Stephens Andrew Frome (Orcid ID: 0000-0002-2271-750X)
Wickramarachchi Avishka (Orcid ID: 0000-0003-2623-7009)
Burrell Aidan JC (Orcid ID: 0000-0001-8430-9678)
Gregory Shaun David (Orcid ID: 0000-0002-5448-1917)

The Hemodynamics of Small Arterial Return Cannulae for Venoarterial Extracorporeal Membrane Oxygenation

Andrew F. Stephens, BEng, PhD[1,2*], Avishka Wickramarachchi, BEng[1,2], Aidan J.C. Burrell, MD, PhD[3], Rinaldo Bellomo, MD, FRACS, FCICM, PhD[4,5,6,7], Jaishankar Raman, MBBS MMed, FRACS, PhD[8], Shaun D Gregory, BEng, MSc, PhD[1,2]

[1]Cardio-respiratory Engineering and Technology Laboratory, Baker Heart and Diabetes Institute, Melbourne, Australia

[2]Department of Mechanical and Aerospace Engineering, Monash University, Melbourne, Australia

[3]Intensive Care Unit, Alfred Hospital, Melbourne, Australia

[4]Intensive Care Unit, Austin Hospital, Melbourne, Australia

[5]Department of Critical Care, The University of Melbourne, Melbourne, Australia

[6]Australian and New Zealand Intensive Care Research Centre, Monash University, School of Public Health and Preventive Medicine, Melbourne, Australia

[7]Department of Intensive Care, Royal Melbourne Hospital, Melbourne, Australia

[8]Cardiothoracic Surgery, University of Melbourne, Austin, & St Vincent's Hospitals, Melbourne, Australia

[*]Corresponding Author – research.andrew.stephens@gmail.com, Lab 2, Level 3, Baker Heart and Diabetes Institute, 75 Commercial Rd, Melbourne, AU, 3004, ORCiD: 0000-0002-2271-750X

Conflict of Interest

The authors declare no conflicts of interest related to this work.

Acknowledgements

This work was supported by Monash University. SG was supported by the National Heart Foundation of Australia (102062) and the National Medical Health and Research Council of Australia (APP2002567).

Running Title

Small Return Cannulae in VA ECMO

Summary of Author Contributions

All authors were involved in the study design, AS and AW conducted the experiments, all authors contributed to the analysis and interpretation of the results, all authors contributed significantly to the preparation and review of the manuscript. Funding and equipment for this study was secured by AS, SG, and JR.

Key Words

ECMO, Return Cannula, Arterial Cannula, Bleeding, Ischemia, Out of Hospital Cannulation, ECPR, Vascular Injury

Abstract

Background: Venoarterial extracorporeal membrane oxygenation (ECMO) provides mechanical support for critically ill patients with cardiogenic shock. Typically, the size of the arterial return cannula is chosen to maximize flow. However, smaller arterial cannulae may reduce cannula-related complications and be easier to insert. This *in vitro* study quantified the hemodynamic effect of different arterial return cannula sizes in a simulated acute heart failure patient.

Methods: Baseline support levels were simulated with a 17 Fr arterial cannula in an ECMO circuit attached to a cardiovascular simulator with targeted partial (2.0 L/min ECMO flow, 60-65 mmHg mean aortic pressure - MAP) and targeted full ECMO support (3.5 L/min ECMO flow and 70-75 mmHg MAP). Return cannula size was varied (13-21 Fr), and hemodynamics

were recorded while keeping ECMO pump speed constant and adjusting pump speed to restore desired support levels.

Results: Minimal differences in hemodynamics were found between cannula sizes in partial support mode. A maximum pump speed change of +600 rpm was required to reach the support target and arterial cannula inlet pressure varied from 79 (21 Fr) to 224 mmHg (13 Fr). The 15 Fr arterial cannula could provide the target full ECMO support at the targeted hemodynamics; however, the 13 Fr cannula could not due to the high resistance associated with the small diameter.

Conclusions: A 15 Fr arterial return cannula provided targeted partial and full ECMO support to a simulated acute heart failure patient. Balancing reduced cannula size and ECMO support level may improve patient outcomes by reducing cannula-related adverse events.

Introduction

Venoarterial extracorporeal membrane oxygenation (ECMO) provides mechanical support for the heart and lungs during cardiogenic shock and circulatory collapse. Typically, peripheral ECMO consists of a larger (19-25 Fr) drainage cannula placed percutaneously in the femoral or jugular vein with the tip in the vena cava or right atrium.[1] Blood is removed via this cannula by the ECMO pump, oxygenated externally and returned by a smaller arterial cannula placed percutaneously, most commonly in the common femoral artery with the tip advanced to the descending aorta.[1] The arterial return cannula may cause many adverse events, including vascular injury and dissection, bleeding, thrombus formation, and distal limb ischemia.[2] Vascular injury, bleeding, and lower limb ischemia are among the most frequently occurring cannula-related adverse events, are associated with in-hospital mortality, and in severe cases,

may require surgical intervention.[3–8] Bleeding and ischemia have both been reduced by using smaller arterial return cannulae.[9,10]

Historically, arterial cannula sizes are chosen to provide high flow (3.5 - 5 L/min) based on the patient's vessel size.[11] However, recent studies have suggested that outcomes can be improved with smaller cannulae by reducing incidences of bleeding and limb ischemia.[9,10,12] Furthermore, opting for a smaller arterial cannula may allow for easier cannulation in the out-of-hospital setting for extracorporeal cardiopulmonary resuscitation purposes (ECPR) and remote ECMO retrievals. While benefits have been reported when using smaller ECMO cannulae, there have only been limited comparisons showing how ECMO arterial return cannula size affects circuit or patient hemodynamics.[13]

This study aimed to quantify the hemodynamic effects of smaller arterial return cannulae during venoarterial ECMO support. Experiments were conducted to verify the pressure head-flow (HQ) characteristics of the cannulae and determine the hemodynamic effect of cannula size in a simulated adult acute heart failure patient under two fixed speeds and adjusted to provide partial and full ECMO support targets. Hemodynamics of interest were the simulated mean aortic pressure (MAP), ECMO flow rate, ECMO pump speed, and arterial cannula inlet pressure.

Methods

ECMO Circuit and Equipment

Based on a typical ECMO circuit at the author's institution, the circuit consisted of a 23 Fr venous drainage cannula (Ultraflex 97023, Medtronic, Dublin, Ireland) connected to the ECMO pump inlet (Bio-Medicus 550 Bio-Console with a Rotaflow adaptor and pump head, Medtronic Inc., Dublin, Ireland) by 200 cm of 3/8th inch (0.95 cm) inner diameter tubing. Seventy cm of 3/8th inch tubing was used to connect the ECMO pump outlet to the oxygenator,

which was then connected to the return cannula by a further 200 cm of 3/8th inch tubing. Arterial return cannulae sizes varied from 13 to 21 Fr and were sourced from two manufacturers based on availability (HLS, Getinge, Gothenburg, Sweden – 13 and 15 Fr; Bio-Medicus, Medtronic, Dublin, Ireland – 17, 19, and 21 Fr). In specified experiments, drainage cannula size was increased to 30 Fr (LV89530, Edwards Lifesciences, CA, USA) to investigate the effects of the venous drainage cannula size on flow capacity.

The working fluid was a water and glycerol mixture (60%/40% w/w – 3.6 cP), within the normal range of blood viscosity at 37°C.[14] All pressures were acquired by TruWave disposable pressure sensors (Edwards Lifesciences, CA, USA), while flow rates were acquired by ultrasonic flow rate sensors (ECMO flow – 9PXL with TS410 Flow Meter, Transonic Inc, NY, USA; cardiac output – SonoTT with Digiflow EXT flow meter; em-tec GmbH, Finning, Germany). All data was acquired by a dSPACE 1202 MicroLabBox (dSPACE GmbH, Paderborn, Germany) at 200 Hz.

Pressure Head-Flow Characteristics

A simple circuit was created to evaluate the HQ (pressure head-flow) characteristics of each return cannulae size (Figure 1 - A). The 23 Fr drainage cannula was placed in a tank of water/glycerol solution and secured to prevent occlusion of the drainage holes. The return cannula was secured to the top of the tank (in air) horizontally to ensure all flow returned to the tank with no gravitational effects. One pressure sensor was located at the arterial return cannula sidearm Luer port (arterial cannula inlet pressure), and another was exposed to atmosphere at the same height as the return cannula outlet (arterial cannula tip pressure). Pressure sensors were zeroed to atmosphere, and the ECMO pump was turned on. Pump speed was increased from 1000 to 4000 rpm in 200 rpm steps to generate a range of pressure head (the difference between arterial cannula inlet pressure and atmospheric pressure readings) and

ECMO flow rate values. These values were then extracted and fitted to a third-order polynomial function for plotting.

Hemodynamic Experiments

A mechanical cardiovascular simulator (mock circulatory loop - MCL) was used to evaluate the effect of arterial return and venous drainage cannula size on different hemodynamics. The MCL is a five-element Windkessel model and includes lumped pulmonary and systemic circulations, a Frank-Starling mechanism, and auto-regulated vascular resistances. The MCL is described in detail elsewhere.[15] The 23 Fr drainage cannula was connected to the MCL's right atrium, and the return cannulae were connected to the MCL's descending aorta after the compliance chamber (Figure 1 – B). Pulmonary vascular resistance and heart rate were maintained at 250 dyne·s·cm^{-5} and 80 beats per minute throughout. The MCL was set to simulate a patient in acute left-sided heart failure without right ventricular involvement (as might occur in myocardial infarction), with a MAP of 67 mmHg, a cardiac output of 1.6 L/min, left and right atrial pressures of 16 and 7 mmHg respectively, a mean pulmonary artery pressure of 22 mmHg, and a systemic vascular resistance of 2800 dyne·s·cm^{-5}.[16] The 17 Fr arterial return cannula was used to establish the baseline supported condition and restored hemodynamics to the desired level under targeted partial support (2.0 L/min ECMO flow, 3.5 L/min total cardiac output) and full support (3.5 L/min ECMO flow, 4.4 L/min total cardiac output) based on the authors' institutional practice (Table 1).[11] Systemic vascular resistance was reduced from 2800 to 1300 dyne·s·cm^{-5} simulating the use of vasodilators.

Each of the different cannula sizes (13, 15, 19, and 21 Fr) were then used to support the simulated patient and compared against the 17 Fr baseline at 2600 rpm and 3600 rpm. The ECMO pump speed was also adjusted for each cannula size until the desired hemodynamics were achieved (Table 1), and the speed was noted, resulting in N=20 experiments.

To determine the effect of the venous cannulae on flow restriction, additional experiments were conducted with a larger venous drainage cannula to determine if a larger drainage cannula would provide more flow to the smaller arterial return cannulae. Venous drainage cannulae size was increased from 23 to 30 Fr. The larger drainage cannula was then combined with a smaller subset of arterial return cannulae of sizes 13, 17, and 21 Fr to find the differences in the baseline at the extremes. Experiments were again run at two fixed speeds and under targeted partial and full support resulting in a further N = 12 experiments.

Figure 1: A - Experimental test rig for determining pressure head-flow characteristics of different sized EMCO arterial return cannulae (return cannula tip is located above the tank in air). B -Schematic of the mock circulatory loop used to simulate cardiogenic shock.

AOC, PAC, PVC, SVC – aortic and pulmonary arterial, pulmonary and systemic venous compliance chambers; SQ, PQ, EQ – systemic, pulmonary, and ECMO flow meters; Pump, Ox – ECMO pump and oxygenator; LA, LV, RA, RV – left and right atria and ventricles; MV, AV, TV, PV – mitral, aortic, tricuspid and pulmonary valves; SVR, PVR – systemic and pulmonary vascular resistance pinch valves; ID – inner diameter; Green Circle – arterial cannula inlet pressure measurement.

Table 1: Baseline cardiogenic shock and target hemodynamic variables for targeted full and partial extracorporeal membrane oxygenation (ECMO) support. MAP – mean aortic pressure; SVR – systemic vascular resistance.

Results

Pressure Head-Flow Experiments

Experimental data produced fitted HQ curves for each of the tested cannulae. Experimental data closely matched data reported in the datasheets for the cannulae, with an additional pressure drop due to the water/glycerol solution used in the experiments, which has a higher viscosity than the water used in the datasheets (Figure 2).[17,18] The maximum flow through the

13 Fr cannula was 2.7 L/min with a pressure drop (inlet pressure - tip pressure) greater than 300 mmHg (maximum measurable by the pressure sensors); achieved under the maximum speed (4470 rpm) of the Bio-Medicus pump used in these experiments. These values can be used to calculate the pressure drop across a given cannula at a known flow rate when situated in the MCL.

Figure 2: Pressure head-flow (HQ) curves generated experimentally and compared to data published in datasheets. [17,18]

Hemodynamic Experiments (23 Fr Drainage)

A pump speed of 2600 rpm was found to meet the partial support target with the 17 Fr baseline cannula, while a pump speed of 3600 rpm provided the full support target; all other cannula sizes were compared to this baseline. At the set speed of 2600 rpm, there was only an 8 mmHg difference in MAP and 0.9 L/min in ECMO flow rate between the 21 and 13 Fr cannulae. Arterial cannula inlet pressure ranged from 89 mmHg (21 Fr) to 150 mmHg (13 Fr) (Table 2). At the set speed of 3600 rpm, there was a greater difference in MAP (13 mmHg) and ECMO flow rate (1.7 L/min) between the 21 and 13 Fr cannulae due to the exponential increase in the cannula HQ characteristics (Table 2). At 3600 rpm, arterial cannula inlet pressure ranged from 132 mmHg (21 Fr) to a supra-physiologic 282 mmHg (13 Fr). Other hemodynamic variables were unremarkable.

Table 2: Hemodynamics for different cannula sizes at fixed pump speeds of 2600 rpm and 3600 rpm and following speed adjustment when targeting the specific levels of partial and full extracorporeal membrane oxygenation (ECMO) support.

ECMOQ – extracorporeal membrane oxygenator flow rate; CO – cardiac output = ECMO flow + ventricular output; LAP – left atrial pressure; RAP – right atrial pressure; MAP – mean aortic pressure; MPAP – mean pulmonary artery pressure.

Results for restoration of target partial and full support hemodynamics via ECMO pump speed adjustments are shown in Table 3. For partial support, all cannulae reached the target level of support, and all hemodynamics were matched to the baseline (17 Fr support) within sensor precision (± 0.1 L/min and ± 2 mmHg) (Table 2). The largest change in speed required to reach the partial support target was from 2600 to 3200 rpm (+600 rpm) for the 13 Fr cannula. ECMO arterial cannula inlet pressure ranged from 79 mmHg (21 Fr) to 224 mmHg (13 Fr). For full support, the 15 to 21 Fr cannulae were able to reach the full-support target, and all hemodynamics were again matched to baseline within sensor precision (Table 2). Meanwhile, the 13 Fr cannula was unable to reach the targeted full-support, providing only 3.2 L/min outflow at the pump's maximum speed (4470 rpm). This speed was the largest change for the full support scenario (+870 rpm for 3600 to 4470 rpm). Arterial cannula inlet pressures varied from 116 mmHg (21 Fr) to above 300 mmHg (pressure sensor maximum) with the 13 Fr cannula (Figure 3).

Figure 3: Arterial cannula inlet pressure at target partial (left) and full (right) extracorporeal membrane oxygenation (ECMO) support. Datapoint text indicates pump speed in RPM. Δ data point did not reach the target level and was greater than the maximum inlet pressure of 300 mmHg.

Hemodynamic Experiments (30 Fr Drainage)

Hemodynamics for fixed speed ECMO support with an increased (30 Fr) drainage cannula size were comparable to the 23 Fr drainage cannula experiments at 2600 and 3600 rpm, restoring baseline within the tolerances of the sensors (Table 3). Meanwhile, similar pump speeds to the

23 Fr drainage cannula (± 100 rpm) were found to restore hemodynamics to the partial and full support target levels, demonstrating that a larger drainage cannula did not drastically change hemodynamics related to the ECMO circuit (Table 3). Finally, the 13 Fr cannula still did not reach the 3.5 L/min target support level, even with a larger drainage cannula, reaching only 3.3 L/min with the 30 Fr cannula (compared to 3.2 L/min with the 23 Fr drainage cannula).

Table 3: Hemodynamics produced at fixed speeds of 2600 and 3600 rpm and after adjusting pump speed to meet the target partial and full support levels with different arterial return cannula sizes and a 30 Fr venous drainage cannula.

ECMOQ – ECMO flow rate; CO – cardiac output = ECMO flow + ventricular output; MAP – mean aortic pressure.

Discussion

This study compared the effects of ECMO arterial return cannula size on both patient and circuit hemodynamics. The study found that a 15 Fr cannula could provide the targeted full ECMO support in the simulated patient but that a 13 Fr cannula could not, even at the maximum speed of the Bio-Medicus pump (4470 rpm). At low flow rates (2600 rpm and partial support mode), there were only minor differences in hemodynamics for different cannula sizes, with the most notable difference being the pressure at the arterial cannula inlet. For high flow rates (3600 rpm and full support), the differences in hemodynamics were greater. In this study, increasing the venous drainage cannula from 23 to 30 Fr only resulted in a 0.1 L/min increase in maximal ECMO flow rate through the 13 Fr arterial return cannula. This is in keeping with previous studies using small neonatal cannulae where venous drainage size had a lesser effect on the ECMO flow capabilities.[19] Characterizing the differences in hemodynamics between cannula sizes is useful, as smaller cannulae may be safer and reduce cannula-related adverse events.

In a single-center study of 101 patients, Takayama et al. demonstrated that a lower level of ECMO support coupled with a smaller cannula resulted in no difference in 30-day survival while reducing bleeding and ischemia.[9] The study found no significant difference in 30-day survival with large cannulae compared to small cannulae but did find more cannula related adverse events and significantly more cannula bleeding events for the large cannulae. The lowest support level used in that study was similar to the highest support level used in this study; however, that patient cohort may not represent the global population due to the smaller patient cohort size.

Similarly, Kim et al. demonstrated non-inferiority of small cannulae (14-15 Fr) on survival to discharge in 165 patients compared to large cannulae (16-21 Fr).[10] They also demonstrated a significantly shorter ECMO duration and significantly less limb ischemia with the smaller cannulae. The results from our study complements the previous clinical work through a controlled and repeatable analysis in a simulated patient with further characterization of the hemodynamics, demonstrating that full flow can be achieved with smaller cannulae within the pump speed ranges of the Rotaflow pump and Bio-Medicus controller.

Despite reaching target flows with minimal changes in patient hemodynamics, this study also revealed a supra-physiological inlet pressure in smaller cannulae at higher flows, > 300 mmHg in the 13 Fr cannula, resulting in a large pressure drop across the cannula to the aortic pressure levels recorded between 65 – 75 mmHg. The pressure drop across the cannula depends on the flow rate and viscosity of the working fluid and the cannula properties themselves. Other studies have investigated the pressure drop across smaller venous and arterial return cannulae, but are difficult to compare to this study as they used whole human blood (a non-Newtonian fluid) and reported their pressure drop with respect to speed, which is pump-brand dependent, unlike flow rate (pump independent) used in this study.[20,21] However, such studies did show that the tip configuration (number of side holes, orientation of side holes) did not significantly

affect the pressure drop across the cannulae. The tip configuration may affect the exit velocity of the cannulae; however previous studies have shown that even in non-dispersing cannulae with a single hole at the tip, blood velocity decreases to physiological levels (< 1.5 m/s) within 40-50 mm of the cannula tip.[22,23] This may result in higher dynamic pressures in the outflow jet, but the averaged dispersed pressure will be the mean aortic pressure. The effect of sandblasting of the arterial wall by smaller cannulae with higher velocities is currently under investigation by the author's group through simulation and particle image velocimetry studies. The measured pressures in an ECMO or cardiopulmonary bypass circuit may be misleading, as they represent the cannula inlet pressure rather than the tip. This difference in pressure may lead to an assumption of harmful tip pressures and may mislead practitioners into using larger cannulae.

The high pressures at the inlet of the cannulae may cause concern about hemolysis. However, pressure alone does not cause hemolysis, which is a function of shear stress, exposure time, and blood-surface interaction.[24] Several studies have investigated the links between pressure and hemolysis and have determined that blood can withstand extremely high and low static pressures (in the range of 1000 to -700 mmHg).[25,26] However, one study has suggested that hemolysis may be more likely in the presence of high positive pressures at high shear rates.[27] Clinically, ECMO cannula hemolysis has been previously investigated in smaller ECMO cannulae at different flow rates. At low flow rates (≤ 2.5 L/min), Appelt et al. found no significant difference in hemolysis between 17 and 15 Fr cannulae in 500 patients in a single-center study.[28] At high flow rates (> 3 L/min), that study reported significantly higher plasma free hemoglobin with a 15 Fr cannula compared to a 17 Fr cannula, indicating more hemolysis. Conversely, there were greater reductions in plasma free hemoglobin for the 15 Fr cannula than the 17 Fr cannula in the ECPR setting (34% vs 22% within one day after ECMO initiation),

perhaps indicating a complicated interaction between biological hemolysis caused during heart failure and mechanical hemolysis caused by the pump and cannulae. Future studies could focus on the benefits of a smaller cannula to vascular complications (ischemia and bleeding) while looking for indicators of hemolysis. A tendency to use smaller cannulae at reduced support levels may also have benefits outside of the hospital setting.

Extracorporeal cardiopulmonary resuscitation (ECPR) is an emerging method of advanced life support that has been recently added to the American Heart Association Advanced Life Support Guidelines.[29] ECPR has been performed in an out-of-hospital setting and is gaining popularity after recent successes in resuscitating refractory cardiac arrest patients.[30–32] In an out-of-hospital setting, smaller cannulae may be easier and, therefore, faster to insert. Partial support (as simulated in this research) may be adequate to support the patient until they reach the hospital, at which time full ECMO support and additional interventions can be considered.

Limitations

The main limitation of this study is that it was conducted in a mock circulatory loop (MCL). The MCL has been validated to simulate hemodynamics over a range of cardiovascular states but does not mimic many biological and anatomical processes. The absence of a Baroreflex, inability to simulate access insufficiency (vessel collapse), and the absence of anatomical features (related to cannula positioning) will result in different hemodynamics than what may be observed clinically. Furthermore, this study used a Newtonian mixture of water and glycerol as a blood analogue. In reality, blood is non-Newtonian and may have a different flow response to what was observed in this study, particularly at the high shear rates likely occurring in the small cannulae. Not using blood in this study has also prevented the investigation of hemolysis and Von Willebrand factor effects associated with small cannulae run at higher ECMO speeds with more pump heat generation, which should be the focus of future work. This study only

simulated an adult patient with a single disease etiology and will not be representative of all patient types, for instance, patients with severe right heart failure and elevated right atrial pressures. About 55% of the patients who receive ECMO are pediatric and neonates, and this data may not extend to those populations.[33]

Conclusion

This study aimed to quantify the effects of smaller arterial return cannulae on simulated patient and circuit hemodynamics. This study demonstrated that smaller arterial return cannulae (15Fr) could provide the targeted partial and full ECMO blood flow rates in a simulated acute heart failure model. The study supports mounting clinical evidence, suggesting smaller cannulae may provide adequate hemodynamic support while also being safer to insert. Further investigations should explore if smaller canulae result in fewer vascular injuries and the possible incidence of hemolysis caused by small cannulae at high pressure and pump speeds. Outcomes from such research may provide guidelines on balancing cannula size to reduce vascular injury, bleeding, and ischemia while avoiding harmful hemolysis, thereby improving patient outcomes.

References

1. Pavlushko E, Berman M, Valchanov K. Cannulation techniques for extracorporeal life support. Ann Transl Med. 2017;5(4).

2. Cheng R, Hachamovitch R, Kittleson M, Patel J, Arabia F, Moriguchi J, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: A meta-analysis of 1,866 adult patients. Ann Thorac Surg. 2014;97(2):610–6. Available from: http://dx.doi.org/10.1016/j.athoracsur.2013.09.008

3. Yang F, Hou D, Wang J, Cui Y, Wang X, Xing Z, et al. Vascular complications in adult postcardiotomy cardiogenic shock patients receiving venoarterial extracorporeal membrane oxygenation. Ann Intensive Care. 2018;8(1). Available from: https://doi.org/10.1186/s13613-018-0417-3

4. Aubron C, Cheng AC, Pilcher D, Leong T, Magrin G, Cooper DJ, et al. Factors associated with outcomes of patients on extracorporeal membrane oxygenation support: a 5-year cohort study. Crit Care. 2013;17(2):R73.

5. Tanaka D, Hirose H, Cavarocchi N, Entwistle JWC. The Impact of Vascular Complications on Survival of Patients on Venoarterial Extracorporeal Membrane Oxygenation. Ann Thorac Surg. 2016;101(5):1729–34. Available from: http://dx.doi.org/10.1016/j.athoracsur.2015.10.095

6. Rupprecht L, Lunz D, Philipp A, Lubnow M, Schmid C. Pitfalls in percutaneous ECMO cannulation. Hear lung Vessel. 2015;7(4):320–6.

7. Pozzi M, Koffel C, Djaref C, Grinberg D, Fellahi JL, Hugon-Vallet E, et al. High rate of arterial complications in patients supported with extracorporeal life support for drug intoxication-induced refractory cardiogenic shock or cardiac arrest. J Thorac Dis. 2017;9(7):1988–96.

8. Lotz C, Streiber N, Roewer N, Lepper PM, Muellenbach RM, Kredel M. Therapeutic Interventions and Risk Factors of Bleeding during Extracorporeal Membrane Oxygenation. ASAIO J. 2017;63(5):624–30.

9. Takayama H, Landes E, Truby L, Fujita K, Kirtane AJ, Mongero L, et al. Feasibility of smaller arterial cannulas in venoarterial extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg. 2015;149(5):1428–33. Available from: http://dx.doi.org/10.1016/j.jtcvs.2015.01.042

10. Kim J, Cho YH, Sung K, Park TK, Lee GY, Lee JM, et al. Impact of Cannula Size on Clinical Outcomes in Peripheral Venoarterial Extracorporeal Membrane Oxygenation. ASAIO J. 2019 Aug;65(6):573–9. Available from: https://journals.lww.com/00002480-201908000-00009

11. Extracorporeal Life Support Organization. ELSO Guidelines for Cardiopulmonary Extracorporeal Life Support. Extracorpor Life Support Organ. 2017;(August):1–26. Available from: https://www.elso.org/Resources/Guidelines.aspx

12. Bonicolini E, Martucci G, Simons J, Raffa GM, Spina C, Coco V Lo, et al. Limb ischemia

in peripheral veno-arterial extracorporeal membrane oxygenation: A narrative review of incidence, prevention, monitoring, and treatment. Crit Care. 2019;23(1):1–17.

13. Landes EL, Truby L, Mundy L, Yang J, Kirtane AJ, Mongero L, et al. Partial Flow with 15F Arterial Cannula Provides Sufficient Circulatory Support in Veno-Arterial Extracorporeal Membrane Oxygenation. J Hear Lung Transplant. 2014;33(4):S250. Available from: http://dx.doi.org/10.1016/j.healun.2014.01.655

14. Rand P, Lacombe E, Hunt H, Austin W. VISCOSITY OF NORMAL HUMAN BLOOD UNDER NORMOTHERMIC AND HYPOTHERMIC CONDITIONS. J Appl Physiol. 1964 Jan;19(1):117–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14104265

15. Gregory SD, Pauls JP, Wu EL, Stephens A, Steinseifer U, Tansley G, et al. An advanced mock circulation loop for in vitro cardiovascular device evaluation. Artif Organs. 2020 Jun 3;44(6):aor.13636. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/aor.13636

16. Fincke R, Hochman JS, Lowe AM, Menon V, Slater JN, Webb JG, et al. Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock: A report from the SHOCK trial registry. J Am Coll Cardiol. 2004;44(2):340–8. Available from: http://dx.doi.org/10.1016/j.jacc.2004.03.060

17. Maquet Getinge Group. HLS Cannulae Brochure [Internet]. Rastatt; 2015. p. 1–6. Available from: https://www.getinge.com/dam/hospital/documents/english/hls_cannulae_brochure-en-non_us_japan.pdf

18. Medtronic. Bio-Medicus NextGen Brochure [Internet]. Minneapolis; 2019. p. 1–8. Available from: https://europe.medtronic.com/content/dam/medtronic-com/products/cardiovascular/cannulae/soft-flow-arterial-cannulae/documents/Bio-Medicus_NextGen_Brochure_1.pdf

19. Qiu F, Clark JB, Kunselman AR, Ündar A, Myers JL. Hemodynamic evaluation of arterial and venous cannulae performance in a simulated neonatal extracorporeal life support circuit. Perfusion. 2011;26(4):276–83.

20. Broman LM, Prahl Wittberg L, Westlund CJ, Gilbers M, Perry da Câmara L, Swol J, et al. Pressure and flow properties of cannulae for extracorporeal membrane oxygenation I: return (arterial) cannulae. Perfus (United Kingdom). 2019;34(1_suppl):58–64. Available from: https://doi.org/10.1177/0267659119830521

21. Broman LM, Prahl Wittberg L, Westlund CJ, Gilbers M, Perry da Câmara L, Westin J, et al. Pressure and flow properties of cannulae for extracorporeal membrane oxygenation II: drainage (venous) cannulae. Perfus (United Kingdom). 2019;34(1_suppl):65–73. Available from: https://doi.org/10.1177/0267659119830514

22. McDonald CI, Bolle E, Lang HF, Ribolzi C, Thomson B, Tansley GD, et al. Hydrodynamic evaluation of aortic cardiopulmonary bypass cannulae using particle image velocimetry. Perfus (United Kingdom). 2016;31(1):78–86.

23. Lemétayer J, Broman LM, Prahl Wittberg L. Confined jets in co-flow: effect of the flow rate ratio and lateral position of a return cannula on the flow dynamics. SN Appl Sci.

2020;2(3):1–15. Available from: https://doi.org/10.1007/s42452-020-2077-9

24. Leverett LB, Hellums JD, Alfrey CP, Lynch EC. Red Blood Cell Damage by Shear Stress. Biophys J. 1972;12(3):257–73. Available from: http://dx.doi.org/10.1016/S0006-3495(72)86085-5

25. Pohlmann JR, Toomasian JM, Hampton CE, Cook KE, Annich GM, Bartlett RH. The relationships between air exposure, negative pressure, and hemolysis. ASAIO J. 2009;55(5):469–73.

26. Chambers SD, Laberteaux KR, Merz SI, Montoya PJ, Bartlett RH. Effects of Static Pressure on Red Blood Cells on Removal of the Air Interface. ASAIO J. 1996 Nov;42(6):947–50. Available from: http://journals.lww.com/00002480-199642060-00005

27. Yasuda T, Funakubo A, Miyawaki F, Kawamura T, Higami T, Fukui Y. Influence of static pressure and shear rate on hemolysis of red blood cells. ASAIO J. 2001;47(4):351–3.

28. Appelt H, Philipp A, Mueller T, Foltan M, Lubnow M, Lunz D, et al. Factors associated with hemolysis during extracorporeal membrane oxygenation (ECMO)—Comparison of VA- versus VV ECMO. PLoS One. 2020;15(1):1–14. Available from: http://dx.doi.org/10.1371/journal.pone.0227793

29. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, et al. Part 7: Adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18):S444–64.

30. Lamhaut L, Hutin A, Deutsch J, Raphalen JH, Jouffroy R, Orsini JP, et al. Extracorporeal Cardiopulmonary Resuscitation (ECPR) in the Prehospital Setting: An Illustrative Case of ECPR Performed in the Louvre Museum. Prehospital Emerg Care. 2017;21(3):386–9.

31. Stub D, Bernard S, Pellegrino V, Smith K, Walker T, Sheldrake J, et al. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial). Resuscitation. 2015;86(2015):88–94. Available from: http://dx.doi.org/10.1016/j.resuscitation.2014.09.010

32. Singer B, Reynolds JC, Lockey DJ, O'Brien B. Pre-hospital extra-corporeal cardiopulmonary resuscitation. Scand J Trauma Resusc Emerg Med. 2018;26(1):1–8.

33. Extracorporeal Life Support Organization. ECLS Registry International Summary - July 2020 [Internet]. Ann Arbor, Mi; 2020. p. 1. Available from: https://www.elso.org/Registry/Statistics/InternationalSummary.aspx

Tables

Table 1: Baseline cardiogenic shock and target hemodynamic variables for targeted full and partial extracorporeal membrane oxygenation (ECMO) support. MAP – mean aortic pressure; SVR – systemic vascular resistance.

Condition	ECMO Flow Rate	ECMO Speed	MAP (mmHg)	SVR (dyne·s·cm^{-5})

	(L/min)	(rpm)		
Cardiogenic Shock	-	-	67	2800
Partial Support	2.0	2600	60-65	1300
Full Support	3.5	3600	70-75	1300

Table 2: Hemodynamics for different cannula sizes at fixed pump speeds of 2600 rpm and 3600 rpm and following speed adjustment when targeting the specific levels of partial and full extracorporeal membrane oxygenation (ECMO) support.

ECMOQ – extracorporeal membrane oxygenator flow rate; CO – cardiac output = ECMO flow + ventricular output; LAP – left atrial pressure; RAP – right atrial pressure; MAP – mean aortic pressure; MPAP – mean pulmonary artery pressure.

Condition	Speed (rpm)	ECMOQ (L/min)	Arterial Cannula Inlet Pressure (mmHg)	CO (L/min)	MAP (mmHg)
Cardiogenic Shock	-	-	-	1.6	67
Fixed Speed - 2600 rpm					
21 Fr	2600	2.4	89	3.7	65
19 Fr	2600	2.2	100	3.5	64
17 Fr*	2600	2.1	112	3.5	63
15 Fr	2600	1.8	126	3.4	61
13 Fr	2600	1.5	150	3.1	57
Fixed Speed - 3600 rpm					
21 Fr	3600	4.1	132	4.6	78
19 Fr	3600	3.9	160	4.5	76
17 Fr*	3600	3.5	189	4.4	75
15 Fr	3600	3.1	229	4.2	73
13 Fr	3600	2.4	282	3.7	65
Target Partial Support					
21 Fr	2360	2.0	79	3.4	61
19 Fr	2400	2.0	91	3.4	62
17 Fr*	2600	2.0	112	3.5	63
15 Fr	2800	2.0	143	3.5	63
13 Fr	3200	2.0	224	3.4	62
Target Full Support					
21 Fr	3260	3.5	116	4.3	73
19 Fr	3400	3.5	146	4.4	74
17 Fr*	3600	3.5	189	4.4	75
15 Fr	4000	3.5	282	4.4	75
13 Fr	4470^	3.2	>300^	4.2	72

*ECMO Baseline ^Maximum limit of pressure sensor and ECMO pump speed

Table 3: Hemodynamics produced at fixed speeds of 2600 and 3600 rpm and after adjusting pump speed to meet the targeted partial and full support levels with different arterial return cannula sizes and a 30 Fr venous drainage cannula.

ECMOQ – ECMO flow rate; CO – cardiac output = ECMO flow + ventricular output; MAP – mean aortic pressure.

Condition	Speed (rpm)	ECMOQ (L/min)	Arterial Cannula Inlet Pressure (mmHg)	CO (L/min)	MAP (mmHg)
Cardiogenic Shock	-	-	-	1.6	67
Fixed Speed - 2600 rpm					
21 Fr	2600	2.4	88	3.6	64
17 Fr*	2600	2.1	110	3.5	62
13 Fr	2600	1.5	149	3.1	56
Fixed Speed - 3600 rpm					
21 Fr	3600	4.1	131	4.6	77
17 Fr*	3600	3.5	190	4.2	73
13 Fr	3600	2.5	279	3.7	65
Target Partial Support					
21 Fr	2360	2.0	79	3.4	61
17 Fr*	2600	2.1	110	3.5	62
13 Fr	3200	2.0	208	3.4	60
Target Full Support					
21 Fr	3260	3.5	115	4.3	73
17 Fr*	3600	3.5	190	4.2	73
13 Fr	4470^	3.3	>300^	4.1	71

*ECMO Baseline ^Maximum limit of pressure sensor and ECMO pump speed

Legends

Graphical Abstract: Smaller extracorporeal membrane oxygenation cannulae provided targeted partial and full support in a mechanical cardiovascular simulator with minimal differences in patient hemodynamics but exponential changes in arterial cannula inlet pressures.

AOC, PAC – Aortic and pulmonary arterial compliance chambers; SVC, PVC – Systemic and pulmonary venous compliance chambers; LV, RV, LA, RA – Left and right ventricles and atria; AV, MV, PV, TV – Aortic, mitral, pulmonary, and tricuspid valves; SVR, PVR – lumped systemic and pulmonary vascular resistance; SQ, PQ, EQ – Systemic, pulmonary, and ECMO flow meters; Pump, Ox – ECMO blood pump and oxygenator.

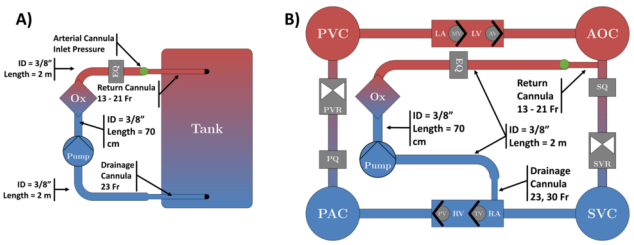
Figure 1: A - Experimental test rig for determining pressure head-flow characteristics of different sized EMCO arterial return cannulae (return cannula tip is located above the tank in air). B -Schematic of the mock circulatory loop used to simulate cardiogenic shock.

AOC, PAC, PVC, SVC – aortic and pulmonary arterial, pulmonary and systemic venous compliance chambers; SQ, PQ, EQ – systemic, pulmonary, and ECMO flow meters; Pump, Ox

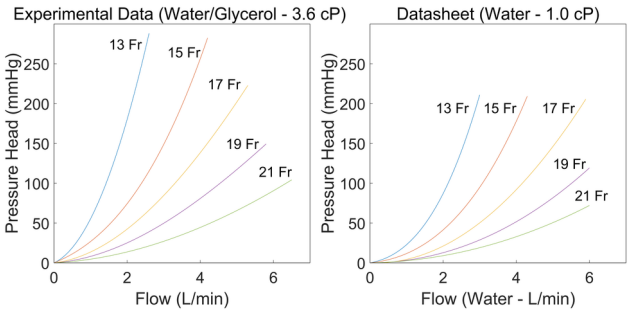
– ECMO pump and oxygenator; LA, LV, RA, RV – left and right atria and ventricles; MV, AV, TV, PV – mitral, aortic, tricuspid and pulmonary valves; SVR, PVR – systemic and pulmonary vascular resistance pinch valves; ID – inner diameter; Green Circle – arterial cannula inlet pressure measurement.

Figure 2: Pressure head-flow (HQ) curves generated experimentally and compared to data published in datasheets. [17,18]

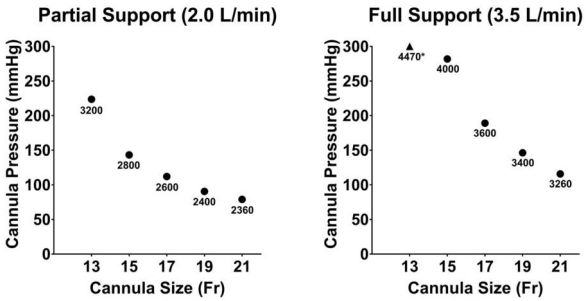
Figure 3: Arterial cannula inlet pressure at target partial (left) and full (right) extracorporeal membrane oxygenation (ECMO) support. Datapoint text indicates pump speed in RPM. Δ data point did not reach the target level and was greater than the maximum inlet pressure of 300 mmHg.



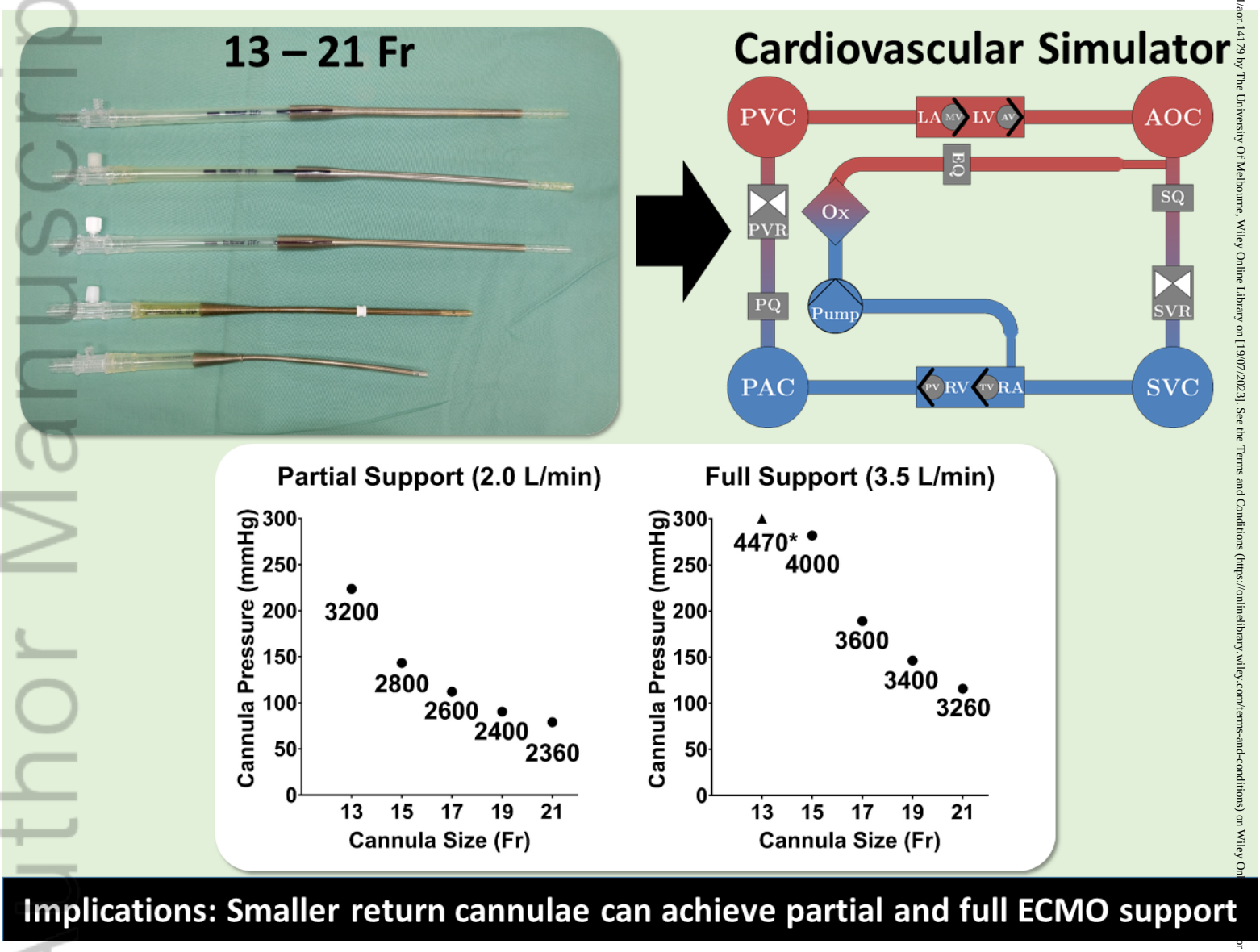
AOR_14179_Figure 1 - MCL and Tank.tif



AOR_14179_Figure 2 - HQ Curves.tif



AOR_14179_Figure 3 - Compare.jpg



Implications: Smaller return cannulae can achieve partial and full ECMO support