



# EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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## INTRODUCTION

Though it was initially developed in the 1960s to support infants and children with advanced respiratory failure, extracorporeal membrane oxygenation, or ECMO, is now being utilized with increasing frequency in adults. In 2009, the H1N1 influenza pandemic caused a large number of cases of adult respiratory distress syndrome (ARDS) that became refractory to conventional medical (ventilator) therapy.<sup>1</sup> Interest in adult extracorporeal support was renewed by contemporary studies that demonstrated improved survival in severe ARDS patients treated with ECMO.<sup>2</sup> As the number of adult ECMO implants continued to grow, improvements in hardware and circuit technology translated into safer implants, improved outcomes, and expansion of ECMO applications to other disease

states. With this growth in usage, specialized ECMO centers developed to allow for regional transport of a patient to a facility that could provide ongoing management, with the ultimate goal of the patient's recovery and explantation of the device.

The Extracorporeal Life Support Organization (ELSO) is an international agency that was established in 1989 to support institutions offering ECMO therapy, and currently tracks more than 170 institutions using this technology in more than 50 countries worldwide.<sup>3</sup> It records ECMO utilization in a robust registry that had captured more than 19,000 adult ECMO implants as of 2016. From 2006 to 2011, for example, the volume of adult ECMO cases increased more than 400%, for reasons noted above. (LGH became an ELSO member in 2017.)

## ECMO: Cardiac (Venoarterial) Support

### Peripheral venoarterial ECMO cannulation approach

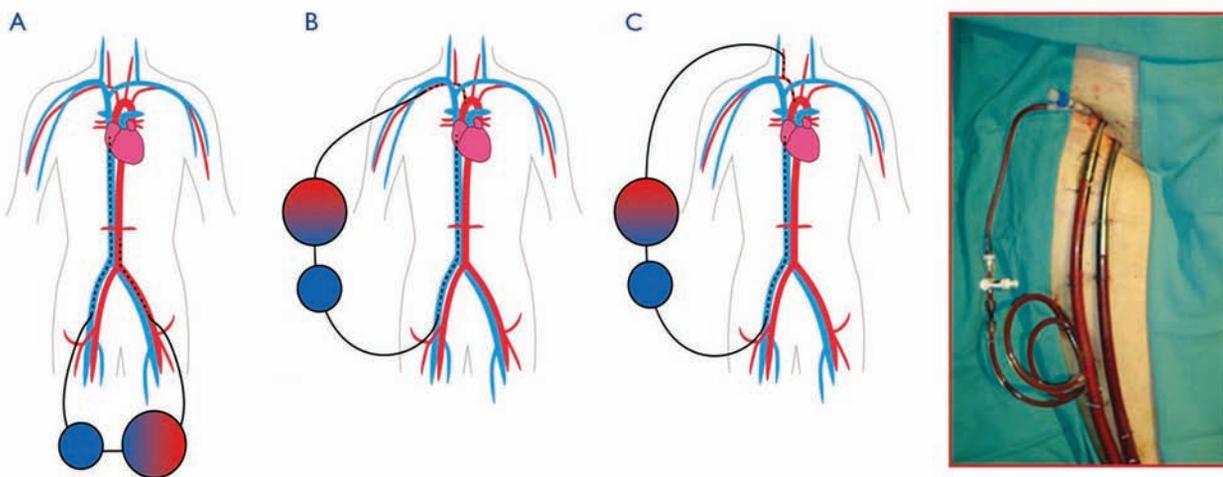


Fig. 1. Circuit for venoarterial ECMO:

- A. A venous cannula placed centrally via the femoral vein, with reinfusion after oxygenation into the abdominal aorta via the femoral/ilic artery.
- B. Arterial reinfusion into the aortic arch via the axillary artery.
- C. Arterial reinfusion into the aortic arch via the common carotid artery.

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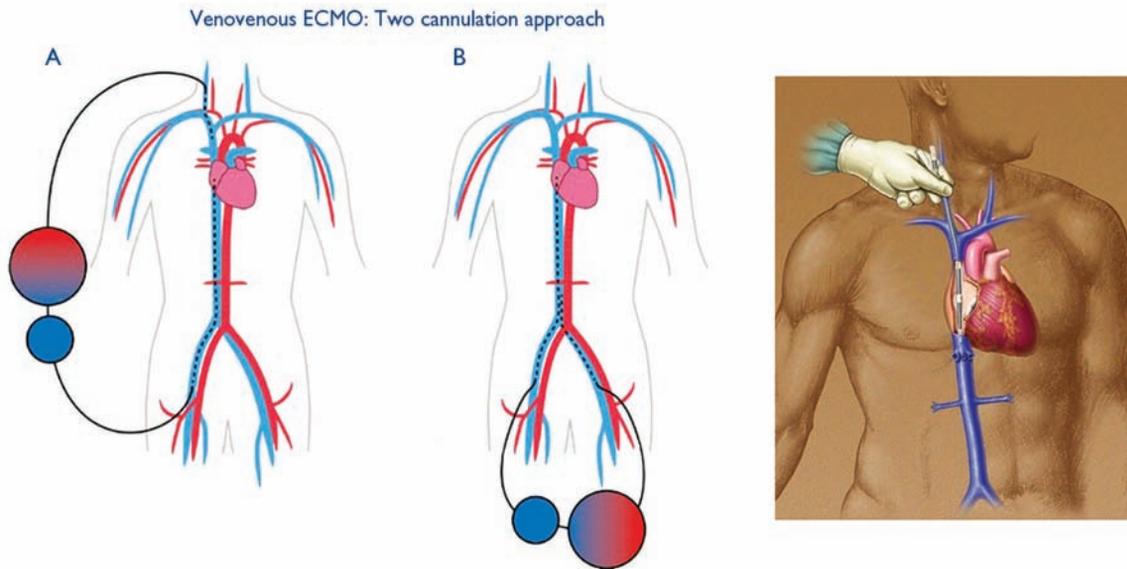
**ECMO: Pulmonary (Venovenous) Support**

Fig. 2. Circuit for venovenous ECMO:

A. Venous cannulation for drainage via the femoral/iliac venous system and reinfusion after oxygenation into the internal jugular vein.  
 B. Venous cannulation for drainage from the lower vena cava with reinfusion of oxygenated blood into the right atrium via a second venous cannula placed from the contralateral vein. (NOTE: This drawing incorrectly shows the oxygenating circuit in reverse.)

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**TECHNIQUES**

The basic components of ECMO include a blood pump, membrane oxygenator, blood tubing, as well as cannulae for drainage and reinfusion. ECMO has the ability to support the failing lungs, heart, or a combination of the two.<sup>2</sup> Venovenous (VV) ECMO offers support to those patients with isolated respiratory failure, whereas venoarterial (VA) ECMO is utilized to treat patients afflicted with cardiac or cardiopulmonary failure. The difference in these two forms of therapy simply lies in the location of the cannulae.

VA ECMO utilizes a centrally located venous drainage cannula, which drains deoxygenated blood from the patient. Following extracorporeal oxygenation, this blood is then reinfused into the patient through a peripheral or central artery, thus bypassing the failing heart and lungs, and providing complete support of the systemic circulation.<sup>4</sup> (Fig. 1, preceding page.)

VV ECMO drains central deoxygenated blood from the patient similarly, but in contrast to VA support, it returns oxygenated blood back to the venous system at the right side of the heart. This strategy depends upon preserved cardiac function to pump the oxygenated blood not only across the pulmonary circuit (which is no longer tasked with gas

exchange), but eventually to the periphery. Both VV and VA ECMO have the ability to offer days to weeks of support, thus offering valuable time for either recovery of cardiac or pulmonary function, or – in the case of irreversible heart or lung failure – initiation of an alternative long-term treatment strategy. (Fig. 2)

**INDICATIONS**

VV ECMO support can be considered for any patient afflicted with a potentially reversible cause of acute lung failure. This category includes those with acute respiratory distress syndrome from a variety of causes, including severe bacterial or viral pneumonia, aspiration pneumonitis, alveolar proteinosis, severe pulmonary contusion and transfusion-related acute lung injury.

Persistent impairment of gas exchange despite maximum ventilator therapy is indicated by a PaO<sub>2</sub>/FiO<sub>2</sub> ratio of < 100, and carbon dioxide retention despite airway plateau pressures of > 30 mmHg. These parameters portend a high pulmonary-related mortality with conventional ventilator therapy alone. Studies suggest that consideration for VV ECMO should be made early in this scenario to optimize survival benefit.<sup>2</sup>

VV ECMO is also useful for events that cause abrupt loss of oxygenation, such as airway obstruction,

### ECMO: Indications for Cardiac (VA) Support

- ✓ **Cardiogenic shock. Severe cardiac failure due to almost any cause:**
    - acute coronary syndrome
    - cardiac arrhythmic storm refractory to other measures
    - sepsis with profound cardiac depression
    - drug overdose/toxicity with profound cardiac depression
    - myocarditis
    - pulmonary embolism
    - isolated cardiac trauma
    - acute anaphylaxis
  - ✓ **Post cardiotomy: Inability to wean from cardiopulmonary bypass after cardiac surgery**
  - ✓ **Post heart transplant: Primary graft failure after heart or heart-lung transplantation**
  - ✓ **Chronic cardiomyopathy:**
    - as a bridge to longer term VAD support, or
    - as a bridge to decision
  - ✓ **Periprocedural support for high-risk percutaneous cardiac interventions**
  - ✓ **Bridge to transplant**
- Refractory low cardiac output**

  - Cardiac Index < 2.2L/m<sup>2</sup>
  - Systolic BP < 90 mmhg
  - On high dose pressors
  - IABP ineffective
  - Adequate intravascular volume

Fig. 3. ECMO: Indications for Cardiac (VA) Support.

massive hemoptysis, or pulmonary hemorrhage. Finally, VV ECMO is routinely employed to not only bridge patients to lung transplant in the case of end-stage pulmonary failure, but also to support a failing pulmonary allograft following lung transplantation.

VA ECMO support is indicated for cardiogenic shock due to cardiac failure from a variety of causes.<sup>5</sup> Cardiogenic shock is defined as persistent hypotension and refractory low cardiac index (<2.2 L/m<sup>2</sup>) despite the use of high dose inotropes and/or intra-aortic balloon pump therapy in a patient with adequate intravascular volume. Fig. 3 lists those etiologies of cardiogenic shock for which VA ECMO is now routinely employed.<sup>6</sup>

#### LGH EXPERIENCE

The Lancaster General Hospital (LGH) ECMO program began in 2012. To date, we continue to offer both VA and VV device implantation. During our program's infancy, our standard was to perform device implantation here at LGH, stabilize the patient's gas exchange or end-organ perfusion, then transfer the supported patient to an outside facility for ongoing ECMO management.

Our practice changed in October 2015, when we were approved by the Department of Health as a specialized ECMO Center, which gave us the opportunity not only to initiate support here at LGH, but to continue the care of our patients throughout the course of support and beyond. To gain Department of Health approval we established an ECMO management team comprised of cardiac surgeons (device implanters), heart failure cardiologists, pulmonary/critical care specialists, perfusionists, nursing staff with specialized ECMO training, and palliative medicine specialists.

Our ECMO team evaluates the indication for device implantation, scrutinizes patient candidacy to receive the device, performs the ECMO implantation, and manages the patient on a continuum throughout their period of support. Ultimately, the team determines the appropriate goal of therapy, which may include device removal in the case of organ recovery, termination of support in anticipation of patient death, or transition to a more durable platform such as a long-term implantable left ventricular assist device.

The ECMO-supported patient is evaluated daily with a multidisciplinary approach. Each ECMO case is peer reviewed not only to evaluate the appropriateness

of implantation, but to identify device-related complications, and critique management decisions. From these discussions, we have evolved our ECMO implant guidelines in light of observed trends (both positive and negative) in our patient cohort.

Prior to DOH approval in October 2015, robust patient data were sparse, owing to the transfer of so many patients to an outside facility. Since January 2016, however, each patient implanted at LGH (i.e. those who receive ongoing ECMO management at LGH) is entered into the worldwide ELSO registry. The following results will focus on this cohort.

## RESULTS

The first ECMO implantation at LGH took place in the spring of 2012. Venoarterial support was offered to a 68-year-old gentleman who presented with acute occlusion of the left main coronary artery resulting in cardiogenic shock. Device implantation immediately stabilized this patient's systemic perfusion and shock state, allowing for safe inter-hospital transfer to a regional ECMO center for continued management.

From that first case in 2012 to September 2018,

we performed a total of 151 ECMO implants in 142 patients. (Nine patients underwent conversion of their mode of support, accounting for the "extra" nine implants.) Sixty-five percent of ECMO implants occurred in males, 35% in females. Our yearly ECMO volume displays a general upward trend in the total number of implants over the program's first six years. There has been a relatively steady increase in the annual number of ECMO implants, with a peak in 2017. Given our current trends, that figure is expected to be matched, if not surpassed, when the data for the last quarter of calendar year 2018 are completed. (Fig. 4)

Over the past three years, we have performed 75 initial VA ECMO implants, 20 initial VV ECMO implants and nine ECMO mode conversions for a total of 104 total implants. Including the cases in which an arterial circuit was added during ECMO conversions (three of nine patients), 75% (78/104) of our total implant volume of the past three years has provided total cardiopulmonary (VA) support. Although, at this stage in our program, VV ECMO implants represent only 25% of our total ECMO volume, this mode of

## LGH ECMO Volume

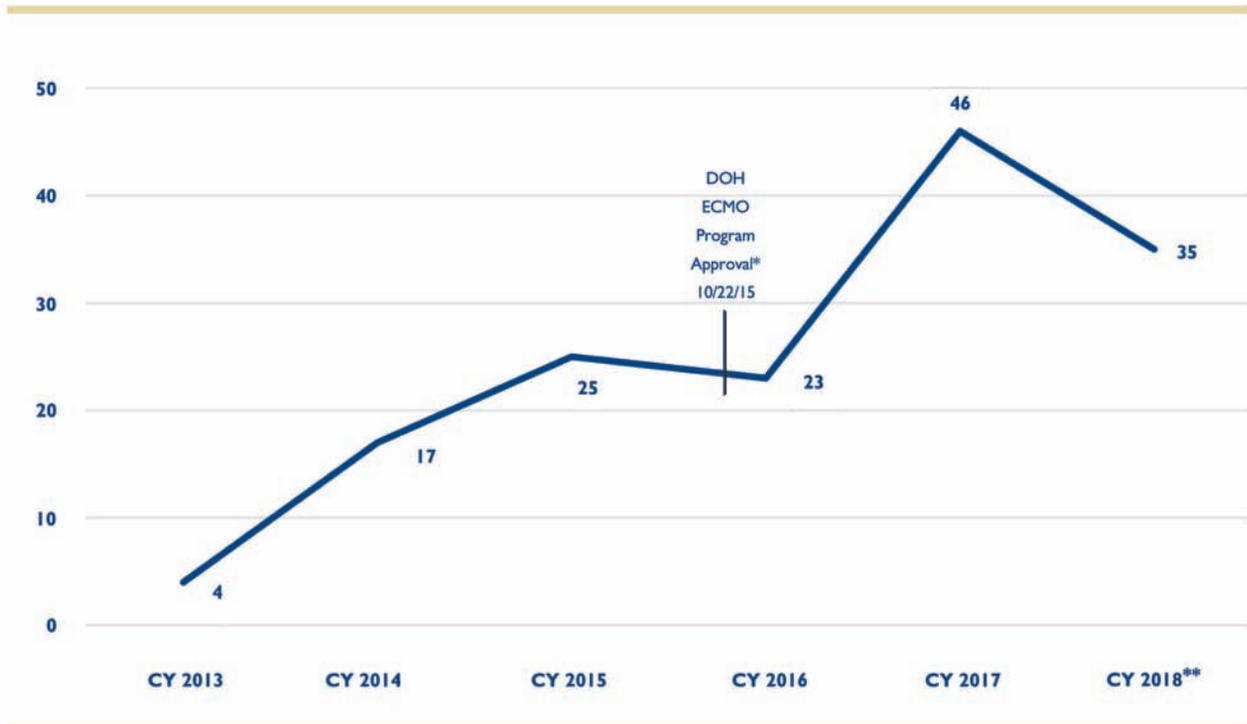


Fig. 4. LGH ECMO Volume.

\* LGH can keep patients on ECMO instead of transferring out to another DOH-approved Center.

\*\* Through the first nine months of 2018.

**Total Volume of ECMO Runs by Calendar Year**

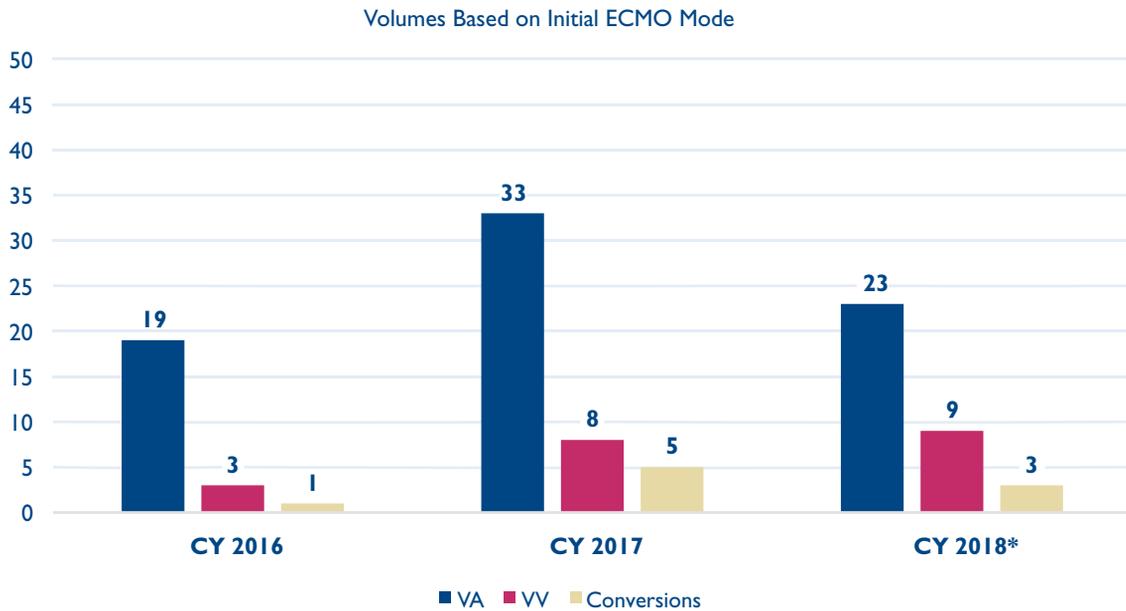


Fig. 5. Total Volume of ECMO Runs by Calendar Year. \* Volumes reported for 2018 are through September.

**VA ECMO Indication 2016-September 2018**

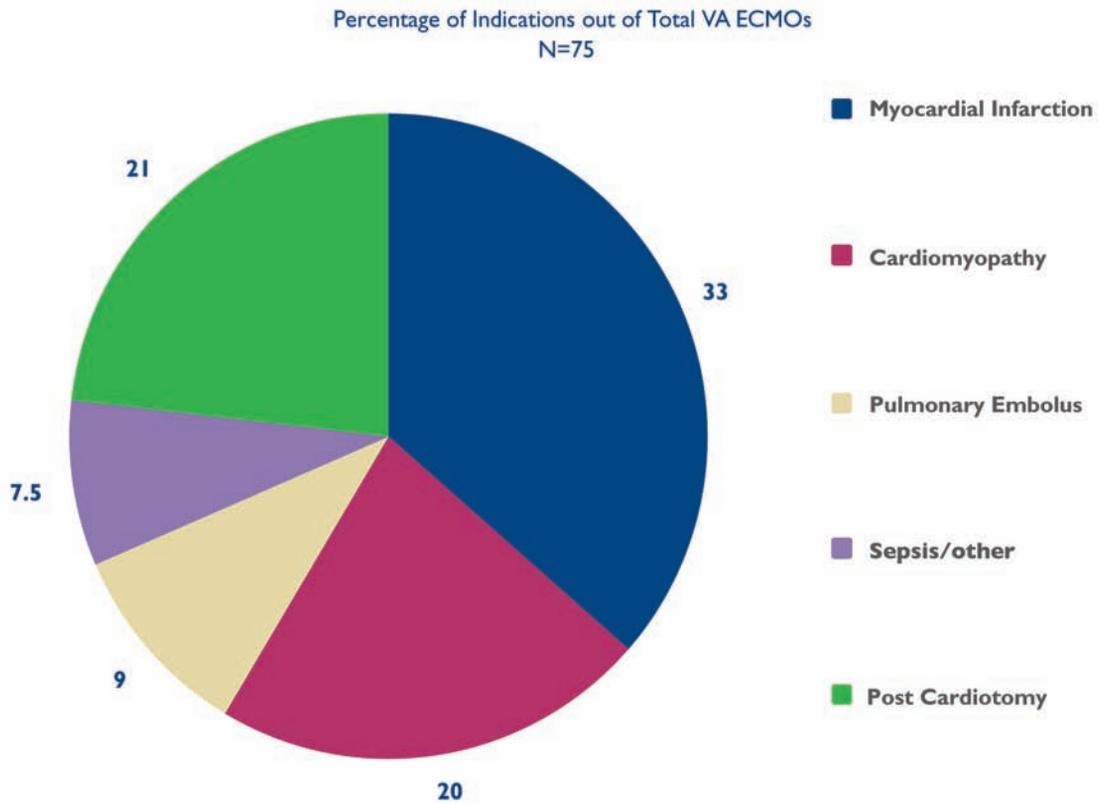


Fig. 6. VA ECMO Indication 2016-September 2018.

support is growing, as illustrated in Fig. 5 (previous page), which lacks the last quarter of calendar year 2018.

Nearly one-third of our VA ECMO implants are done to support patients with cardiogenic shock from a myocardial infarction. The next largest subset of patients is those with a known, pre-existing cardiomyopathy who present with acute decompensation and shock. Over the past three years, we have supported 14 patients with VA ECMO who were unable to be weaned from heart lung support following complex or complicated open-heart surgery (post-cardiotomy shock).<sup>5</sup> Fig. 6 (previous page) summarizes our indications for VA ECMO implantation.

In descending order of frequency, we most commonly perform VA ECMO implants for patients with cardiogenic shock as a result of:

1. Myocardial infarction
2. Post-cardiotomy cardiac failure
3. A pre-existing chronic cardiomyopathy.

Throughout the study period (2016-2018), the mean duration of ECMO support for the VA (n=75) and VV (n=20) cohorts has been 4.33 and 4.96 days, respectively (overall mean of 4.25 days).

The survival rate to explantation of the device

was 47% (35 of 75 patients) for patients originally implanted with VA ECMO, and 55% (11 of 20), for those originally implanted with VV ECMO. Figs. 7 and 8 illustrate patient survival to device explant for both VA and VV ECMO patients for each of the three study years. (See below for discussion of results.)

Survival to device implantation for VA ECMO in patients with shock following myocardial infarction was 45% (10/22); for those with refractory shock following open-heart surgery (post-cardiotomy) it was 85% (12/14); and for those with acute shock in the setting of decompensated chronic heart failure, survival was 42% (6/14). We should note that one additional post-cardiotomy patient was implanted with VV ECMO in a delayed fashion for isolated lung failure. This patient did not survive and is not included in the above VA ECMO data for post-cardiotomy shock.

**COMPLICATIONS**

ECMO is associated with a broad range of complications, some of which can have a significant impact on patient morbidity and mortality. The incidence and risk of ECMO-related complications are often difficult to determine in light of the heterogeneity of patients, pre-ECMO severities of illness, variable reporting among centers, and a lack of standardized

**VA Runs—Survival to Explant by Calendar Year**

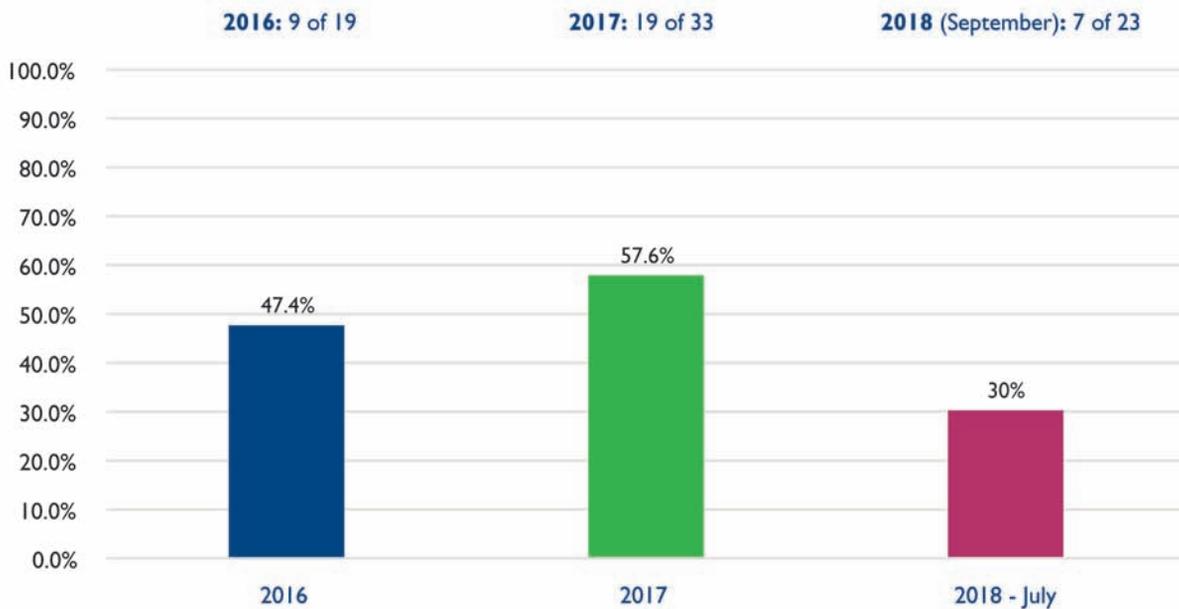


Fig. 7. VA Runs—Survival to Explant by Calendar Year.

**VV Runs—Survival to Explant by Calendar Year**

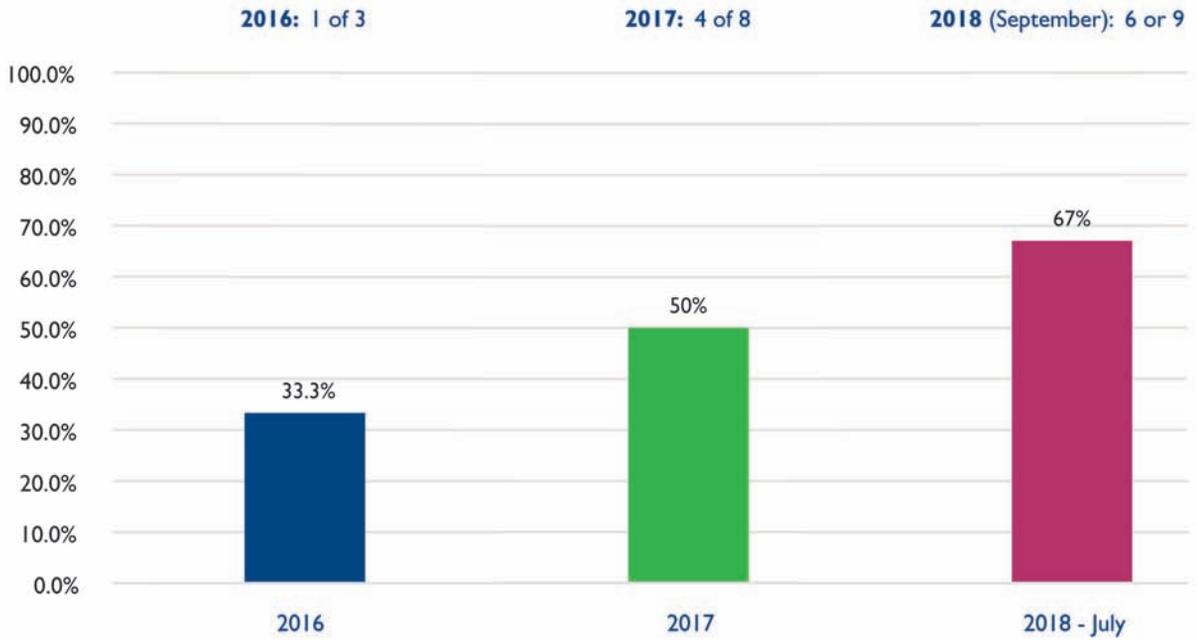


Fig. 8. VV Runs—Survival to Explant by Calendar Year.

**Complications 2016-2018**

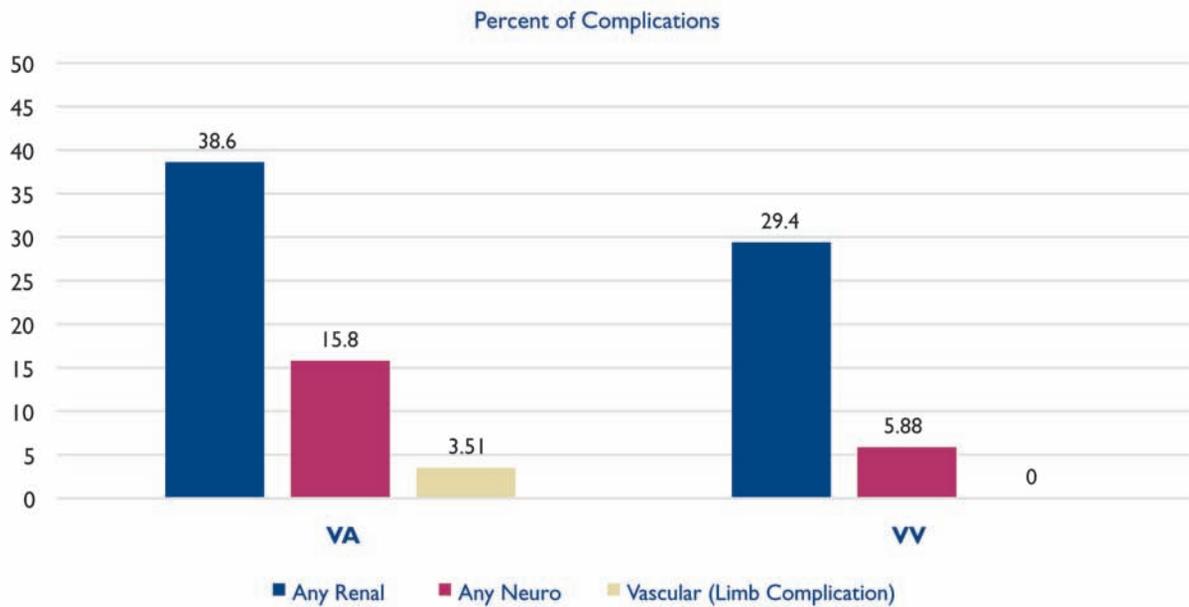


Fig. 9. Complications 2016-2018.

definitions in randomized trials.

Complications can arise from patient factors, or from malfunction of the ECMO circuit's components. Common complications arising from ECMO fall into four broad categories: renal, neurologic, vascular/ischemic, and hemorrhagic. Fig. 9 displays our ELSO recorded complication rates for all ECMO implants (VA and VV) from 2016 to 2018.

ECMO supported patients are susceptible to an estimated 40% risk of bleeding, which can occur at the cannula insertion site, surgical site (in case of post-cardiotomy support), or intracranially as a result of required anticoagulation. Clotting factors and blood elements become activated when they contact extracorporeal tubing. Most ECMO patients become thrombocytopenic during mechanical support, which may further potentiate their risk of bleeding.

The definition of acute kidney injury across studies is highly variable. The mode of ECMO (VA vs. VV) generally is not associated with a statistically significant difference in the incidence of acute kidney injury. In our series, there is a trend toward less acute renal injury with VV ECMO.

A broad range of neurological complications have been associated with ECMO, and can be devastating. These include subclinical cognitive impairment, seizures, neuropathy, ischemic and hemorrhagic strokes, and global hypoxic injury with death. In the LGH series, 15.8% of patients implanted with VA ECMO over the past three years have displayed some form of neurological complication, which is similar to the ELSO incidence of approximately 13%.<sup>3</sup> As is the case at LGH, the incidence of all neurologic complications is expected to be lower in VV ECMO, since the arterial system is not accessed and there is less risk of cerebral embolic events from diseased central or peripheral arteries.

From 2012 to 2015, we estimated a 14% incidence of major vascular/ischemic complications in all ECMO patients at LGH, of whom the vast majority received VA ECMO. In our early experience with VA ECMO, seven patients developed critical limb ischemia, and all ultimately died. In contrast, our most recent three years of data reveal a marked reduction to 3.51% in the overall rate of vascular/ischemic limb complications with VA ECMO. The routine addition of a distal leg perfusion sheath to the VA ECMO circuit is primarily responsible for the decrease in our vascular complication rate.

## DISCUSSION

As the number of adult ECMO cases continues to grow, it is vital that those who care for patients who could require ECMO become familiar with its basic mechanisms, update their knowledge of expected ECMO outcomes, and recognize those patients who might benefit from this technology. Cardiogenic shock from a variety of etiologies, including acute myocardial infarction, open-heart surgery, fulminant myocarditis, and decompensated chronic cardiomyopathy, remains a lethal disease that carries a mortality risk ranging widely between 50%-90%.

For patients with cardiogenic shock, VA ECMO can be used as a bridge to myocardial recovery, to cardiac transplantation, or to an implantable device for long-term mechanical circulatory support (LVAD). Mechanical circulatory support offers the potential to increase systemic perfusion without the adverse effects of inotropic and vasopressor agents, which increase myocardial oxygen consumption, often leading to myocardial ischemia, arrhythmias, and end-organ hypoperfusion. ECMO, in particular, also offers the advantage of rapid insertion (which can take place hospital-wide), biventricular support, and the ability to oxygenate and ventilate the patient who may also be suffering from respiratory failure. Optimal patient selection and timing of ECMO implantation are key to optimize outcomes. At LGH, our ECMO circuit is portable, and we routinely perform device implantation in the emergency department, intensive care unit, operating room, and cardiac catheterization suite.

As our ECMO program continues to grow, so do our implant volumes. LGH currently possesses the hardware to offer simultaneous ECMO support to three patients simultaneously. As noted above, between January 2016 and September 2018, we supported 75 patients with VA ECMO for cardiogenic shock deemed refractory to conventional medical therapy. Our survival rate of 47% (35 of 75 patients were discharged from the hospital) compares favorably with contemporary data for VA ECMO, which cite an overall survival to discharge of roughly 40%.<sup>3</sup>

In our series, patient survival to VA ECMO explantation peaked in 2017 at 57%, which likely reflects our growing experience in managing the ECMO patient through to recovery. The subsequent drop in survival in 2018 probably reflects our growing confidence in the benefit of ECMO, and our decision to offer device implantation to several patients whose disease state, upon review, was too advanced for ECMO to benefit.

This again, highlights the importance of patient selection and timeliness of implant.

As noted earlier (Fig. 6), post-cardiotomy cardiac failure is second only to myocardial infarction as an indication for mechanical support, as it carries a nearly 100% mortality in the absence of mechanical support. In the first few years of our ECMO program, our success with post-cardiotomy VA ECMO support was suboptimal, with < 30% of patients surviving to device explant.

At LGH, we perform approximately 600 cardiac surgical cases annually. Over the past three calendar years, we identified 14 cases of refractory post-cardiotomy shock unresponsive to conventional medical therapy, an incidence of 0.8%. Our ability to wean 85% of these patients from VA ECMO is a particularly attractive component of our evolving ECMO program. Although our series is small in comparison with other reports of ECMO for post-cardiotomy shock, our results are favorable.<sup>5</sup> Our ECMO program now allows salvage of postoperative shock patients who would otherwise die.

When myocardial recovery is inadequate, we have

also used VA ECMO to bridge patients to implantation of a durable left ventricular assist device at LGH.<sup>7</sup> One patient was successfully bridged to LVAD following acute myocardial infarction and remains alive nearly three years after LVAD implant. Two patients presenting with decompensated chronic heart failure were bridged to LVAD implantation following successful stabilization with VA ECMO. One of these patients is alive 12 months following LVAD implant, and the other died four days after LVAD implant due to irreversible brain injury.

## CONCLUSION

ECMO is no longer an experimental therapy, but is now an established, essential component of advanced adult cardiac and pulmonary care at Penn Medicine LGH. It has been responsible for salvage of patients with cardiac or pulmonary insufficiency from a broad array of conditions. All clinicians who care for adult patients who might experience cardiac or pulmonary failure should become familiar with the basic indications and uses of both venovenous (VV) and venoarterial (VA) support.

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