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Recirculation in venovenous extracorporeal membrane oxygenation

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ABSTRACT

Despite the increasing use of venovenous extracorporeal membrane oxygenation (ECMO) to treat severe respiratory failure, recirculation remains a common complication that may result in severe hypoxemia and end-organ damage. The present review, therefore, examines updated evidence for the causes, measurement, and management of recirculation. Six electronic databases were searched from their dates of inception to January 2016, and 38 relevant studies were selected for analysis. This review revealed that, currently, recirculation is typically calculated from measurement of blood oxygen saturations, although limited evidence suggests that oxygen content may provide a more accurate measure. Dilutional ultrasound may play an additional role in dynamic quantitative monitoring of recirculation, but further human studies are required to validate its clinical use. Although cannula configuration appears to be a key contributor to recirculation in addition to factors such as ECMO flow rate, there are insufficient comparative clinical studies to recommend an optimal cannulation technique for minimizing recirculation. Existing evidence suggests that the dual-lumen cannula may have a low recirculation fraction, but only if correctly positioned. This review underscores the need for more robust clinical and laboratory studies to effectively evaluate and address the persistent problem of recirculation.

1. Introduction

In recent years, there has been renewed interest in the use of venovenous extracorporeal membrane oxygenation (VV-ECMO) for severe acute respiratory distress syndrome because it facilitates protective lung ventilation and has been shown to improve survival [1,2]. Furthermore, VV-ECMO is associated with fewer vascular complications compared with other extracorporeal pulmonary support devices that require arterial cannulation, such as the pumpless interventional lung assist and veno-arterial ECMO [3,4].

However, unlike these devices, VV-ECMO can be complicated by recirculation. This occurs when a fraction of oxygenated blood delivered by the infusing cannula is withdrawn by the draining cannula before entering the systemic circulation. High recirculation volumes markedly decrease the efficacy of VV-ECMO and may contribute to severe hypoxemia and end-organ damage. It is therefore essential that this complication is recognized and managed. The present review examines the causes, measurement, and management of recirculation.

2. Material and methods

A literature review was performed by searching 6 electronic databases, including MEDLINE, EMBASE, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Reviews of Effects, from their dates of inception to January 2016. To maximize the sensitivity of the search, the following terms were combined: (ECMO OR extracorporeal circulation OR ECMO) AND (recirculation), as either keywords or MeSH terms. The reference lists of articles obtained were also reviewed to identify additional relevant studies.

Both in vitro and in vivo studies, including mock loop, animal, and human trials, were included in the review. When institutions published duplicate studies with overlapping sample populations, only the most recent articles were reviewed. Case reports and conference abstracts were also analyzed. Only studies published in the English language were selected.

3. Mechanism of recirculation

Recirculation occurs when oxygenated blood infused by the return cannula is withdrawn by the access cannula before it reaches the systemic circulation. This may result in insufficient oxygen delivery with subsequent hypoxemia and is one of the main factors that limit the efficacy of VV-ECMO [5,6].

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Because the distance between the infusing and draining cannula tips is one of the main determinants of recirculation, ECMO cannula configuration has been the focus of most studies on recirculation [5]. However, few studies have quantitatively compared recirculation among commonly used VV-ECMO cannulation configurations, including femorofemoral and femorojugular techniques. Mock circulation loop studies by Jayewardene et al [7] and Xie et al [8] demonstrated higher recirculation fractions for femorofemoral and femorojugular configurations compared with dual-lumen cannulation, based on oxygen content calculations in crystalloid solution. Current blood-based mock loop studies, meanwhile, have not yielded consistent results [8].

Other contributors to recirculation include patient movement (such as rotation of the head and neck), which may affect cannula position, volume status, cardiac output, and ECMO flow rate [9–13]. Higher ECMO flow rate, in particular, has been shown in multiple studies to increase recirculation fractions. Sreenan et al [11] and Van Heijst et al [13] both demonstrated that increased recirculation occurred at higher VV-ECMO pump flows, using a dual-lumen cannula in animal models and measuring recirculation based on thermodilution and oxygen saturation calculations, respectively. Broman et al [10], using a mock circulation loop, similarly showed a positive correlation between recirculation (based on oxygen saturation measurements) and ECMO flow rate up to 5 L/min with various cannula placements in the right atrium and vena cavae. Togo et al [12] demonstrated similar findings in goats, cannulated in various configurations (including the right atrium and/or vena cavae). However, they also found that oxygen saturation and partial pressure (Pa_{O_2}) increased at higher ECMO flow rates, indicating that oxygen delivery increased in spite of increased recirculaton [12].

Nonetheless, it should be noted that these studies all had limitations, including small sample sizes, animal-based or in vitro design, and considerable variation in methodology for quantifying recirculation.

4. Quantification of recirculation

A range of techniques has been developed in the attempt to accurately measure recirculation.

4.1. Formulae for recirculation

Recirculation is calculated as a proportion of the volume of oxygenated blood infused by the ECMO circuit that is then immediately withdrawn into the draining ECMO cannula, as expressed by Equation 1.

$$\text{Recirculation (\%)} = \frac{\text{Oxygenated blood drained from infusing cannula}}{\text{Net blood drained}} \times 100\%$$

Formula 1: Simplified recirculation equation. Blood drained is expressed in liters per minute.

Applying the law of conservation of mass of oxygen gives rise to the following formula:

$$\text{Recirculation (\%)} = \frac{ctO_{2\ \text{Draining}} - ctO_{2\ \text{Mixed ven}}}{ctO_{2\ \text{Infusing}} - ctO_{2\ \text{Mixed ven}}} \times 100\%$$

Formula 2: Recirculation formula based on oxygen content. $ctO_{2\ \text{Draining}}$ indicates oxygen content (g/dL) in draining cannula; $ctO_{2\ \text{Infusing}}$, oxygen content (g/dL) in infusing cannula; $ctO_{2\ \text{Mixed ven}}$, oxygen content (g/dL) of mixed venous blood before oxygenation by ECMO.

Most commonly, oxygen saturation (measured by oximetry or blood gas analysis) has been used to calculate recirculation in Formula 2 [13]. The main limitation of this method is the difficulty in measuring the mixed venous oxygen (ie, before oxygenation by the ECMO circuit) because of the differing oxygen content in the superior vena cava (SVC) and inferior vena cava (IVC) [13,14].

Van Heijst et al suggested that the most accurate technique for estimating mixed venous oxygen in ECMO patients [13] is to temporarily cease ECMO sweep gas flow and use the ventilator to achieve an arterial oxygen saturation equivalent to that achieved on ECMO support. The oxygen saturation of blood in the venous drainage cannula (measured using oximetry) would represent the true mixed venous oxygen saturation. Although this technique is more accurate than the central venous measurement of oxygen saturation, it is time-consuming, prone to measurement error, and may not be tolerated in highly ECMO-dependent patients [13].

However, because blood that is highly oxygenated by ECMO also has higher levels of dissolved oxygen, measurement of recirculation using oxygen content may be more accurate. This has been demonstrated in animal and in vitro studies [14,15]. However, other authors have argued that in clinical settings, where oxygen saturation is typically less than 95%, the contribution of dissolved oxygen is negligible and therefore saturation is appropriate for use in recirculation formulae [10].

Lindstrom et al [14] developed an alternative strategy to assess recirculation based on oxygen content measurements in a dog on cavoatrial VV-ECMO. Using a bypass loop to create a known level of recirculation, they found that measurement of recirculation using oxygen content had an excellent correlation with true recirculation ($r^2 = 0.89$) (with a bias of +18.6%), which was more accurate than measurement using oxygen saturation.

4.2. Dilutional ultrasound

Dilutional ultrasound is based on changes in ultrasound velocity in response to saline injection. Ultrasonic flow sensors are placed on the access and return cannulae. Injecting a saline bolus into the return cannula changes the velocity properties of ultrasound, producing a "dilution curve." Recirculated saline subsequently generates a second dilution curve, which is detected by the ultrasonic probe on the access cannula. The ratio of the areas under the 2 dilution curves then determines the recirculation fraction (Formula 3) [16].

$$\text{Recirculation (\%)} = \frac{S_{\text{access cannula}}}{S_{\text{return cannula}}} \times 100\%$$

Formula 3: Recirculation formula for dilutional ultrasound. *S* indicates area under the curve.

This technique was first validated in the measurement of arteriovenous fistula recirculation in hemodialysis patients [17]. Since then, several studies have investigated its use in VV-ECMO [13,16,18–20]. Van Heijst et al [13] and Darling et al [16] conducted animal trials of VV-ECMO but found no significant difference between recirculation calculated using dilutional ultrasound vs the standard recirculation formula. Clements et al [18] reported the first use of dilutional ultrasound for measuring recirculation in a neonate and noted considerable changes in recirculation over time (range, 15%-57%), especially with patient movement. Korver et al [20] used dilutional ultrasound to demonstrate increased recirculation fractions (45% and 38%) in two patients with a malpositioned dual-lumen cannula, reinforcing the potential of this technique in monitoring VV-ECMO patients. Similarly, Gehron et al measured recirculation fractions of 25% to 30% in 5 VV-ECMO patients, although this level of recirculation did not adversely affect their level of oxygenation [19].

Other applications of dilutional ultrasound in VV-ECMO have also been examined. Using the principles of the standard recirculation formula based on oxygen saturation, Walker et al [15] used recirculation values derived from ultrasound dilution to calculate true mixed venous saturation. A blood-based mock circulation loop was used with a fixed recirculation fraction. However, significant differences in actual vs calculated mixed venous saturation were found at systemic oxygen saturations greater than 60%. In common with other authors [12], they concluded that the standard recirculation formula is inaccurate if oxygen saturation is used and, in a subsequent study, demonstrated improved accuracy if oxygen content was used instead [21]. However,