoperative 3-dimensional computed tomographic reconstruction depicting hemiarch repair of type A aortic dissection with right axillary-bifemoral bypass.

level of the sinotubular junction was completed upon resumption of total body reperfusion and rewarming. Myocardial perfusion was achieved by anterograde and retrograde cold-blood cardioplegia.

Upon rewarming there were no identifiable Doppler signals in the lower extremities. The axillary artery graft was tunneled inferiorly and the Y limb of the bifemoral crossover graft was tunneled superiorly. The 2 grafts were anastomosed for completion of a right axillary-bifemoral bypass (Fig. 2). Doppler signals were then present and bilateral 4-compartment fasciotomies were performed. The patient was transferred to the cardiac intensive care unit (CICU).

The patient's hospital course was complicated by atrial fibrillation and acute kidney injury requiring hemodialysis. The patient was downgraded from the CICU on postoperative day 14. He was discharged to inpatient rehab on postoperative day 35 and has done well clinically on follow-up.

Discussion

Acute TAAD represents a challenging diagnosis associated with high in-hospital mortality. Indeed, the International Registry of Acute Aortic Dissection study reported an in-hospital mortality rate of 25%.⁵ Surgical intervention is the mainstay of treatment and results in decreased mortality when provided in a timely fashion.⁶

Even with emergent surgery, TAAD with malperfusion is associated with decreased mortality and other adverse surgical outcomes.^{7–9} The extent of malperfusion prior to and during an operation can be useful in operative planning and predicting outcomes. The degree of malperfusion can be correlated by measuring acidosis. Thus, easily obtained laboratory analysis of base deficits may be useful.¹⁰ Despite poorer outcomes associated with malperfusion syndrome, optimal surgical treatment for patients with TAAD and malperfusion is not well defined.

Surgical options for repair of TAAD include hemiarch replacement with entry tear repair or total arch replacement using a classic 2-stage or frozen elephant trunk technique.^{11–13} The chosen technique should account for the extent of dissection, integrity of the aortic root/valve, and involvement of the supra-aortic vessels.¹⁴ Regardless of the chosen technique, malperfusion complicates the operation as longer operations primarily focused on aortic repair can jeopardize ischemic tissue but delays in aortic repair can result in fatal rupture. In some cases, repair of the proximal aorta and restoration of antegrade blood flow to the true lumen may allow for resolution of the malperfusion syndrome.

In the present case, we elected for urgent repair with a conservative hemiarch replacement approach simultaneously restoring blood flow to the true lumen and ischemic peripheral tissue. Creation of the axillary-bifemoral connection allowed for early reconstitution of bilateral lower-extremity blood flow in addition to aortic repair. Given the satisfactory outcome, we advocate for early multidisciplinary management and efforts to resolve malperfusion syndrome concurrently with proximal aortic repair.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Percutaneous Pulmonary Vein Stenting to Treat Severe Pulmonary Vein Stenosis After Surgical Reconstruction

Innovations
2020, Vol. 15(4) 381–384
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sagepub.com/journals-permissions
DOI: 10.1177/1556984520933962
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Abstract

A 36-year-old female underwent left lower lobectomy with left atrial and left upper pulmonary vein (LUPV) reconstruction with a bovine pericardial patch for an intrathoracic pheochromocytoma. Postoperatively, she developed shortness of breath and transesophageal echocardiography demonstrated LUPV stenosis with increased velocities. Computed tomography angiogram of the chest revealed LUPV stenosis at the left atrium ostium with an area of 39 mm². Under angiographic and echocardiographic guidance, a 10 × 19 mm Omnilink Elite uncovered stent was deployed in the LUPV ostia. While reported following left atrial ablation, pulmonary vein stenting can be successful in a pulmonary vein surgically reconstructed with bovine pericardium.

Keywords

pulmonary vein stenosis, endovascular, percutaneous, stent

Introduction

Pulmonary vein (PV) stenosis most commonly occurs as a complication from radiofrequency ablation during PV isolation to treat atrial fibrillation, occurring at an incidence of 0% to 5% in recent series.¹ The stenosis can lead to shortness of breath, decreased exercise tolerance, cough, and hemoptysis. Balloon dilation or stenting is used to treat PV stenosis.² We describe a case of left upper pulmonary vein (LUPV) stenosis as a result of surgical reconstruction with a pericardial patch, which was treated with a percutaneous PV stent 1.5 years after the original surgery.

Case Report

A 36-year-old female underwent left lower lobectomy with partial circumferential left atrial and LUPV reconstruction with a bovine pericardial patch for an intrathoracic pheochromocytoma. Since surgery, she experienced New York Heart Association Class II dyspnea with inability to walk up a flight of stairs or perform basic activities of daily living.

Transesophageal echocardiography (TEE) demonstrated PV stenosis with elevated LUPV peak velocity at 151 cm/s and normal right upper and lower PV velocities (normal range 30 to 80 cm/s). There was overall preserved right and left ventricle function. Computed tomography angiogram (CTA) of the chest demonstrated the LUPV narrowest segment to be at the ostium

with a diameter of 7.3 mm and an area of 39 mm² (Fig. 1a–c). Right superior PV diameter was 14 mm and area 200 mm². In addition, there was no evidence of left upper lobe edema as a result of the LUPV stenosis. Three-dimensional reconstruction of the left atrium (Fig. 1d) using Aquarius 3D Workstation (TeraRecon, San Mateo, CA, USA) was used to assist procedural planning. The case was discussed at the multidisciplinary heart team conference and the decision was made to proceed to percutaneous LUPV stenting.

Under general anesthesia, the right femoral vein was accessed under ultrasound guidance with a Micropuncture needle (Cook Medical, Bloomington, IN, USA) followed by a 6-French sheath (Terumo, Tokyo, Japan). Preclosure was performed with a Perclose Proglide Vascular Closure device (Abbott Vascular, Chicago, IL, USA). Electrocautery-assisted, transseptal puncture of the mid-septum was performed under TEE guidance, using an 8.5-French SL-1 catheter (St Jude Medical, Minneapolis, MN, USA) and BRK needle (St Jude

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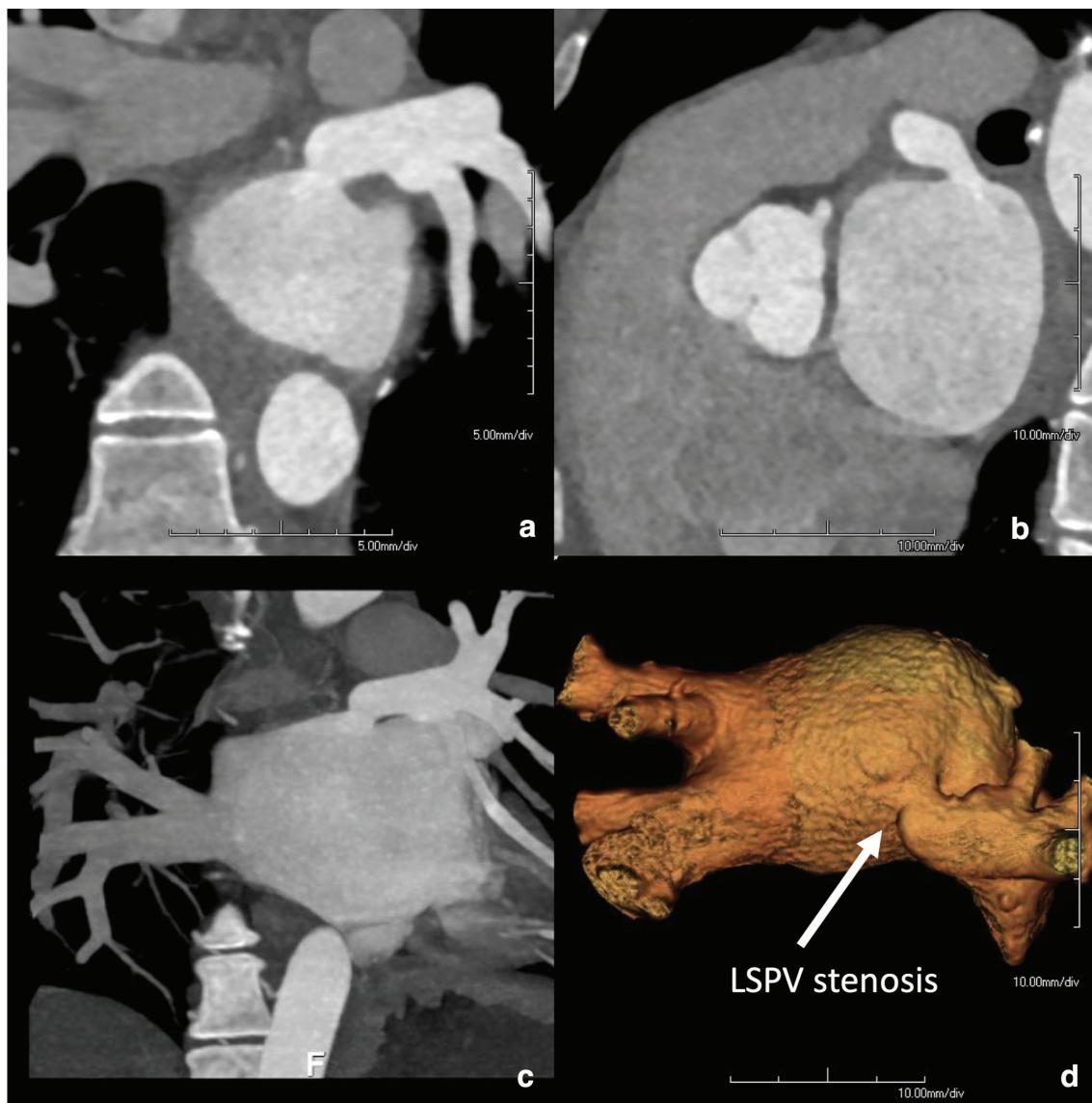


Fig. 1. (a) Coronal and (b) sagittal reformatted computed tomographic images demonstration of LSPV stenosis at the ostium of the reconstructed vein. (c) and (d) Three-dimensional reformatting of the left atrium with severe stenosis of the LSPV. LSPV, left superior pulmonary vein.

Medical, Minneapolis, MN, USA). A 7-French multipurpose guide catheter (Cordis, Santa Clara, CA, USA) was introduced into the left atrium and a mean pressure of 20 mmHg was recorded. The LUPV was then wired with a 200 cm 0.018" V18 control wire (Boston Scientific, Boston, MA, USA), the multipurpose guide catheter then advanced across the ostial lesion into the body of the LUPV, and a mean LUPV pressure of 37 mmHg was recorded. LUPV angiography was performed to confirm the vessel size, course, and angiographic position of the stenosis (Fig. 2a).

A 0.035" Amplatz Superstiff Guidewire (Boston Scientific, Boston, MA, USA) was then advanced into the body of the LUPV. Predilatation was performed with a 6 × 20 mm Armada

balloon (Abbott Vascular, Chicago, IL, USA). Under angiographic guidance, a 10 × 19 mm Omnilink Elite stent (Abbott Vascular, Chicago, IL, USA) stent was deployed at nominal pressure across the ostium of the LUPV into the left atrium with a 2 mm overhang (Fig. 2b). Post-dilatation was performed with a 12 × 20 mm Armada balloon (Abbott Vascular, Chicago, IL, USA) to flair the stent at both ends, preventing migration and creating a smooth transition to the distal PV that measured 14 mm on preoperative imaging. Invasive hemodynamics revealed resolution of the 17 mmHg gradient to 0 mmHg across the LUPV ostium and TEE demonstrated normal LUPV flow velocity.

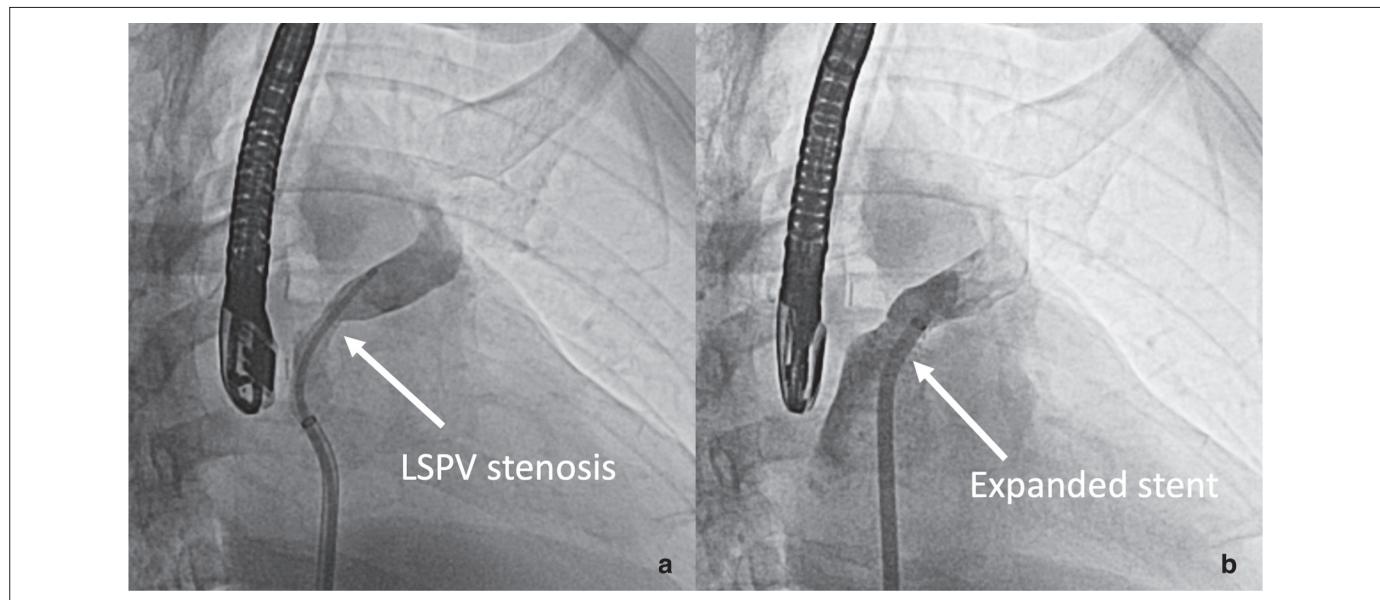


Fig. 2. (a) LSPV ostial stenosis seen on selective angiography. (b) Resolution of stenosis after stent deployment. LSPV, left superior pulmonary vein.

The patient had an uneventful recovery and was discharged the following day. Postoperative transthoracic echocardiogram demonstrated no procedural complications and continued patency of the LUPV stent without a gradient. One and 3-month follow-up CTA showed continued patency and proper positioning of the LUPV stent (Fig. 3).

The patient had significant relief of symptoms immediately after the procedure with continued improvement in exercise

tolerance after 1 month. She is being treated indefinitely with dual antiplatelet therapy.

Discussion

PV stenting has been described in patients with congenital heart disease, after pulmonary transplantation or post-PV isolation ablation (PVIA). A similar case has been reported in a 53-year-old

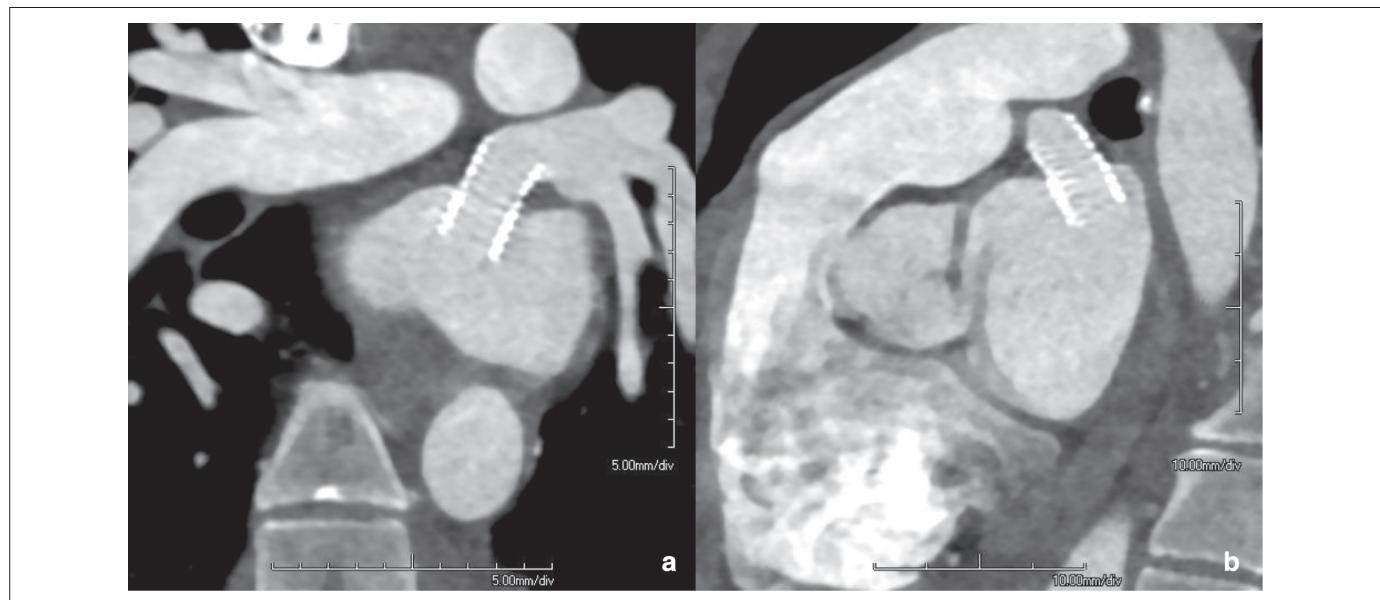


Fig. 3. (a) Coronal and (b) sagittal reformatted computed tomographic images demonstrate stented left superior pulmonary vein with resolution of stenosis 3 months postprocedure.

female who developed PV stenosis after PVIA with failed surgical reconstruction although efficacy of the procedure was not reported.²

While this patient's PV stenosis did not appear critical on CT, a gradient of 17 mmHg is categorized as severe, given that most patients develop symptoms with a gradient above 8 to 10 mmHg. In the past, pulmonary angioplasty was typically used in patients with PV stenosis after PVIA while PV stenting reserved for patients with PV dissection or restenosis after angioplasty.³ Although there was improved PV flow and symptoms, long-term outcomes were poor with almost 50% having significant restenosis at 6 months after primary intervention.⁴ A recent meta-analysis revealed that balloon angioplasty carries a higher risk of restenosis requiring repeat intervention compared to PV stenting while procedure-related complications were comparable between the two.³

Although well tolerated, PV stenting can have major procedural complications including stent embolization, malposition, adjacent PV obstruction, and perforation.⁵ A large single-center registry of 124 patients with post-PVIA PV stenosis treated with balloon angioplasty or stenting found that 94% had acute procedural success and 3.5% experienced major procedural complications.⁶ This and other reports mostly describe balloon-expandable, uncovered stent use, reserving covered stents for the instance of PV injury or rupture. Given the low velocities of flow across the PVs, most centers have treated patients with dual antiplatelet therapy postoperatively.

A study of outcomes in patients less than 18 years old with PV stenting for congenital or postoperative PV stenosis found that freedom from reintervention was 63% at 6 months and 43% at 12 months after primary intervention. Furthermore, stent implantation diameter ≥ 7 mm was associated with improved durability (hazard ratio = 0.32, $P < 0.05$).⁵

In conclusion, PV stenting is a feasible and an effective option for symptomatic postoperative PV stenosis following PV reconstruction.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Zone 0 Thoracic Endovascular Repair After Aortic Wrapping for Acute Aortic Syndrome

Innovations
2020, Vol. 15(4) 385–387
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DOI: 10.1177/1556984520933966
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Abstract

We report a successful treatment of type A acute aortic syndrome (AAS)-associated aortic arch aneurysm in a 71-year-old man with major comorbidities. The ascending aorta was wrapped with artificial graft, and supra-aortic debranching was constructed. Then, Zone 0 thoracic endovascular aneurysm repair (TEVAR) with plug occlusion of the left subclavian artery was successfully performed. The patient was discharged in good physical condition without any complications. To our knowledge, this is the first reported case in the literature of successful Zone 0 TEVAR after ascending aorta wrapping and supra-aortic debranching with type A AAS associated with aortic arch aneurysm.

Keywords

acute aortic syndrome, Zone 0 thoracic endovascular aneurysm repair, external wrapping, supra-aortic debranching

Introduction

We herein report successful Zone 0 thoracic endovascular aneurysm repair (TEVAR) after ascending aortic wrapping and supra-aortic debranching in an extremely high-risk patient with type A acute aortic syndrome (AAS)-associated aortic arch aneurysm.

Case Report

The patient was a 71-year-old man with a medical history of old cerebral infarction, hypertension, continuous atrial fibrillation, untreated diabetes mellitus, and smoking without any medication because of low compliance. At midnight, he had sudden back pain and was unresponsive. He was emergently transported to a tertiary medical facility. Computed tomography (CT) showed a 7-cm aortic arch aneurysm and type A intramural hematoma (IMH) with penetrating atherosclerotic ulcer, and obvious cardiac tamponade (Fig. 1). He was transferred to our hospital. At arrival, 8 hours had already passed from the onset of his condition, and he showed deep coma and shock vitals with inotropic support. The estimated standard European System for Cardiac Operative Risk Evaluation (EuroSCORE) II result was 63.7 for the patient.

Median sternotomy was performed, and cardiopulmonary bypass was implemented through femoral arterial cannulation and single 2-stage venous cannulation via right atrial appendage.

Intraoperative transesophageal echocardiography demonstrated no aortic regurgitation. The ascending aorta was carefully separated from the pulmonary artery trunk and the right pulmonary artery. Pieces of a Triplex artificial graft® (Vascutek Terumo, Tokyo, Japan) were tailored and placed around the aorta from the coronary ostia to the innominate artery and approximated to tightly wrap the ascending aorta to 36 mm (Fig. 2a, Fig. 2b). The wrapped ascending aorta was tangentially side-clamped and proximal side-to-side anastomosis with 2-branch graft was performed (Fig. 2c, Fig. 2d). A longitudinal incision involving both the wrapped graft and the ascending aorta was made to perform proximal anastomosis. Suturing involving both the ascending aorta and the wrapped graft was performed in order to obtain the best fixation. Distal anastomoses were sequentially constructed in an end-to-end fashion to the right innominate artery and left carotid artery (Fig. 2e). Since preoperative CT demonstrated good communication between the left vertebral artery and the left subclavian artery, the left subclavian artery was not bypassed. The

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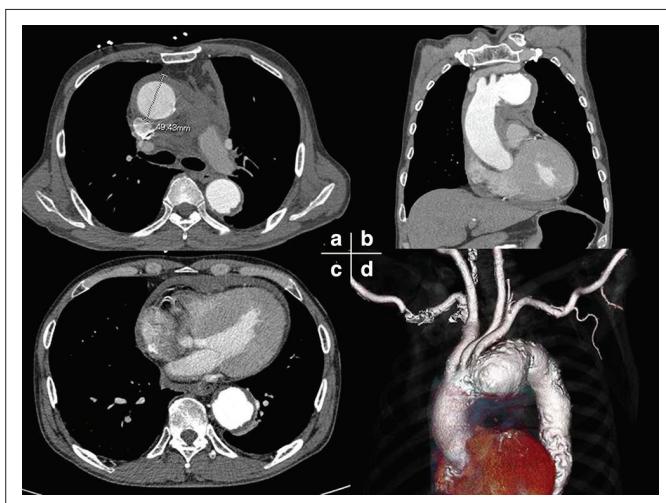


Fig. 1. (a) Transverse view of a preoperative plain computed tomographic scan demonstrating type A intramural hematoma. (b) Coronal view of a preoperative computed tomographic scan demonstrating intramural hematoma with aortic arch aneurysm and penetrating atherosclerotic ulcer (arrow). (c) Transverse view of a preoperative computed tomographic scan demonstrating massive bloody effusion surrounding the heart. (d) Preoperative 3-dimensional reconstruction of the thoracic aorta demonstrating acute aortic dissection with aortic arch aneurysm.

left atrial appendage was closed with 40 mm of AtriClip® (AtriCure, Mason, OH, USA), because his CHA₂DS₂-VASc score was 6. TEVAR was performed after the aortic wrapping and 2 debranching procedures. An extra-stiff wire was passed through a femoral access point to reach the aortic valve. The stent graft was advanced over the wire and placed at the level of the

ascending aorta (Zone 0). A 10% oversized aortic stent graft (Valiant Navion®: Medtronic, Santa Rosa, CA, USA) was used for proximal landing in correspondence with the wrapped ascending aorta because of its flexibility and small delivery system. The aortic stent graft was deployed (Fig. 2f), and the left subclavian artery was occluded at the proximal portion with an Amplatzer vascular plug® (Abbott Cardiovascular, St Paul, MN, USA). Operation time was 149 minutes and cardiopulmonary bypass time was 52 minutes (Supplemental Video).

The length of hospitalization was 16 days, including 3 days in the intensive care unit at the time of the primary operation. No neurological complications or minor complications occurred. Postoperative CT showed that the stent graft was properly positioned without any endoleak with good patency of the debranching stent and good brain perfusion. The patient was discharged in good physical condition without any complications, and no new lesions were detected on postoperative CT scan (Fig. 3).

Discussion

To our knowledge, this is the first reported case in the literature of successful Zone 0 TEVAR after ascending aorta wrapping and supra-aortic debranching in a high-risk patient with type A AAS associated with aortic arch aneurysm.

The application of TEVAR has dramatically changed the treatment paradigm for aortic disease of the descending thoracic aorta. It may be a viable rescue option for patients with AAS who are not eligible for open surgical repair. The first successful report of TEVAR in a patient with acute aortic dissection was published by Dorros et al.¹ Subsequently, several other investigators reported similar successes using TEVAR for AAS.²⁻⁴ However, treatment with TEVAR for AAS remains challenging because of the

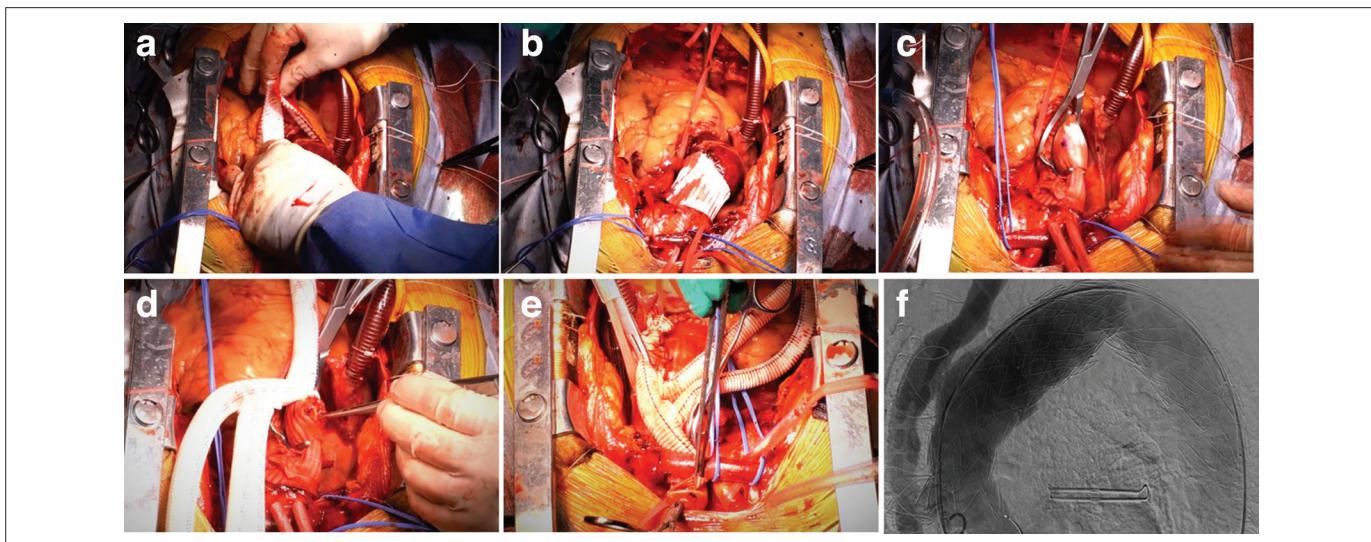


Fig. 2. The operative process. a) A piece of an artificial graft placed around the ascending aorta. b) The artificial graft was approximated to tightly wrap the ascending aorta. c) The wrapped ascending aorta was tangentially side-clamped. d) Proximal side-to-side anastomosis with a 2-branch graft. e) Distal anastomosis to the right innominate artery and left carotid artery. f) A deployed aortic stent graft.

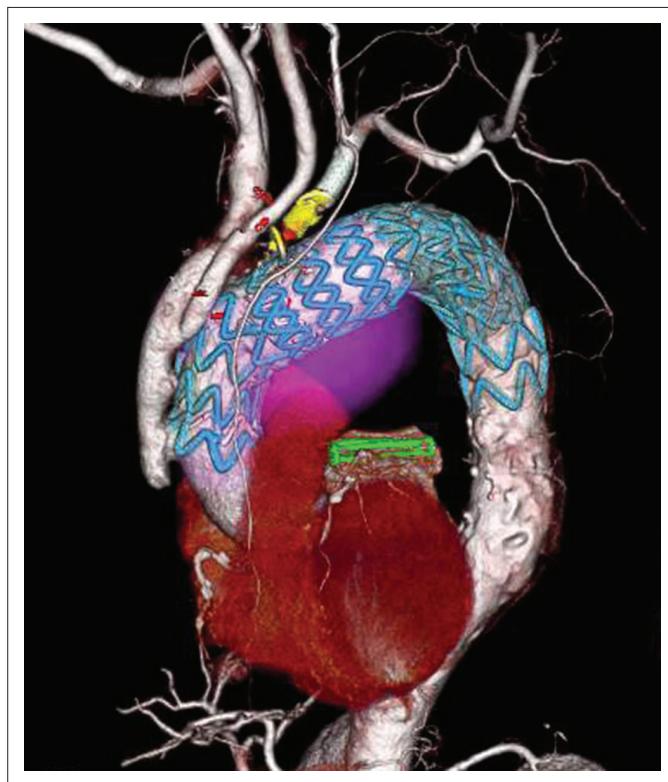


Fig. 3. Postoperative 3-dimensional reconstruction of the thoracic aorta demonstrating successful thoracic endovascular stent-graft deployment without any endoleak and patent neck vessels after ascending aortic wrapping and debranching graft, anastomosed to the right innominate artery and left carotid artery. The left atrial appendage was closed with an AtriClip.

anatomical vicinity of the ascending aorta to the aortic valve, coronary artery, and brachiocephalic artery. The hemodynamic forces also differ between the ascending aorta and descending aorta.⁵ Excessive hemodynamic forces in the ascending aorta typically lead to variations in diameter of the normal ascending aorta by at least 8%.⁶ These changes may compromise the precise deployment of devices and can also increase the risk of late migration. In addition, the fragility of the diseased ascending aorta may increase the risk of aortic rupture or retrograde dissection during stent graft deployment. For AAS, the aorta proximal to the branches is not normal, and an ancillary procedure may be needed in order to reduce the diameter of the ascending aorta and better conform to the aortic stent graft. In the current case, the size of the ascending aorta was 49.4 mm. Aortic wrapping was useful for reducing the diameter to accommodate the aortic stent graft and creating the best anastomosis site for debranching.

The gold standard surgery for AAS is still conventional ascending and arch graft replacement. In addition, our procedure

is also not suitable for acute aortic dissection with a patent false lumen. Furthermore, even in aortic dissection with a thrombosed false lumen, a thick thrombosed false lumen is difficult to manage because side-clamping is impossible. However, in select patients with an extremely high risk, wrapping of the ascending aorta plus debranching TEVAR may be a viable alternative to therapeutic abstention or conventional surgery. Since a high incidence of late rupture of wrapped aneurysms has been previously reported,⁷ further careful follow-up care will be needed.

Conclusions

Wrapping the ascending aorta plus debranching TEVAR should be considered, especially in patients for whom open surgery is extremely risky.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Supplemental Material

Supplemental material for this article is available online.

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Massive Left Atrial Thrombus After a Left Atrial Surgical Ablation and Bioprosthetic Mitral Valve Replacement

Innovations
2020, Vol. 15(4) 388–391
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DOI: [10.1177/1556984520934632](https://doi.org/10.1177/1556984520934632)
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Abstract

Variability exists regarding the timing and duration of anticoagulation after surgical ablation for atrial fibrillation and bioprosthetic mitral valve replacement (MVR). We report a case in which a patient developed a massive left atrial (LA) thrombus after MVR and left-sided radiofrequency ablation (LRFA). Despite acutely elevated gradients across the bioprosthetic valve, the patient remained asymptomatic and hemodynamically stable; thus, a multidisciplinary, patient-centered discussion was had and the patient was treated successfully with oral anticoagulation.

Keywords

thrombus, thrombolytics, anticoagulation

Introduction

Intracardiac thrombus after cardiac surgery is rare. While guidelines exist regarding the use of systemic anticoagulation after bioprosthetic mitral valve replacement (MVR) and intracardiac ablation for atrial fibrillation (AF),^{1–4} adherence and clinical practice remain variable.^{5–7} Moreover, the guidelines do not advise on what patient-specific factors should be considered in determining initiation of anticoagulation postoperatively. The purpose of this report is to (1) highlight risk factors that may be associated with increased thrombotic risk in a patient undergoing MV surgery and a left-sided radiofrequency ablation (LRFA) and (2) to discuss management considerations when an intracardiac thrombus is discovered postoperatively.

Case Report

A 64-year-old female with nonischemic cardiomyopathy, severe mitral regurgitation, marked left atrial (LA) enlargement (indexed area 62 mL/m^2), and paroxysmal AF underwent MVR with a 27-mm Magna pericardial valve. A concomitant extended left atrial surgical ablation was also performed with LA appendage (LAA) amputation. The LRFA lesion set included pulmonary vein isolation, roof and floor lines, as well as a free wall ablation and a lesion to the mitral isthmus (Fig. 1). Cryotherapy was utilized for completion of the mitral valve (MV) isthmus lesion. Intraoperative transesophageal echocardiogram (TEE) demonstrated a postoperative ejection fraction (EF) of 30% on inotropes, with normal

bioprosthetic MV function and no paravalvular leak. The patient's surgical course was unremarkable, without any recurrence of AF, but notable for the extended use of inotropes due to left ventricular dysfunction. Oral anticoagulation (OAC) was started on the day of discharge (postoperative day 15) with the plan to continue warfarin for a minimum of 3 months. A routine transthoracic echocardiogram (TTE) obtained at discharge demonstrated an EF of 25% to 30%, preserved LA function by pulse wave Doppler, and no paravalvular regurgitation. However, a large thrombus within the left atrium was found that extended onto the prosthetic MV leaflets. Bioprosthetic leaflet mobility was reduced and gradients were elevated (Fig. 2). The patient was systemically heparinized and a subsequent TEE that day confirmed a massive $5.5 \times 3.5 \text{ cm}$ LA thrombus extending to the MV annulus and onto the MV leaflets. The mean gradient (MG) by TEE assessment was 14 mmHg (heart rate [HR] = 97 bpm).

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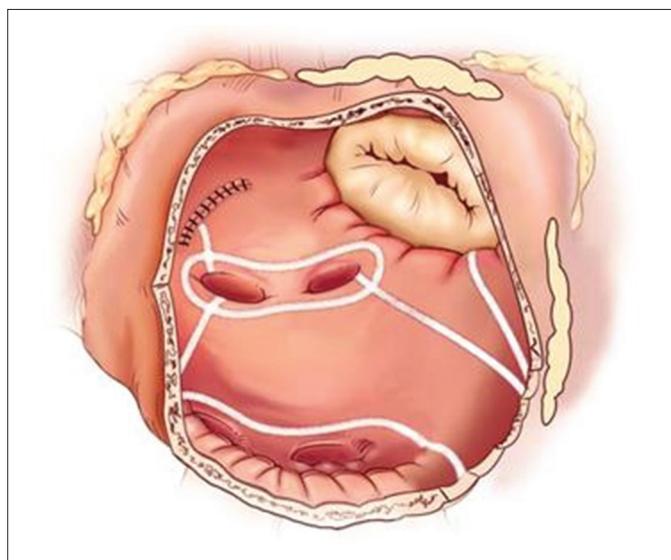


Fig. 1. Schematic of the left atrial radiofrequency ablation performed. All ablation lines are performed with a bipolar radiofrequency clamp except for an endocardial cryoablation at the mitral annulus and an epicardial cryoablation over the coronary sinus. Reproduced with permission from Weimar et al. (2012).¹²

In spite of the acute MV dysfunction, the patient remained asymptomatic and hemodynamically stable. A multidisciplinary, patient-centered discussion was had and management options were presented. The options included redo surgery, intravenous thrombolytic therapy, or systemic anticoagulation. Given the high risk for redo surgery and the risk for embolization with thrombolytics, the patient chose to continue treatment with intravenous heparin and warfarin. Serial TTEs over the next few days demonstrated a gradual reduction in the size of the thrombus and MV gradient.

Ten days after the thrombus had been discovered, the patient reached the specified international normalized ratio (INR) goal (INR 2.5 to 3.5). Her heparin infusion was discontinued and she was discharged on warfarin. At the time of discharge, the MV MG by TTE assessment was 6 mmHg (HR = 90 bpm) and the thrombus had decreased in size. The patient was maintained on OAC and serial TTEs over the next several months demonstrated a continued reduction in the LA thrombus burden with normalization of the MV gradient. The patient has remained on warfarin with her most recent TTE at 18 months postoperatively demonstrating a complete resolution of thrombus and normal prosthetic valve function (Fig. 2f).

Discussion

This case illustrates 2 important management discussions. The first is regarding the management strategy for an LA and bioprosthetic MV thrombus discovered incidentally after cardiac surgery. The second discussion specifically surrounds the decision and timing of when to initiate routine systemic

anticoagulation in the perioperative period after bioprosthetic MVR and surgical intracardiac ablation.

As stated for this patient, once the LA thrombus was identified, the options included redo surgery, intravenous thrombolytic therapy, or systemic anticoagulation. The 2017 American College of Cardiology/American Heart Association valvular guidelines convey multiple factors to consider when assessing surgery or fibrinolysis for prosthetic valve thrombosis.¹ Factors favoring surgery in this patient included readily available surgical expertise and large thrombus size (5.5×3.5 cm). Guidelines suggest that thrombi >0.8 cm² may be best treated with surgical extraction, while factors favoring fibrinolysis include high surgical risk, New York Heart Association I symptoms, and hemodynamic stability. Fibrinolysis, particularly with thrombus >1.0 cm in diameter, is associated with a 2.4-fold higher rate of complications per 1.0 cm² increase in thrombus size.² While reoperative surgery is always a consideration, this patient's reduced EF postprocedurally (left ventricular EF 25%) and the prospect of reoperation 2 to 3 weeks following surgery was considered to be an extremely high-risk option. After discussing the risk and benefits of redo surgery and intravenous thrombolytic therapy, the patient opted to forgo surgery and thrombolysis in favor of continued intravenous anticoagulation with heparin and OAC with warfarin. While there are limited data for anticoagulation in the setting of perioperative prosthetic valve thrombosis, a small prospective study from the Mayo Clinic described a success rate of 83% for the treatment of valve-associated thrombus with OAC. The patients in that study by Egbe et al. had thrombus identified much later, at an average of 86 ± 24 weeks postoperatively, but had a similar burden of prosthetic valve thrombus (MG 14 ± 4 mmHg versus 14 mmHg in this case).⁸

As prevention of this complication is the ideal strategy, discussion must be had regarding the importance of timing and duration of OAC among patients undergoing MV surgery and then specifically with concomitant surgical ablation. Anticoagulation after bioprosthetic MVR remains an Class II A guideline for a period of 3 to 6 months postoperatively in order to minimize leaflet thrombosis and improve clinical outcomes;^{1,2} however, there is substantial surgeon and hospital variability on this practice.⁵ Schwann et al. suggest that the bimodal "very few or almost all" pattern is likely driven by the lack of convincing evidence for or against warfarin in the current clinical practice guidelines and legacy regional biases for or against postoperative anticoagulation after bioprosthetic MVR.⁵

This patient, having also undergone surgical ablation, had an additional indication for anticoagulation. Patients undergoing surgical ablation (with or without LAA amputation) are routinely anticoagulated for 3 months.^{3,4} This recommendation of the Society of Thoracic Surgeons³ is utilized at our institution, and at 3 months, OAC is discontinued if there is no evidence of AF on 24-hour monitoring, no evidence of LA stasis or thrombus by echocardiogram, and the patient has no other indication for systemic anticoagulation. This practice pattern has been shown to be effective in minimizing the need for long-term anticoagulation without increasing the risk of neurological thromboembolic events at a mean 6 years of follow-up.⁹

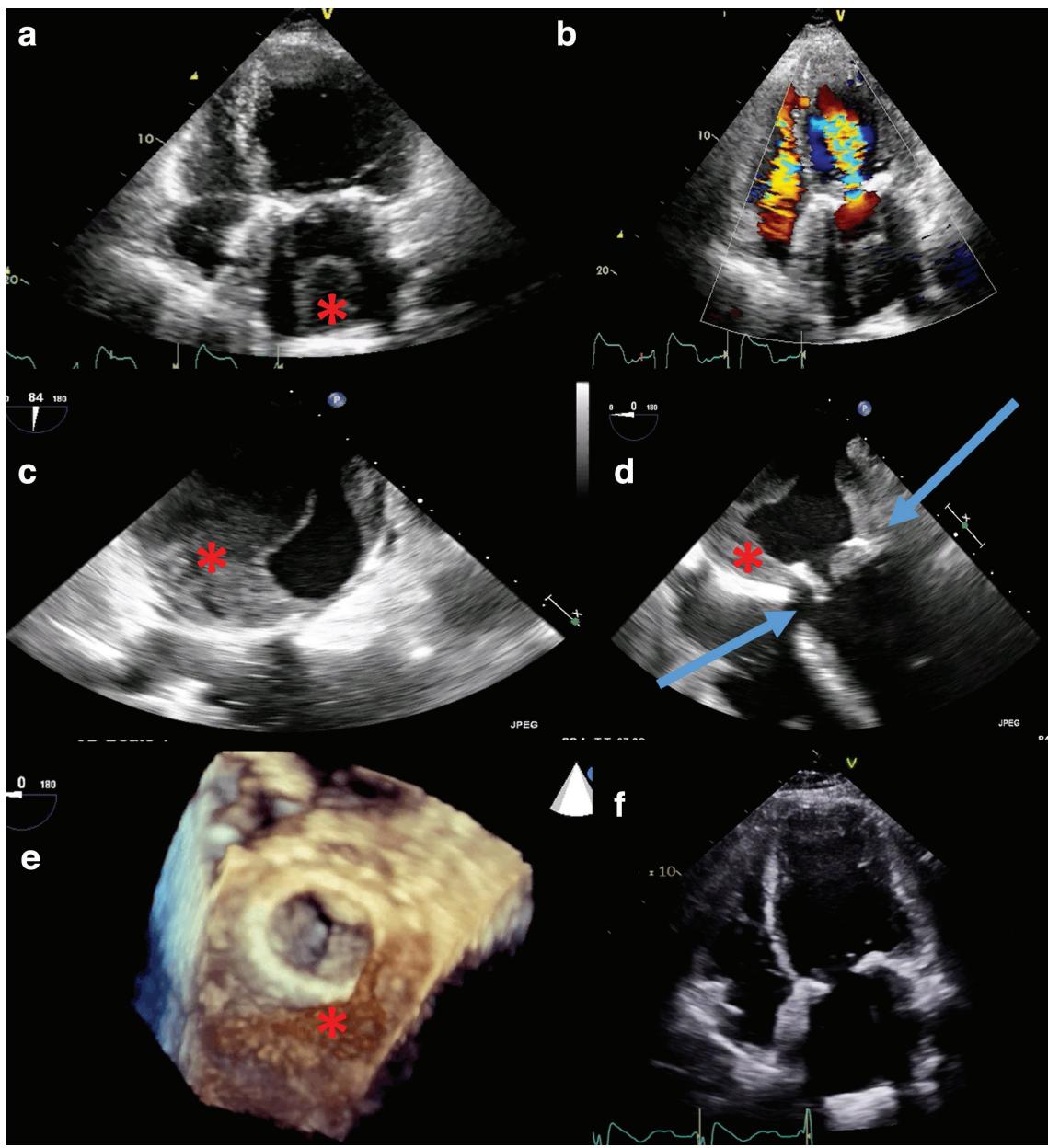


Fig. 2. (a) TTE on POD 15 illustrating a circumferential echodensity in the LA (star). (b) Color Doppler across the MV illustrating turbulence with a mean gradient of 14 mmHg. (c) POD 16 TEE demonstrating massive thrombus at the posterior wall of the LA (star). (d) POD 16 TEE illustrating that the thrombus (star) extending onto and involving the 27-mm Magna pericardial MV prosthesis (arrows). (e) POD 16 3-dimensional TEE en-face view of the LA demonstrating thrombus (star) on the posterior LA wall. (f) TTE 18 months after hospital discharge demonstrating resolution of the LA/MV thrombus while on oral anticoagulation. LA, left atrial; MV, mitral valve; POD, postoperative day; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

As the decision of when to initiate anticoagulation for a specific patient must be individualized, it is this exact variability that results in marked differences within clinical practice and limits the utility of guidelines with respect to postoperative timing of systemic anticoagulation after mitral replacements and even more so for surgical ablations.^{6,7} Specifically, risks for bleeding are too specific for a given patient, which creates a gap within the practice guidelines.¹⁻⁴ Thus, the use of OAC

after bioprosthetic MVR and the timing of OAC after surgical ablation at our institution remain quite variable.

This patient had several risk factors that likely predisposed her for the formation of an LA thrombus. Observational studies and case reports have identified several risk factors for thrombus after surgical LA ablation and MVR.^{6,7,10,11} Specifically, AF recurrence, decreased LV systolic function, LA enlargement, and decreased LA contractile function are associated

with the development of intracardiac thrombus. Despite maintaining normal sinus rhythm following the procedure, this patient had decreased LV systolic function, a bioprosthetic MVR, marked LA enlargement, and newly performed ablation lines from her LRFA. In retrospect, given these multiple risk factors, this patient may have benefited from earlier systemic anticoagulation, particularly once her bleeding risks were deemed lower.

In summary, while guidelines recommend systemic anticoagulation after a surgical LA ablation and bioprosthetic MVR for a minimum of 3 months postoperatively, consensus does not exist as to when to start anticoagulation in the postoperative setting. This case represents the unusual complication of a massive LA thrombosis after a bioprosthetic MVR and LRFA procedure. Systemic anticoagulation should be initiated promptly after surgical LRFA when bleeding risks are mitigated and especially in those with multiple risk factors for LA thrombus formation. If intracardiac thrombus is identified postoperatively, each patient should be evaluated for the risk and benefits of reoperation, intravenous thrombolytic therapy, or conservative therapy with OAC and close monitoring.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

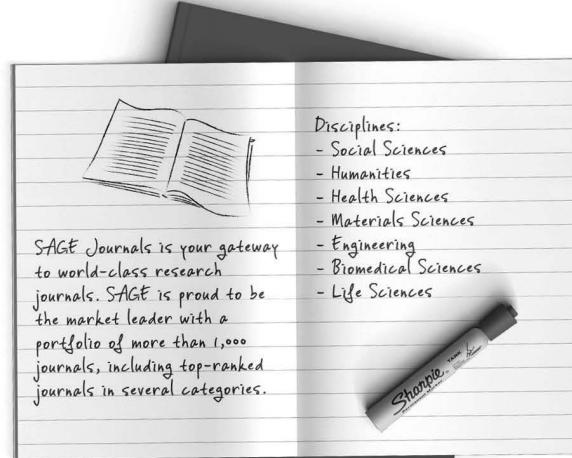
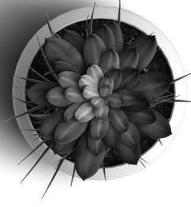
The author(s) received no financial support for the research, authorship, and/or publication of this article.

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