

Quantification of Carbon Dioxide Removal at Low Sweep Gas and Blood Flows

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Abstract: Advancement in oxygenator membrane technology has further expanded the boundaries in the clinical application of extracorporeal carbon dioxide removal (ECCO₂R). Despite the advent of modern poly-4-methyl-1-pentene (PMP) membranes, limited information exists on the performance of these membranes at low sweep gas and blood flows. Moreover, physiological relationships for CO₂ removal at these flows are less explored. Hence, CO₂ removal was quantified in an in vitro setting using a PMP membrane oxygenator. ECCO₂R was performed using a .8 m² surface pediatric oxygenator in an in vitro setting with freshly drawn single-source porcine blood. In this setting, low blood flows of either 200 or 350 mL/min were generated, with sweep gas flow rates of 100, 200, and 400 mL/min, respectively. CO₂ transfer ranged from 14.05 ± 4.35 mL/min/m² to 18.76 ± 4.26 mL/min/m² at a sweep gas to a blood flow ratio of .5:1 to 2:1

($p < .01$). Decreasing this ratio i.e., increasing the blood flow (.5:1.75 and 2:1.75) resulted in a lower CO₂ transfer of 10.00 ± 4.77 mL/min/m² to 16.87 ± 5.09 mL/min/m², which was still statistically significant ($p < .01$). Alternatively, decreasing the sweep gas to blood flow ratio, while maintaining a constant gas flow, did not show a significant increase in CO₂ extraction ($p > .05$). At these test parameters, an increase in sweep gas improved the CO₂ transfer, whereas an increase in blood flow resulted in a lower CO₂ transfer. These results indicate that CO₂ removal in low-flow ECCO₂R is mainly sweep gas flow driven. Although these settings might not be applicable for clinical use, this study gives tangible information about the important factor involved in ECCO₂R. **Keywords:** extracorporeal carbon dioxide removal, low sweep gas flow, low blood flows. *J Extra Corpor Technol. 2017;49:257–261*

Extracorporeal carbon dioxide removal (ECCO₂R) is a technique that was principally developed to support patients with acute respiratory distress syndrome to facilitate lung-protective mechanical ventilation (1–3). As ECCO₂R primarily removes CO₂ rather than provide oxygenation, its application has expanded to support patients with hypercapnic respiratory failure (4–6). Through time, a more alluring technique that uses lower blood flows, which require smaller cannulas and hence, a potentially wider clinical application has been developed to reduce the potential complications (2,7).

At these low flows (200–500 mL/min), approximately 30–150 mL/min of CO₂ is transferred (7,8). Variables that influence the CO₂ extraction rate have been extensively

described utilizing silicone membrane oxygenators at relatively higher blood flows (7,9). Accordingly, factors such as blood flow, sweep gas flow, and surface area are known to influence CO₂ extraction. In the current ECCO₂R circuit, a poly-4-methyl-1-pentene (PMP) membrane oxygenator is incorporated instead of the earlier silicone membrane oxygenator. Potentially, an in vitro study would allow to independently investigate the major physiological factors involved in CO₂ transfer. Hence, we conducted this study to quantify the amount of CO₂ transferred in relation to the PMP membrane surface area at low-flow situations (sweep gas and blood flow) to determine whether ECCO₂R is mainly blood flow or gas flow driven at low sweep gas and blood flow settings.

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MATERIALS AND METHODS

The study was carried out at the Experimental Laboratory of the department of Cardiothoracic Surgery, Maastricht University Medical Center.

Overview of the Study

The in vitro setting (Figure 1) consisted of a soft-shell venous reservoir (BMR 1900, Sorin Livanova, Mirandola, Italy), a roller pump (Sorin Livanova, Mirandola, Italy), a membrane oxygenator (1.8 m², Quadrox-i adult, Maquet Cardiopulmonary, Rastatt, Germany), and a modified dialysis system (Baxter BM11, Baxter Healthcare Corporation, Deerfield, IL) incorporated with a PMP membrane oxygenator (.8 m², Quadrox-iD pediatric, Maquet Cardiopulmonary), by means of a perfusion adaptor connected to the dialysis tubing, that was assessed for low-flow ECCO₂R application. The whole circuit comprised of a high-flow and a low-flow subunit representing a hypercapnic patient and a low-flow ECCO₂R technique, respectively. The high flow was maintained at 4.5 L/min with a roller pump, which was placed between the soft-shell venous reservoir and the adult oxygenator, while the dialysis unit guaranteed low flows (200 and 350 mL/min) for ECCO₂R application.

The circuit was primed with approximately 1.5 L of normal saline to ensure that no air was present within the circuit. Freshly drawn, single-source porcine blood containing 25,000 IU heparin was used. The blood was introduced into the circuit through a hard-shell reservoir

(HKV 2000, Maquet Cardiopulmonary), which filtered off larger particulates to prevent damage to the circuit and blood. The priming volume was discarded simultaneously through the low-flow circuit while the circuit was filled with porcine blood to achieve a hematocrit of $25 \pm 3\%$. The blood temperature was maintained at 37.5°C using a heater cooler unit. A high-pressure CO₂ tank connected via a gas blender with the gas inlet port of the adult oxygenator acidified the blood in the circuit through a standardized procedure applying sweep gas flow at 100 mL/min. Oxygen (100%) was delivered into the pediatric oxygenator via a blender, enabling CO₂ removal from the circuit at fixed sweep gas flow of 100, 200, and 400 mL/min.

Conduct of the Study

A predetermined protocol was not available in the literature; hence, several test runs were required to standardize the process of acidification and CO₂ removal. Each blood flow to gas flow ratio lasted for 45 minutes; during this period, four samples of blood were drawn at each of the two sampling ports (pre- and post-oxygenator). The first sample point at the beginning of the experiment was termed as $t_0 = 0$ minutes. Consecutive samples drawn were termed as $t_1 = 15$ minutes, $t_2 = 30$ minutes, and $t_3 = 45$ minutes.

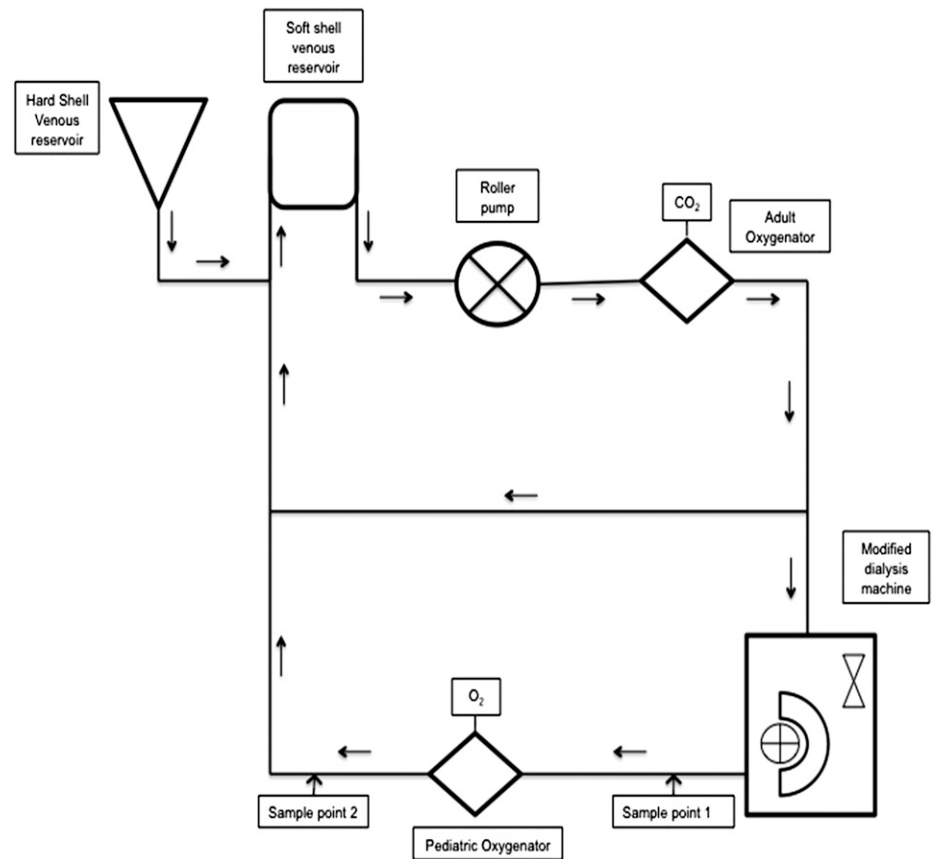


Figure 1. Schematic diagram of the in vitro circulation used to quantify carbon dioxide transfer in a low-flow system.

At the beginning of each experiment, acidification of blood took place [partial CO₂ pressure of 20 kPa {150 mmHg} and a pH of 6.8] after which the CO₂ supply was stopped. Then CO₂ removal was measured from t₀ to t₃ at blood flows of 200 and 350 mL/min, in combination with fixed sweep gas flows of 100, 200, and 400 mL/min, respectively. This resulted in sweep gas to blood flow ratios of .5:1; 1:1; 2:1 and .5:1.75; 1:1.75; 2:1.75, respectively as seen in Table 1. For each such ratio, six experiments were conducted. A new system was used after each set of ratios making the total number of systems six, leading to no breach of manufacturers' instructions for use.

Sample Analysis

Blood samples were drawn to measure pCO₂, pH, bicarbonate, and hematocrit. Blood gas analysis was performed on the Gem Premier blood gas analyzer (Gem Premier 3000, Instrumentation Laboratory, Lexington, MA).

Data Analysis

CO₂ extraction was calculated from the amount of total CO₂ (TCO₂) at the beginning of each experiment subtracted from TCO₂ values that were measured at the end of each experiment. TCO₂ was calculated with the modified Henderson–Hasselbalch equation taking bicarbonate concentration into consideration:

$$TCO_2 = HCO_3 + (\alpha \times pCO_2)$$

where TCO₂ = total content of carbon dioxide (in mmol/L), solubility coefficient of CO₂ (α) = .03, pCO₂ = partial pressure of CO₂ in blood (in mmHg), and HCO₃ = concentration of bicarbonate in blood (in mmol/L).

TCO₂ was expressed in mL/min using the following conversion formulae:

$$TCO_2(\text{in mmol/L}) \times 22.3 \text{ mL} = TCO_2(\text{in mL/L}) \quad (1)$$

$$\begin{aligned} \text{Priming volume (in L)} \times TCO_2(\text{in mL/L}) \\ = TCO_2(\text{in mL}) \text{ in the circuit.} \end{aligned} \quad (2)$$

The TCO₂ in mL was then converted to a final value that would be mL/min/m² to give the amount of CO₂ removed per minute per square meter of chosen oxygenator.

Table 1. Different blood flow to gas flow ratios with total amount for each setting.

	Amount	Gas Flow		
Blood flow	n	100 mL/min	200 mL/min	400 mL/min
200 mL/min	6	.5:1	1:1	2:1
350 mL/min	6	.5:1.75	1:1.75	2:1.75

Statistical Analysis

For statistical analysis, IBM SPSS Statistics version 21 (SPSS, Chicago, IL) was used. Data were compared with Mann–U–Whitney test. A p-value of .05 was considered significant. Continuous data were expressed as the mean ± SD.

RESULTS

Increasing the sweep gas to blood flow ratio from .5:1 to 2:1 resulted in a significantly higher CO₂ extraction, (from 14.05 ± 4.35 mL/min/m² to 18.76 ± 4.26 mL/min/m² (p < .01), as shown in Figure 2. Decreasing this ratio, i.e., increasing the blood flow (.5:1.75 and 2:1.75) resulted in a lower CO₂ transfer of 10.00 ± 4.77 mL/min/m² to 16.87 ± 5.09 mL/min/m² (p < .01). Furthermore, there was a greater CO₂ transfer per square meter of surface area at higher sweep gas than at low sweep gas flows (Figure 3) independent of changes in blood flow rate (p < .01). Moreover, comparing the ratios of .5:1.75 and 2:1 or .5:1 and 2:1.75 resulted also in a statistically significant increase of CO₂ transfer (p < .01). Maximum CO₂ transfer in relation to oxygenator membrane surface area was 18.76 mL/min/m² and occurred at a blood flow of 200 mL/min and a sweep gas flow of 400 mL/min (ratio 2:1). Comparison of sweep gas to blood flow ratios of .5:1 and .5:1.75, 1:1 and 1:1.75, and 2:1 and 2:1.75 did not result in a significant difference in CO₂ extraction (p > .05).

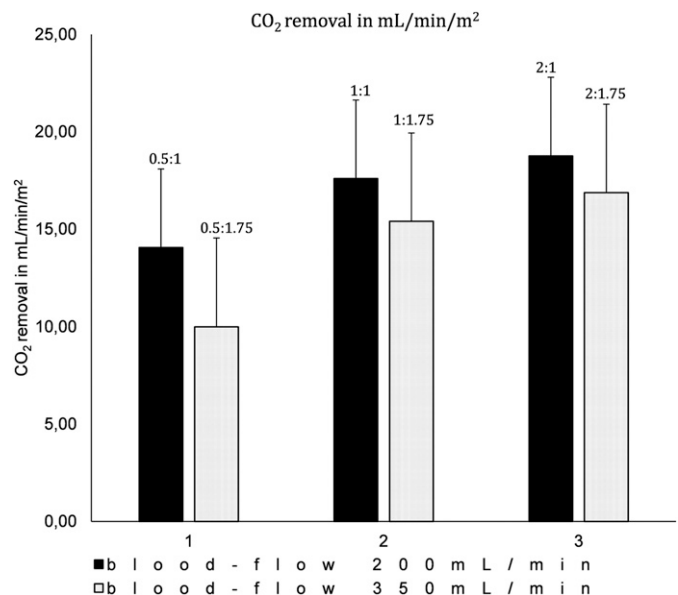


Figure 2. CO₂ removal at various low blood flows. The p-values for the categories 1, 2, and 3 are p = .2, p = .4, and p = .65, respectively.

DISCUSSION

CO₂ transfer was significantly dependent on sweep gas flow at these testing parameters. In contrast, CO₂ transfer was not influenced by the increase of blood flow; it even showed a tendency toward inverse proportionality. These findings reinforce the theory that CO₂ transfer in a membrane oxygenator is mainly driven by gas flow and that low blood flow may be sufficient to remove CO₂ when matched with a correspondingly high sweep gas flow (10).

One of the earliest studies carried out in 1977 by Kolobow and Gattinoni, found that CO₂ transfer (35–65 mL/min) using an ECCO₂R technique with a silicone rubber membrane oxygenator at constant sweep gas flow of 2.5 L/min were dependent on blood flow rates (400–1,000 mL/min) and pre-membrane pCO₂ levels (9). In 2006, Cardenas et al. (11) reported a higher CO₂ extraction (31–150 mL/min), which was dependent on the blood flow (500–1,000 mL/min) and sweep gas flow (2–15 L/min), using a polypropylene microporous hollow fiber membrane oxygenator with an unspecified surface area. Recently, Karagiannidis et al. reported CO₂ transfer rates of 25–100 mL/min at blood flow rates of 200–400 mL/min and sweep gas flows of 8–16 L/min in a PMP membrane oxygenator (12). They inferred that higher CO₂ extraction transfer rates were predominantly influenced by blood flow rather than sweep gas flow (12). Obviously, this observation contradicts our findings where sweep gas flow mainly determined the CO₂ transfer rate.

Alternatively, heterogenic study outcomes can also be a product of different types of oxygenator membrane properties, which itself is an important parameter of gas exchange (13). Moreover, apart from the size of membrane surface, design and material, sweep gas and blood flows, other factors also influence gas transfer, which include

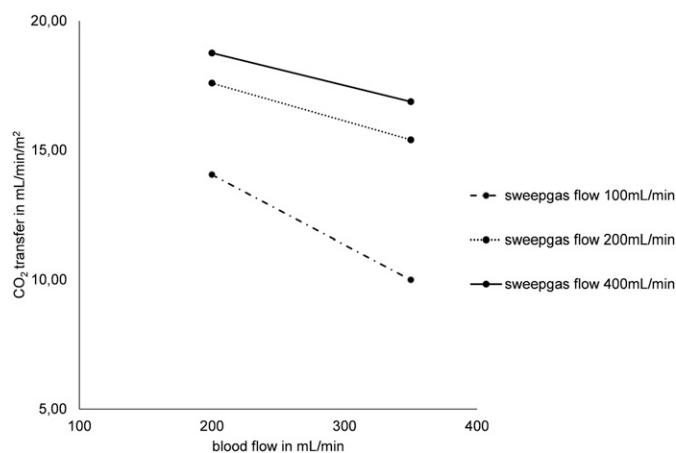


Figure 3. CO₂ transfer in relation to blood flow. Increasing the sweep gas from 100 to 400 mL/min results in a significant improvement of CO₂ transfer at a blood flow of 200 mL/min ($p = .02$) and at a blood flow of 350 mL/min ($p = .015$).

blood channel depth, temperature, and hemoglobin (14). Therefore, optimal setting is important to study the varying influencing factors on CO₂ transfer and an in vitro study can ably provide that condition.

Gas transfer in oxygenator membrane physiology is akin to native lung tissue, where a ventilation perfusion match facilitates CO₂ transfer, a subject of multifactorial dependency (15). In other words, an increase of only one parameter like the surface area of the artificial membrane will not automatically increase CO₂ transfer. The gas exchange may even be less efficient. It is rather a combination of different physiological factors that lead to better gas exchange (16). Furthermore, we expressed the CO₂ transfer in relation to the membrane surface area to emphasize that the artificial membranes have a limited functional capacity restricted by surface area and decremented properties of the membrane.

We realize that our study had noticeable limitations. Firstly, this study was performed on a very small scale, whereas larger-scale studies are needed to bring about a better understanding of this subject. Secondly, design limitations like measuring CO₂ extraction rates at lower blood flow range and lower sweep gas range have led to some insignificant outcomes in our study; mainly although CO₂ extraction does occur, these low sweep gas flows might not be enough in clinical practice to effectively reduce a hypercarbic patient's CO₂ levels. From our bench-top trials, measurements with higher sweep gas without continuous CO₂ supply were not feasible as observed in our setting as the elimination of CO₂ occurs very rapidly. Nevertheless, the present study gives tangible information about the amount of CO₂ extraction and provides essential knowledge about the most important factors that are involved in gas exchange at low blood and sweep gas flows in a PMP membrane oxygenator.

In conclusion, at low-flow ECCO₂R, CO₂ transfer is pre-eminently dependent on sweep gas flow rather than the blood flows in this setup with low blood flow and corresponding low sweep flow.

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