Venoarterial Extracorporeal Membrane Oxygenation

If You Cannot Measure It, You Cannot Improve It

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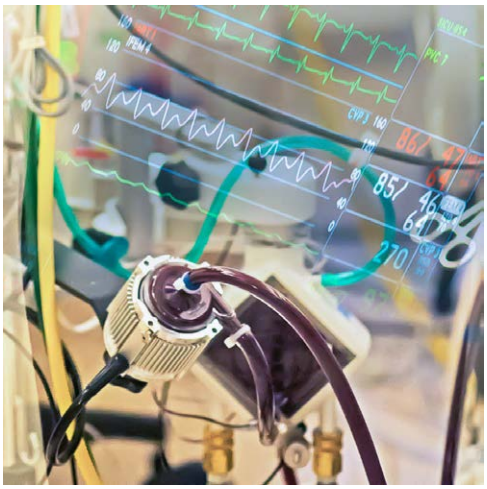
THE circulation of the blood was first described in detail by William Harvey. Harvey's famous work, *De Motu Cordis et Sanguinis*, was published in 1628. In it, he described the action of the heart and the consequent movement of the blood around the body in a circuit, thereby challenging Galen's accepted view of the liver as the origin of venous blood. Harvey had noticed that tying the veins of a fish would lead to an empty heart. However, when the arteries were tied, the heart would swell up. These simple observations still have profound implications in the setting of temporary mechanical circulatory support techniques, such as venoarterial extracorporeal membrane oxygenation that create additional complexities unknown to the native circulation described by Harvey. In this setting, effective integration of native circulation with temporary mechanical circulatory support to minimize iatrogenic insults is an evolving science. Physiologic measurements that enhance our understanding of pathophysiology and guide optimal application of mechanical circulatory support may be a good place to start. As Lord Kelvin, a Scottish mathematician and physicist who developed the Kelvin scale of temperature measurement famously said, "If you cannot measure it, you cannot improve it." Inability to reliably measure right ventricular output and function during venoarterial extracorporeal membrane oxygenation support makes it difficult to provide cardioprotective venoarterial extracorporeal membrane oxygenation support and ultimately wean patients from venoarterial extracorporeal membrane oxygenation.



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In this issue of ANESTHESIOLOGY, Bachmann *et al.*[1] describe a modified thermodilution technique to calculate cardiac output (CO) and assess right ventricular function during central venoarterial extracorporeal membrane oxygenation support in a porcine model. During central venoarterial extracorporeal membrane oxygenation, venous blood drained through a cannula typically placed in the right atrium is returned to the ascending aorta after passing through a membrane oxygenator for extracorporeal gas exchange. Central venoarterial extracorporeal membrane oxygenation requires a sternotomy/thoracotomy and is usually applied in patients who develop postcardiotomy cardiogenic shock. The less invasive, more commonly used peripheral venoarterial extracorporeal membrane oxygenation option in other forms of cardiogenic shock involves returning the blood into distal descending aorta *via* a cannula placed transfemorally. Regardless, their technique requires two pulmonary artery catheters with rapid response thermistors, one positioned in the pulmonary artery and the other in the extracorporeal membrane oxygenation circuit. The thermodilution signal obtained at the extracorporeal membrane oxygenation circuit after an injection into the right atrium can be used to determine the volume of injectate passing through the pulmonary circulation to allow accurate calculations of native CO. There was good agreement seen between these calculations and flow measurements at the pulmonary artery trunk using a high-precision flow probe. However, use of central venoarterial extracorporeal membrane oxygenation in the absence of clinical heart failure represents an artificial scenario, as evidenced by the relatively low left atrial pressures seen in

Image: J. P. Rathmell.

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this experiment. One may assume that this may be due to combination of a properly ejecting left ventricular, partially unloaded right ventricular, and anterograde reinjection into the ascending aorta. In addition, the right ventricular–left ventricular interactions would not reflect the conditions seen with peripheral venoarterial extracorporeal membrane oxygenation in patients with severe left- or biventricular failure. Although the findings are a good foundational step, further validation in large animal models of heart failure using peripheral venoarterial extracorporeal membrane oxygenation, as well as in clinical subjects, is clearly indicated.

Advances in medical therapies in the last three decades have failed to improve mortality[2] from cardiogenic shock. This is despite the rapid uptake of temporary mechanical circulatory support technologies, most notably venoarterial extracorporeal membrane oxygenation and percutaneous ventricular assist devices.[2,3] Encouraging outcomes have been reported in selected groups of cardiogenic shock patients with the use of venoarterial extracorporeal membrane oxygenation (*e.g.,* in myocarditis). However, the cardiogenic shock population supported with venoarterial extracorporeal membrane oxygenation is quite heterogenous. While approximately 60% of patients have sufficient cardiac recovery to wean from venoarterial extracorporeal membrane oxygenation, 44% of patients survive to hospital discharge,[4] and this attrition is largely due to persistent heart failure. Most acute cardiogenic shock patients are not candidates for durable mechanical circulatory support or heart transplant, and therefore it is of critical importance to minimize secondary cardiac injury and maximize cardiac recovery during venoarterial extracorporeal membrane oxygenation. However, the current setup and use of venoarterial extracorporeal membrane oxygenation results in increased left ventricular workload, potentially leading to progressive left ventricular distension, loss of aortic valve opening, intracardiac blood stasis, and thrombosis, with subendocardial ischemic injury and compromised cardiac recovery. Equally, significant impairment of microcirculation seen in cardiogenic shock and venoarterial extracorporeal membrane oxygenation patients, combined with blood component damage and activation of the endothelium, as well as coagulation and inflammatory systems, may all lead to further cardiac injury. Therefore, merely replacing the native pump (patient's own heart) with a nonpulsatile, continuous flow pump (venoarterial extracorporeal membrane oxygenation) without optimizing the microcirculation and unloading the left ventricular may result in suboptimal outcomes (fig. 1).

During venoarterial extracorporeal membrane oxygenation support, one must strike a balance between adequate decompression of the right ventricle through venous drainage and prevention of distension of the left ventricle due to excessive return blood flow into the aorta. This balancing act is generally achieved with repeated echocardiographic assessments of the heart. The technique described by Bachmann *et al.*, if validated in clinical studies and also for the commonly applied peripheral cannulation mode, may provide dynamic cardiovascular monitoring in venoarterial extracorporeal membrane oxygenation patients to allow careful titration of extracorporeal membrane oxygenation blood flows, pharmacologic cardiac support, and other supportive therapies. This includes the degree of left ventricular venting required at any given point in time, and more so as right ventricular function is of pivotal importance for left ventricular overloading during venoarterial extracorporeal membrane oxygenation as the right ventricular drives left ventricular filling. Measurements of pulmonary capillary wedge pressure as a proxy for left ventricular end-diastolic pressure may assist with timely mechanical left ventricular decompression.[5] This technique can also play a key role in the extracorporeal membrane oxygenation weaning process along with echocardiography. The ability to continuously calculate right ventricular ejection fraction and filling volumes may allow for more nuanced venoarterial extracorporeal membrane oxygenation weaning while accounting for right ventricular myocardial mechanics, especially in the setting of a marginal right ventricular. Whether patient management based on these invasive measurements, in addition to echocardiography, will lead to improved venoarterial extracorporeal membrane oxygenation outcomes is a subject for future research.

These potential benefits, of course, should be weighed against potential risks. A typical venoarterial extracorporeal membrane oxygenation run lasts 5 to 7 days and any additional infection risks from leaving a pulmonary artery catheter in for that duration should be taken into consideration. Equally, insertion of a pulmonary artery catheter into the extracorporeal membrane oxygenation circuit

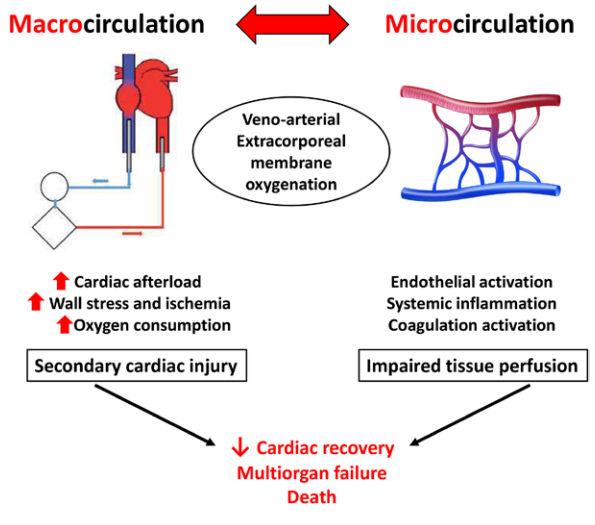

Fig. 1. Interactions among venoarterial extracorporeal membrane oxygenation, macrocirculation, and microcirculation may have unintended consequences.

has unquantifiable medium-to-long-term risks for blood trauma and coagulation. It may be possible to develop extracorporeal membrane oxygenation circuitry with a built-in thermistor and a dedicated injection port for calibration to overcome some of these potential risks. Regardless, this work helps improve our understanding of the interplay between the native and extracorporeal circuits and may allow more sophisticated decision-making.

Hemodynamic measurements during venoarterial extracorporeal membrane oxygenation are a means to an end and may help us better understand and address the research questions in relation to macro- and microcirculation (fig. 1) that may ultimately lead to improved outcomes. In the future, holistic monitoring during venoarterial extracorporeal membrane oxygenation may include continuous monitoring of cardiac mechanics and output, pulmonary pressures, hemostasis, microcirculation, and brain tissue oxygenation. Defining cardiogenic shock patient populations that stand to benefit most in clinical studies, thereby enriching those studies, is also a key priority moving forward. Equally, measuring quality and process metrics for extracorporeal membrane oxygenation is critical to making improvements in an extracorporeal membrane oxygenation program. Future venoarterial extracorporeal membrane oxygenation research should focus on strategies that improve mechanical efficiency of the native heart, the risk-to-benefit ratio of proactive unloading of the left heart and, perhaps, the introduction of synchronized extracorporeal pulsatility. Global collaboration is essential to ensure high quality research in the field.

Competing Interests

Dr. Brodie receives research support from ALung Technologies (Pittsburgh, Pennsylvania) and was previously on their medical advisory board. He has been on the medical advisory boards for Baxter (Deerfield, Illinois), BREETHE (Danvers, Massachusetts), Xenios (Heilbronn, Germany), and Hemovent (Rottstraße, Germany). Dr. Donker receives research support and speaker fees from Getinge Maquet (Gothenburg, Sweden) and Xenios. Dr Shekar receives research support from Metro North Hospital and Health Service (Queensland, Australia).

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