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An experimental model of veno-venous arterial extracorporeal membrane oxygenation

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Abstract

Introduction: Veno-venous arterial extracorporeal membrane oxygenation is a hybrid-modality of extracorporeal membrane oxygenation combining veno-venous and veno-arterial extracorporeal membrane oxygenation. It may be applied to patients with both respiratory and cardio-circulatory failure.

Aim: To describe a computational spreadsheet regarding an ex vivo experimental model of veno-venous arterial extracorporeal membrane oxygenation to determine the return of cannula pairs in a single pump–driven circuit.

Methods: We developed an ex vivo model of veno-venous arterial extracorporeal membrane oxygenation with a single pump and two outflow cannulas, and a glucose solution was used to mimic the features of blood. We maintained a fixed aortic impedance and physiological pulmonary resistance. Both flow and pressure data were collected while testing different pairs of outflow cannulas. Six simulations of different cannula pairs were performed, and data were analysed by a custom-made spreadsheet, which was able to predict the flow partition at different flow levels.

Results: In all simulations, the flow in the arterial cannula gradually increased differently depending on the cannula pair. The best cannula pair was a 19-Fr/18-cm arterial with a 17-Fr/50-cm venous cannula, where we observed an equal flow split and acceptable flow into the arterial cannula at a lower flow rate of 4 L/min.

Conclusion: Our computational spreadsheet identifies the suitable cannula pairing set for correctly splitting the outlet blood flow into the arterial and venous return cannulas in a veno-venous arterial extracorporeal membrane oxygenation configuration without the use of external throttles. Several limitations were reported regarding fixed aortic impedance, central venous pressure and the types of cannulas tested; therefore, further studies are mandatory to confirm our findings

Keywords

Extracorporeal membrane oxygenation, ECMO circuit, V-AV ECMO, V-VA ECMO, computational fluid dynamics, extracorporeal membrane oxygenation cannulae, ex-vivo simulator, artificial lung and respiratory support, cardiac and circulatory support

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Introduction

Veno-venous (V-V) and veno-arterial (V-A) extracorporeal membrane oxygenation (ECMO) are effective treatments for life support in patients with severe pulmonary or cardio-circulatory failure refractory to standard therapy while waiting for organ recovery[1–6] or organ transplantation.[7,8] The kind of choice depends on the patient's clinical situation; in case of life-threatening hypoxemia, the indication would be the configuration of V-V ECMO. However, if the patient presents severe cardiac failure a V-A ECMO must be applied.[4–9] Recently, a hybrid-modality of ECMO combining these two veno-venoarterial (V-VA) ECMO was described[10–13] in several clinical settings. Based on the paper published by Conrad et al.[14] in 2019 on nomenclature and abbreviations for extracorporeal life support, the hybrid-model V-VA can be configured in two ways: V-VA or V-AV depending on whether the initial setting was V-V or V-A, respectively, in which the draining, 'venous' cannula is referred to first, followed by a hyphen indicating the membrane lung, and any return cannulas are, therefore, positioned to the right of the hyphen.

The simultaneous use of a configuration based on the two ECMO modes may represent an advanced treatment for a selected group of patients. For example, in an acute respiratory distress (ARDS) case, the patient can be supported with V-V ECMO when suffering from concurrent cardiac failure, that is, the right ventricular failure due to pulmonary hypertension and an arterial infusion cannula may be implanted for additional cardiac support (V-VA). Furthermore, in a patient on V-A ECMO for cardiac failure experiencing pulmonary complications causing upper body hypoxemia, an additional venous return cannula may be adapted for a V-AV configuration to avoid the North/South syndrome.

Recently, Ius et al.[10] reported a cohort of V-VA ECMO patients: in their institution, they retrospectively analysed characteristics and outcomes of patients who were started on either V-V or V-A ECMO due to respiratory failure and, thereafter, switched to a V-VA or V-AV mode. This was analysed over a 2-year time period. Among the ten patients forming the study population, seven were successfully taken off ECMO; four of them recovered, and three bridged to lung transplantation after a mean period of 11 days. Five patients survived until hospital discharge, and all of them were alive at the end of the follow-up. It was concluded that 'V-VA ECMO is a technically feasible rescue strategy in treating patients presenting with combined respiratory and haemodynamic failure'. Stohr et al. evaluated the effect of different ECMO configuration strategies (V-V, V-A, V-VA and V-AV ECMO) on the outcome in a cohort of 30 patients who received ECMO for severe ARDS in a 2-year single-centre study. The authors reported an insignificant decrease in mortality in the V-VA group when compared to both V-V and V-A groups ($p = 0.057$).[11] Moravec et al. reported two cases of patients undergoing cerebral hypoxemia after 3 days on V-A ECMO for respiratory or haemodynamic failure. Both patients were converted to V-AV ECMO using a haemodialysis catheter inserted into an internal jugular vein as an additional venous return cannula. The two patients were successfully weaned off ECMO, and one was discharged.[12]

With the understanding of the importance of the clinical use of the hybrid-models and the theoretical complexity for forecasting the right return cannulas pairing, we decided to deepen our knowledge on outflow partitioning. The aim of this study is to present a computational spreadsheet that is able to predict the flow in both arterial and venous outflow cannulas related to the input data of cannula sizes and total hypothetical total ECMO flow. The spreadsheet is based on the measured data obtained from the physical ex vivo model, and the experimental model is designed for the determination of venous and arterial return cannula pairs concerning weighted volume flow in a single pump–driven ECMO circuit developed for V-VA ECMO or V-AV ECMO.

Methods

We developed an experimental ex vivo model, displayed in Figure 1, for V-VA from a Permanent Life Support (PLS, Maquet Cardiopulmonary/Getinge Group, Hirrlingen, Germany) system with a Rotaflow centrifugal pump and Quadrox oxygenator (Maquet Cardiopulmonary/Getinge Group). For temperature control, (37.5°C), a heat exchanger (Heater Unit HU 35; Maquet Getinge Group) was used. To the return side of the PLS circuit, a 3/8″ Y-piece was inserted for flow division to the 'arterial' and 'venous' return cannula, respectively. The detailed description of the ex vivo model is reported in Supplemental Appendix I. As a medium and to mimic the physical features of blood, a glucose 15.57% m/v solution with a density of 1.065 g/mL ± 0.001 and a constant viscosity of 4 mPa s ± 0.2 was used for the experiments, taken from previous studies.[15,16] Particular attention was given to the pressure measurements, by positioning the arterial cannula 50 cm above the reference plane, simulating an aortic impedance of approximately 40 mm Hg. This is to simulate a typical mean aortic pressure in a shocked patient. Data were collected for both flow (Q) and pressure (p) for the different cannula pair configurations using a flowmeter (Novalung Emtec Sono TT Ultrasonic, Xenios, Heilbronn, Germany) and a pressure monitoring transducer connected to a monitoring system (TruWave disposable pressure transducers; Edwards Lifesciences Corporation, Irvine, California, USA). We tested the following cannulas: Bio-Medicus NextGen® (Medtronic Europe Sárl, Tolochenaz, Switzerland) 17 Fr/18 cm and 19 Fr/18 cm arterial, Bio-Medicus NextGen 17 Fr/50 cm, 19 Fr/50 cm and 21 Fr/50 cm venous. The total ECMO blood flow was progressively increased from 2 up to 7 L/min, using 1-L/min increments, representing the rated flow of the oxygenator.

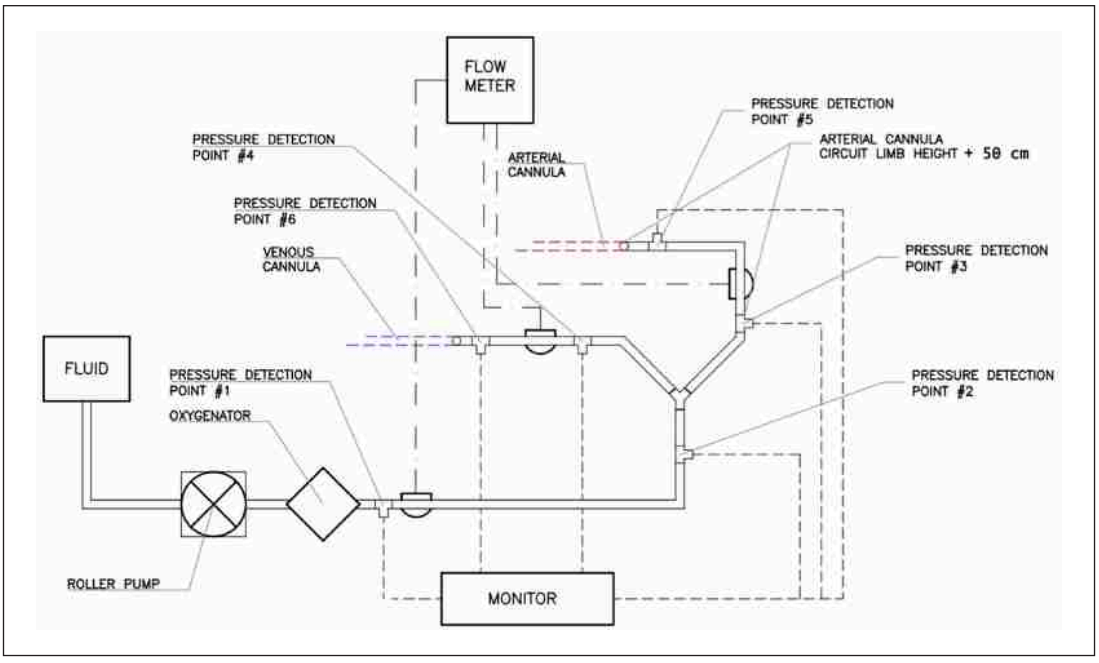


Figure 1. Diagram of the experimental circuit: the 'fluid' is a glucose 15.57% m/v solution with a density of 1.065 g/mL ± 0.001 and a constant viscosity of 4 mPa s ± 0.2; the 'roller pump' is a PLS system with a Rotaflow centrifugal pump (Maquet Cardiopulmonary/Getinge Group, Hirrlingen, Germany); the 'oxygenator' is a Quadrox oxygenator (Maquet Cardiopulmonary/Getinge Group), and the 'flowmeter' is Novalung Emtec Sono TT Ultrasonic (Fresenius-Xenios, Heilbronn, Germany); the 'pressure detection points' are six monitoring transducers connected to a monitoring system TruWave disposable pressure transducers (Edwards Lifesciences Corporation), and the 'arterial cannulas' are Bio-Medicus NextGen® (Medtronic Europe Sárl, Tolochenaz, Switzerland) of different sizes (17 Fr/18 cm and 19 Fr/18 cm); the 'venous cannulas' are Bio-Medicus NextGen (Medtronic Europe Sárl, Tolochenaz, Switzerland) of different sizes (17 Fr/50 cm, 19 Fr/50 cm and 21 Fr/50 cm).

Data were analysed from a custom-made spreadsheet (Excel, Microsoft Office 2010, Microsoft Corporation, Redmond, Washington, USA) simulating the expected flow and pressure in the outflow cannulas as well as the total flow needed to obtain the expected flow in both the 'arterial' and 'venous' return cannulas. These computations were carried out by applying a Lagrangian interpolation polynomial[17] to the measured dataset (Supplemental Appendix II).

The first data inserted into the spreadsheet were flow and pressure from experimental measurements (green cells – Figure 2). Since the flow in different circuit points was known, we were able to use the continuity equation (Supplemental Appendix II, equation 2.1) in order to calculate the fluid speed in the different sections. The same process was applied to calculate cannula outgoing flow speed.

We calculated the circuit tubing area and cannula outflow area (dark blue cells in Figure 2) using the equation 3.1, 3.2 and 3.3 (see Supplemental Appendix II), entering the cannula diameter in French (Fr) and the number of holes and diameter in millimetre (mm), according to the manufacturer.

Cannula outflow pressure (Pa) was calculated using Bernoulli's law, considering a known cannula outflow speed (Supplemental Appendix II, equation 4.2). Thus, all pressures, volume flows and flow velocities at all points of the circuit, from post oxygenator to the cannula outflow, were known. In addition, entering the total ECMO blood flow as a single input, by means of using Lagrange's interpolation law, pre-post cannula speed and pressure and flow in both return venous and arterial cannulas were calculated (red cells in Figure 2; Supplemental Appendix II, equation 6.1). Finally, we entered a determined arterial flow, and we calculated the total ECMO flow needed to reach it, using the 'dichotomy' mathematical method, (orange cells in Figure 2).

Results

Six simulations from different cannula pairs were performed. As shown in Table 1 below, with the higher total circuit flow, the flow in the arterial cannula is gradually increased. At lower flow rates, the venous component dominated due to the pressure applied downstream of the arterial cannula, and for certain settings, the entire flow may be directed to the venous limb. Volume flow and pressure data from the five measuring points of the circuit were collected while performing the simulations; 'pre' and 'post' outflow cannula pressures presented limited variations, and the results are shown in Table 2.

RPM [giri/min]	Q [l/min]	Q [m³/s]	V [m/s]	P Post Oxy [mmHg]	P Pre Y [mmHg]	P Post Y a [mmHg]	P Post Y v [mmHg]	P Pre C a [mmHg]	P Pre C v [mmHg]	Q C a [l/min]	Q C a [m³/s]	V Pre C a [m/s]	Q C v [l/min]	Q C v [m³/s]	V Pre C v [m/s]	H C a [cm]	P C a [mmHg]	P Post C a [mmHg]	P Post C v [mmHg]	V Post C a [m/s]	V Post C v [m/s]
1925	2,04	3,40E-05	0,48	67	57	57	56	55	53	0,38	6,33E-06	0,09	1,66	2,77E-05	0,39	50	39				
2340	3,04	5,07E-05	0,71	91	72	71	70	69	69	1,22	2,03E-05	0,29	1,82	3,03E-05	0,43	50	39	69,09	69,39	0,32	0,53
2770	4,02	6,70E-05	0,94	122	92	90	90	87	86	1,94	3,23E-05	0,45	2,08	3,47E-05	0,49	50	39	87,23	86,51	0,51	0,60
3260	5,02	8,37E-05	1,17	164	122	116	117	110	111	2,66	4,43E-05	0,62	2,36	3,93E-05	0,55	50	39	110,44	111,66	0,70	0,69
3750	6,01	1,00E-04	1,41	215	158	150	151	142	145	3,33	5,55E-05	0,78	2,68	4,47E-05	0,63	50	39	142,68	145,85	0,88	0,78
4255	7,07	1,18E-04	1,65	275	199	191	191	181	186	4,00	6,67E-05	0,94	3,07	5,12E-05	0,72	50	39	181,99	187,12	1,06	0,89

Cannula	
Radius [m]	4,76E-03
Area [m²]	7,13E-05

Density [kg/m³]	
Glucose	1065
Hg	13600

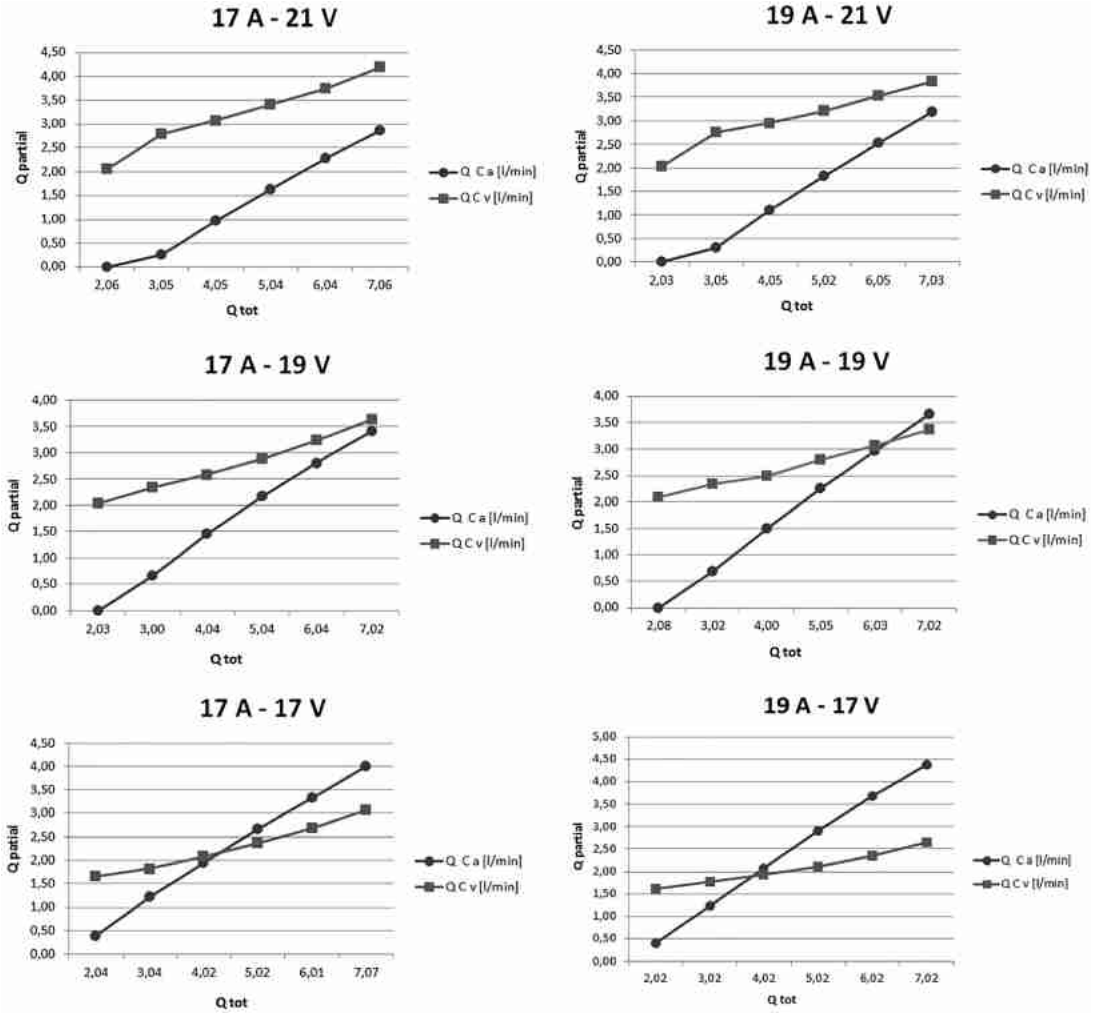
Cannula A	[Fr]	19		
Internal Diameter	[Fr]	17	[mm]	5,67E+000
Lateral Holes	n°	12	Diameter [mm]	2
Area [m²]	6,29198E-05			

Cannula V	[Fr]	17		
Internal Diameter	[Fr]	15	[mm]	5,00E+000
Lateral Holes	n°	12	Diameter [mm]	2
Area [m²]	5,7334E-05			

Q [l/min]	5	P Pre C a	[mmHg]	109,48	V Pre C a	[m/s]	0,83	Q C a	[l/min]	2,65
			[Pa]	14591,906					[m³/s]	4,41E-05
		P Post C a	[mmHg]	109,86	V Post C a	[m/s]	0,70			
			[Pa]	14649,5355						
		P Pre C v	[mmHg]	110,40	V Pre C v	[m/s]	0,55	Q C v	[l/min]	2,35
			[Pa]	14719,1456					[m³/s]	3,9234E-05
		P Post C v	[mmHg]	111,06	V Post C v	[m/s]	0,88			
			[Pa]	14807,0623						

Q C a [l/min]	2,1642	Q [l/min]	4,32647705

Table 1. Simulation results of flow (Q) rates in both outflow arterial (A) and venous (V) cannulas in the six experiments. The total ECMO flow is shown on the X axis, and the partition flows in both the venous and the arterial cannulas are shown on the Y axis.



These data were, as mentioned above, subsequently used for all calculations, and the approach used to calculate the total volume flow (Qtot) needed to obtain the desired flow in the arterial cannula (Qa) for the current V-VA return configurations is provided in Supplemental Appendix II.

Simulation 1: 17 Fr/18 cm arterial and 21 Fr/50 cm venous.

At an ECMO total flow (Qtot) of 2 L/min, there was no flow in the arterial cannula (Qa) and the whole flow was diverted to the venous cannula (Qv).

At a Qtot of 3 L/min, Qa and Qv were 0.3 and 2.7 L/min, respectively.

At a Qtot of 4 L/min, Qa and Qv were 1 and 3 L/min, respectively.

At a Qtot of 5 L/min, Qa and Qv were 1.6 and 3.4 L/min, respectively.

Simulation 2: 17 Fr/18 cm arterial and 19 Fr/50 cm venous.

At a Qtot of 2 L/min, the whole flow was directed via the venous cannula.

At a Qtot of 3 L/min, Qa and Qv were 0.6 and 2.4 L/min, respectively.

At a Qtot of 4 L/min, Qa and Qv were 1.4 and 2.6 L/min, respectively.

At a full Qtot of 5 L/min in this configuration, Qa and Qv were 2.2 and 2.8 L/min, respectively.

Simulation 3: 17 Fr/18 cm arterial and 17 Fr/50 cm venous.

At the lower flows (2 and 3 L/min), a similar pattern as above was observed (Table 1). When reaching a Qtot of 4.3 L/min, the flows were equal in both limbs, and at a flow of 5 L/min, the major flow was via the arterial cannula.

通过伯努利方程可以得到之间的关系

这个表应该是说小孔带来的影响?

Table 2. Simulation results of velocity (v), expressed as metre/second, and pressure (p), expressed as millimetre of mercury data from measuring points: pre-arterial cannula (pre c a) and pre-venous cannula (pre c v) and from custom-made spreadsheet calculations: post-arterial cannula (post c a) and post-venous cannula (post c v). 速度(v)以米/秒表示，压力(p)以毫米汞柱表示。测量点的数据:动脉前插管(pre ca)和静脉前插管(pre c v)，定制电子表格计算:动脉后插管(post ca)和静脉后插管(post cv)

17A		17A-17V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
69.00	1.00	69.10	0.29	0.33	1.22
87.00	0.58	87.25	0.45	0.52	1.94
110.00	0.00	110.47	0.62	0.71	2.66
142.00	2.00	142.74	0.78	0.89	3.33
181.00	1.00	182.07	0.94	1.07	4.00

17V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
69.00	0.58	69.22	0.43	0.49	1.82
86.00	0.58	86.29	0.49	0.56	2.08
111.00	1.53	111.37	0.55	0.63	2.36
145.00	0.58	145.48	0.63	0.72	2.68
186.00	2.52	186.63	0.72	0.82	3.07

19A		19A-17V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
62.00	1.53	61.95	0.29	0.27	1.24
73.00	0.58	72.87	0.49	0.45	2.08
90.00	1.00	89.74	0.68	0.63	2.90
112.00	0.00	111.59	0.86	0.80	3.68
138.00	1.15	137.42	1.02	0.95	4.38

17V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
61.00	1.00	61.21	0.42	0.48	1.78
74.00	0.58	74.25	0.45	0.52	1.94
94.00	0.00	94.30	0.50	0.57	2.12
118.00	1.00	118.37	0.55	0.63	2.34
148.00	1.73	148.47	0.62	0.71	2.64

17A		17A-19V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
52.00	1.00	52.03	0.15	0.18	0.66
68.00	0.58	68.14	0.34	0.39	1.46
86.00	0.58	86.32	0.51	0.58	2.17
112.00	0.00	112.53	0.65	0.75	2.80
138.00	1.15	138.78	0.80	0.91	3.40

19V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
50.00	1.15	49.83	0.55	0.51	2.34
65.00	0.00	64.80	0.60	0.56	2.58
85.00	0.58	84.75	0.67	0.62	2.87
110.00	0.58	109.68	0.76	0.70	3.24
137.00	1.53	136.60	0.85	0.79	3.62

19A		19A-19V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
54.00	1.53	53.99	0.16	0.15	0.68
61.00	1.15	60.93	1.35	0.33	1.50
74.00	0.58	73.84	0.53	0.49	2.26
88.00	0.00	87.73	0.69	0.64	2.96
105.00	0.58	104.60	0.85	0.79	3.65

19V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
50.00	0.58	49.83	0.55	0.51	2.34
60.00	0.58	59.81	0.58	0.54	2.50
72.00	1.53	71.76	0.65	0.61	2.79
89.00	0.58	88.71	0.72	0.67	3.07
109.00	0.00	108.66	0.79	0.73	3.37

17A		17A-21V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
50.00	1.53	50.00	0.06	0.07	0.26
59.00	0.58	59.06	0.23	0.26	0.97
77.00	0.58	77.18	0.38	0.44	1.63
95.00	1.53	95.35	0.54	0.61	2.29
118.00	0.00	118.55	0.67	0.77	2.87

21V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
45.00	0.00	43.77	0.65	0.34	2.79
53.00	0.58	51.50	0.72	0.38	3.08
70.00	1.53	68.17	0.80	0.42	3.41
89.00	2.08	86.78	0.88	0.46	3.75
110.00	1.00	107.23	0.98	0.52	4.19

19A		19A-21V			
p pre c a	SD	p post c a	v pre c a	v post c a	Q partial
51.00	0.58	51.00	0.07	0.07	0.30
58.00	1.53	57.96	0.26	0.24	1.10
69.00	1.15	68.90	0.43	0.40	1.82
82.00	0.58	81.81	0.59	0.55	2.53
95.00	1.00	94.69	0.75	0.69	3.19

21V					
p pre c v	SD	p post c v	v pre c v	v post c v	Q partial
43.00	1.53	41.81	0.64	0.34	2.75
52.00	0.58	50.63	0.69	0.36	2.95
64.00	0.58	62.39	0.75	0.40	3.20
77.00	0.58	75.05	0.82	0.43	3.52
90.00	0.00	87.68	0.90	0.43	3.84

SD: standard deviation.

Simulation 4: 19 Fr/18 cm arterial and 21 Fr/50 cm venous.

In this simulation, there were comparable results as in simulation 1.

Simulation 5: 19 Fr/18 cm arterial and 19 Fr/50 cm venous.

In this simulation, there were comparable results as in simulation 2.

Simulation 6: 19 Fr/18 cm arterial and 17 Fr/50 cm venous.

The results of this simulation were similar to the ones of simulation 3. Particularly, the intersection of flows, which means the same circulating flow in the arterial and venous cannulas, occurred at 3.82 L/min of the total ECMO; at 5 L/min of ECMO total flow, Qa and Qv were 2.9 and 2.1 L/min, respectively.

Discussion

V-VA or V-AV ECMO may be useful in patients already on ECMO support for initial cardiac failure (V-A) who develop profound upper body hypoxemia due to pulmonary impairment or initial respiratory failure (V-V) and who develop cardiac failure or hyperdynamic shock, particularly when the right ventricle is failing. Advantages of the V-VA or V-AV ECMO approach are mainly adopted because the myocardium and the brain receive blood, improved of oxygen, via the coronary arteries, carotid and vertebral arteries. This represents a critical point in ARDS patients supported by V-V ECMO when cardiac failure occurs, especially when the right ventricle support is needed by implanting an arterial return cannula, achieving a partial right ventricle discharge (equal to the flow of the arterial inlet cannula), or real full right ventricle support by implanting the return cannula into the pulmonary artery. Moreover, in patients supported by peripheral V-A ECMO, especially with femoral artery cannulation, suffering from pulmonary complications, the oxygen profile of the blood circulating in coronary and carotid arteries strictly depends on patient's native lung and cardiac function. Limitations of V-AV, particularly in the femoro-femoral V-A ECMO configuration, occur when the majority of, or perhaps, even all the, deoxygenated blood is drained from the inferior vena cava where the DO_2 is determined mainly by venous saturation. When adding a return cannula via the internal jugular vein, the oxygen content increases in the upper part of the body; however, it does not mean that the ECMO oxygen delivery ($D_{ECMO}O_2$) will increase.[18,19] Since V-V ECMO always carries a serious risk for recirculation,[20] it should be noted that an increase in pre-membrane lung saturation immediately reduces the efficiency for the membrane lung to oxygenate the blood. To compensate for this or to increase the $D_{ECMO}O_2$ to the patient, the ECMO blood flow has to be increased, but considering the results of our study, a change in Qtot will affect the balance between the two return cannulas. Therefore, the choice of the cannula size could be crucial, and it should be based on the desired target of the arterial flow. In fact, starting from our results, in the lower flow range (≈ 2 L/min), the entire ECMO flow was directed towards the 'venous' return cannula. On increasing the ECMO flow, the pressure subsequently rises up in the return limb, creating an increased driving pressure over the 'arterial' cannula against the arterial impedance and the ECMO flow is split, differently into the 'venous' and 'arterial' return cannulas, based on the pairs of the cannulas tested.

A well-noted complication is thrombosis of the venous return cannula in this hybrid-modality, particularly for the longer cannula type (50 cm). Indeed, when the flow in the venous return cannula goes below 2 L/min, which may be the case in the total flow below 3 L/min with a venous return cannula of 17 or 19 FR, there is an increased risk of thrombosis, due to the low blood flow velocity; therefore, close daily monitoring of the circuit, anticoagulation levels and inlet pressures of both cannulas is mandatory. Accordingly, the use of a circuit without the throttle valves, as hypothesized by our study, could lead to less side effects, caused by turbulent flow, as thrombosis or haemolysis. In fact, when a double-return ECMO configuration is established, a throttle valve is usually applied to regulate the outflow of blood into the two respective parts of the patient's circulations. This causes turbulent flow, thus leading to haemolysis, when applied for a long time.[21] When the throttle is omitted, one approach to increase resistance in one of the limbs, usually the venous return, is to down size to ¼″ tubing and use the M-number, that is, for the resistance in length.[22] For this reason, to be more optimal, the return cannula should have a ¼″ connector, often limiting that cannula size to at least 14 Fr. According to our clinical experience, turbulence and platelet activation and blood trauma will occur in the 3/8-1/4″ connector. The third option to handle the flow partitioning is to use cannulas of different effective lengths. In a 'standard setting', a combination of Bio-Medicus 17 Fr/18 cm arterial and 15 Fr/50 cm venous, both lighthouse tip design cannulas, will result in similar flows.[23] Considering our results, we found that the best pair of cannulas for most clinical settings was a Bio-Medicus NextGen cannula of 19 Fr/18 cm for arterial outflow, in combination with a 17 Fr/50 cm for the venous outflow cannula. Indeed, this cannula pairing setup permits an arterial cannula flow, even at the lowest ECMO flow tested (Qtot of 2 L/min). An increased ECMO flow delivers more blood through the arterial cannula, compared to the venous cannula. In the clinical scenario, when the patient requires more haemodynamic than respiratory assistance, the flow in the arterial

cannula may be enhanced by increasing the ECMO flow. Pairing the 17 Fr/18 cm as arterial and a 17 Fr/50 cm as venous outflow cannulas, respectively, is clinically acceptable as well, however, with the intersection of the flow aiming at 4.3 L/min.

Volume flow and pressure data were also collected while testing different pairs of cannulas. Observing the inflow and outflow and pressure graphs for the different cannula configurations, both arterial and venous, the trend displays a straight or hyperbolic correlation. In fact, they both progressively increase as the flow increases. Moreover, the results show that 'pre' and 'post' outflow cannula pressures presented limited variations (see Table 2). This is important because it is well known that high pressure is detrimental on the endothelium and on blood cells.

Our study presents several limitations: first, only a fixed arterial impedance and no pulmonary vasculature resistance or abnormal central venous pressure is simulated in the model. Indeed, in a complex clinical scenario of a patient supported by ECMO, the aortic impedance and pulmonary vascular resistances or the right ventricle failure are related to numerous factors, such as systemic and pulmonary resistances, intravascular volume and vasoactive drugs used, and all these factors may influence the onset of systemic and/or pulmonary vascular vasodilation or vasoconstriction. This contributes to the sudden and unpredictable increase or decline of the systemic and pulmonary vascular resistance and, hence, the aortic impedance and venous return cannula flow. With this issue in mind, we decided to start an experimental and pioneering ex vivo model without any previous reference studies, and we chose 40 mm Hg as a fixed value of the aortic impedance, which is mostly observed in this clinical setting, as the first step in this exploration, knowing that the complexity of the real clinical setting needs more advanced and complicated simulation to investigate the effects of different combinations of aortic impedance and central venous pressure. Second, both the experimental and computational models are based on a single type of arterial and venous cannulas, which, for the same external diameter, have a specific outflow area, given by the sum of the various holes present in the outflow tract of the cannula itself. This helped us to standardize the computation in the spreadsheet, and it turned out to be fundamental in the division of the flow in either the arterial or the venous district. At the other end, a single type of cannula limited the wideness of applicability in a real clinical setting where the cannula types are different in terms of length, external diameter, internal diameter and hole numbers and position.

Conclusion

The hybrid-model ECMO is a demanding system, applicable to critically ill patients suffering from concurrent severe heart and lung failure, and it seems to be promising for full ECMO cardio-pulmonary support. The tested spreadsheet was able to predict flow partitioning in a pair of outflow cannulas starting from the input data of cannula sizes and lengths and the total ECMO flow. This could potentially be useful in clinical practice when a V-VA or V-AV is required as a primary ECMO configuration or when there is the need to upgrade to a VV or VA configuration into a single-pump circuit of V-VA or V-AV, respectively, without using any kind of throttle to modulate the blood flow splitting. In conclusion, the return cannula size and their pairing should be carefully taken into consideration before applying a hybrid-model to obtain the desired flow partition into the venous and arterial outflow cannulas, but due to the important limitations of our study, further and more complex experimental studies based on physiological ex vivo models, comprehensive of the pathological conditions (e.g. high central venous pressure and high systemic and/or pulmonary vascular resistances), are mandatory to confirm our findings.

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Supplemental material

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