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Injection of agitated saline to detect recirculation with transthoracic echocardiography during venovenous extracorporeal oxygenation: A pilot study

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ABSTRACT

Purpose: We assessed the security and efficiency of intravenously injected agitated saline in conjunction with transthoracic echocardiography to identify recirculation in patients supported with a venovenous extracorporeal membrane oxygenation (VV ECMO) device.
Materials and Methods: We injected agitated saline 4 consecutive times separated by an interval of 5 minutes in 2 patients supported by VV ECMO. In both patients, the drainage cannula was placed in the left femoral vein, and the return cannula was placed in the right internal jugular vein. Echocardiography was performed during the injection and until the bubbles disappeared. The security of the method was assessed by evaluating the mechanical function of the ECMO and the efficiency of the oxygenator. The value of this method was assessed by visualizing the increase of inferior vena cava's echogenicity as well as by measuring the time required for this change to occur after the injection of agitated saline at different ECMO output levels.
Results: We did not observe any change in ECMO, oxygenation function, or the hemodynamic status of patients after the 4 injections of agitated saline. The echogenicity of the inferior vena cava increased more rapidly as the ECMO's output increased. The recirculation phenomenon was noted even with low levels of ECMO output (<2 L/min).
Conclusions: Transthoracic echocardiography in conjunction with agitated saline administration may be a safe and easily applicable method to evaluate a recirculation phenomenon in patients supported with VV ECMO.

1. Introduction

A venovenous extracorporeal membrane oxygenation (VV ECMO) device has been proposed as a therapeutic option for severe acute respiratory distress syndrome (ARDS) [1]. High-flow VV ECMO performance is very important because it is applied only in patients with severe hypoxemia. However, several sessions of ECMO are not as efficient as expected. A fraction of the oxygenated blood that is infused in the venous circulation can be drained back and not delivered to the patient's circulation. This situation, which is a possible limiting factor in the efficiency of ECMO, is called recirculation [2].

Today, there is no easily applicable method to clinically assess recirculation. Central venous oxygen saturation is not useful for recirculation assessment because it may not accurately reflect the mixed venous oxygen saturation [3]. The ultrasound dilution technique can quantify recirculation [4], but it is not yet a widely applied method [5]. Echocardiography can evaluate the correct position of the catheters [6], but it cannot ensure the absence of recirculation [5]. Intracardiac injections of agitated saline containing microbubbles—a well-described contrast agent—has been used in echocardiography to study different pathologies [7]. However, it has not been evaluated thoroughly in patients supported with ECMO because microbubble accumulation may cause ECMO dysfunction. In light of this fact, we evaluated the safety of microbubbles administration as well as the efficacy of this method to assess recirculation.

2. Methods

We obtained approval from Brugmann University Hospital's Ethics Committee and written informed consent from the patients. We then evaluated 2 patients aged 68 and 70 years who were treated in our unit for severe ARDS secondary to pulmonary infection and were supported by VV ECMO (Stöckert SCPC Centrifugal Pump, SORIN Group, München, Germany; EOS ECMO oxygenator) for more than 20 days. Our patients were not treated with any type of vasoactive drugs, nor did they present signs of peripheral hypoperfusion or right heart dysfunction. Furthermore, the patients were not treated with any renal replacement therapy, nor did they present clinical signs of intra-abdominal hypertension. The drainage cannula (Bio-Medicus, Medtronic, USA 23F

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Table 1
Patients' demographic and clinical characteristics

	Patient 1	Patient 2
Reason of admission	Septic shock, pulmonary infection	Septic shock, pulmonary infection
Comorbidities	Hypertension	COPD, dilated cardiomyopathy
APACHE II[a]	20	23
Pa_{O_2}/F_{IO_2}[b]	70	60
Time on ECMO support	43	31
Time before examination	42	20
Time after examination	1	11
Left ventricular ejection fraction (%)[b]	68	33
Cardiac index[c] ($L\ min^{-1}\ m^{-2}$)	3.6	2.9
TAPSE (cm)[c]	3.4	2.9
$S_{cv}o_2^5$ (%)	60	62
4-d fluid balance (mL)	4611	−4885
Mechanical ventilation parameters[c]		
Mode	Pressure assist control	Volume assist control
Tidal volume (mL)	100	350
Respiratory rate (breaths/min)	20	12
F_{IO_2}	0.4	0.4
PEEP (cm H_2O)	12	12

TAPSE indicates tricuspid annular plane systolic excursion; Pa_{O_2}, partial pressure of oxygen in arterial blood; $S_{cv}o_2$, central venous oxygen saturation; F_{IO_2}, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; COPD, chronic obstructive pulmonary disease; APACHE II, Acute Physiology and Chronic Health Evaluation II.
[a] On the day of admission.
[b] On the day of ECMO support initiation.

× 25 cm) was placed in the left femoral vein, and the return cannula was placed in the right internal jugular vein (Bio-Medicus, 19F × 18 cm). The tips of the return cannulas were within the beginning of cardiac silhouette based on the frontal chest radiographs obtained from both of the patients. The tips of the drainage cannula were not visible in inferior vena cava (IVC) from the classical echocardiography subcostal view. The distance between the tips of the 2 cannulas was approximately 20 to 30 cm.

Two 10-mL syringes were attached to a 3-way stopcock on the jugular central venous catheter (VYGON multicath 3, France 7.5F × 15 cm). One syringe was filled with 9 mL of saline (NaCl 0.9%) and the other syringe was filled with 1 mL of air. The saline was injected rapidly into the syringe with air and inverted 10 times and then immediately injected into the patient through the distal lumen of the catheter. Concurrently, the patients were examined with echocardiography (Vivid S5, GE Healthcare, USA) from the subcostal point of view so that the IVC in its long axis and part of the right atrium would be simultaneously visible. The probe was positioned in that way that allowed imaging of at least 2 cm of the IVC distally to its junction with the suprahepatic vein. The filters were adjusted to ensure that the IVC's borders were distinct. We repeated the test starting with the current ECMO conditions and increasing the ECMO's pump velocity to increase the output by 1 L each time until the increase in the pump velocity was not associated with any further increase in the ECMO output. Each time the examination was repeated by placing the probe to obtain an anatomically comparable image to the first one. No further adjustment to the filters was permitted. After a maximum value was achieved, we repeated the test down to ECMO output values of 2 L. Between each test, we waited for the total disappearance of the bubbles. Five minutes after each injection of contrast, we evaluated the patient's arterial gases, as well as the blood gases from the return cannula.

The presence of air within the centrifugal pump of the ECMO may cause an abrupt decrease of its flow or even a total stoppage [8]. Accordingly, we evaluated the security of this method by assessing any decrease in the ECMO output. Furthermore, we expected that an accumulation of air bubbles within the oxygenator could cause a decrease in the gas exchange efficiency due to a decrease in the oxygenator's efficient surface and thrombus formation because of bubble-induced platelet aggregation [9]. A postoxygenator decrease of P_{O_2} less than 200 mm Hg and/or a P_{CO_2} increase of 10 mm Hg or more were considered to be indicators of oxygenator dysfunction according to the local criteria. Appropriate preparations were made to address either of these 2 complications (ie, air removal from ECMO system and oxygenator change).

We injected the bubbles into the superior vena cava. Therefore, in the absence of recirculation, we expected that the bubbles would not appear within the IVC. Conversely, we presumed that in the case of recirculation, the bubbles would move far from the heart toward the distal side of the IVC; the more intense the recirculation, the more rapidly the bubbles would move in the IVC. Consequently, we evaluated the efficiency of our method by measuring the time that was necessary to increase the echogenicity of the IVC. We analyzed the echocardiographic images off line. Considering time 0 to correspond to the frame with a sign of opacification of the right atrium, we measured the frames until the total opacification of the IVC (ie, the IVC's borders were not visible). Calculating the time that each frame corresponded to (ie, the total time of the strip divided to the total number of frames; both parameters were provided by the ultrasound machine), we estimated the total time that was necessary for the opacification of the IVC. Given that recirculation was expected to be enhanced with augmentation of ECMO output [10], we expected to observe a shorter time needed for total opacification of IVC at the highest achieved ECMO's output compared with the lowest.

3. Results

The characteristics of the patients are listed in Table 1. The first patient was deeply sedated during the examination, and the second patient was at a normal state of consciousness during the examination. This latter patient did not describe any symptoms during or immediately after the end of the examination. The test was repeated 4 times in both patients. We did not observe any problem with the functioning of the ECMO at any time. The parameters of ECMO and the Pa_{O_2} and hemodynamic parameters are presented in Tables 2 and 3. At the end of the study, the postoxygenator P_{O_2} and P_{CO_2} data remained similar to the baseline values. No decrease in the pump velocity or ECMO output was observed after each injection of agitated saline. Furthermore, we did not detect any abnormal noise in the centrifugal pump that might indicate a disengagement of the impeller. Macroscopically, no presence of air bubbles was noted at any point in the ECMO system during the examination. Incidentally, after the end of the examination, we returned the ECMO's velocity to the baseline values and obtained stable outputs for the next hour. Furthermore, there was no need to change the oxygenator over the course of the next 11 days during which the second patient was followed up.

In both patients, we observed a more rapid opacification of the IVC with increasing ECMO output (Figs. 1 and 2). In the first patient, we

Table 2
The parameters of patient 1 5 minutes after the injection of agitated saline under different ECMO outputs

	ECMO Output (L/min)	ECMO velocity (cycle/min)	MAP (mm Hg)	Patient's saturation	Pa_{O_2} (mm Hg)	$P_{pox}o_2$ (mm Hg)	$P_{pox}co_2$ (mm Hg)
First injection	3.3	2399	88	94%	84	522	24
Second injection	4.3	2963	106	95%	105	462	27
Third injection	5.2	3562	99	94%	104	497	27
Fourth injection	1.7	1290	95	65%	32	526	24

MAP indicates mean arterial pressure; Pa_{O_2}, partial pressure of oxygen in arterial blood; $P_{pox}o_2$, partial pressure of oxygen in blood postoxygenator.