Original Article

Non-Destructive Evaluation of Membrane Lung Gas Exchange Performance

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ABSTRACT

This paper describes a method of evaluating the gas exchange effectiveness of hollow fiber oxygenators utilizing gas on both sides of the membrane. The goal of the study was to develop an evaluation technique which was accurate, reliable, and did not harm or contaminate a new, sterile oxygenator. Three pediatric oxygenators were tested and compared: the Medtronic Minimax Plus, the Terumo Capiox 320, and the Sorin Masterflo 34 (all with rated blood flows of 2 - 2.5 L/min). Gas entering the "blood" side was a mixture of CO_2, O_2, and N_2 in a mixture matching typical venous blood partial pressures. The "blood" flows used were 0.5, 1, 1.5, or 2 L/min. Gas entering the gas port had an FiO_2 of 0.4 flowing at 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 L/min. Fractional contents of CO_2 and O_2 at all inlets and outlets were determined using a gas analyzer and converted to partial pressures. Efficacy indices and gas transfer rates were calculated and compared. Of the devices studied, the Masterflo 34 had the highest gas transport rates and effectiveness followed by the Minimax-Plus and the Capiox 320. Reversing the direction of the flow through the "blood" phase of the Minimax-Plus greatly changed its gas exchange effectiveness. The techniques described in this study should allow for a more uniform and consistent evaluation of gas exchange by membrane lungs which can be made inexpensively and relatively quickly. In addition, these methods should allow manufactures to evaluate gas exchange effectiveness and transfer rates of individual units during production as well as reduce the complexity involved when evaluating newly developed oxygenators.

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INTRODUCTION

When in-vitro evaluations of membrane oxygenators are performed, a complex, time consuming method is used which typically entails construction of two separate circuits and the acquisition of large volumes of bovine, porcine, or canine blood (1,2,3). To evaluate an oxygenator, a test loop must include a source of venous blood deoxygenated to standard venous conditions, with known and controllable hemoglobin content, oxygen saturation, pCO_2, and temperature. Also required is a system for propelling the blood at known flow rates through the test oxygenator and a means for measuring blood O_2 and CO_2 partial pressures and hemoglobin concentration and saturation. Such procedures can be time consuming, not only due to the complex system, but also due to the large number of samples which must be run and data that must be collected. In addition, once these tests are performed, manufacturers tend to plot performance data differently. For example, in the Terumo 320 manufacturer's literature, oxygen transfer is expressed as ml/min vs FIO_2, whereas for the Minimax Plus, oxygen exchange is plotted as ml/min vs blood flow at Qb/Qg of 1:1. In addition to reporting inconsistencies, Vocelka et al. (4), contend that manufacturers' performance data are not comparable between brands due to widely differing testing conditions. Therefore, performance comparison is very difficult without a standard, simple method that can be easily applied.

Another important consideration is the fact that it cannot be assumed that every unit manufactured will perform as expected. Unless each oxygenator is individually tested, distribution of inferior oxygenators cannot be prevented. It is therefore desirable to develop an evaluation technique which is nondestructive to the sterile unit to enable testing of every oxygenator during manufacturing so as to prevent distribution of defective units.

Several design characteristics of hollow fiber oxygenators can contribute to their effectiveness for gas exchange and for their ability to transfer large quantities of gas (5). The physical characteristics of the membrane itself are important considerations, including the porosity, average pore size, wall thickness and total surface area. In addition, the physical relationship between the gas pathways and blood pathways are of primary importance in establishing the gradients for diffusion. For example, countercurrent flow designs are much more effective in mass transfer than co-current flow. Also, the geometry of the blood path can be critical to ensure complete diffusion equilibrium, thus avoiding shunting and incomplete gas exchange.

The purpose of this study was to develop a series of tests that could be used to evaluate several aspects of oxygenator function that allow direct comparisons. One important consideration of this study was that the technique not harm or contaminate a new, sterile oxygenator. It was also important that the evaluation procedure requires a minimum number of analyses which can be quickly and reliably performed. To this end, this study utilizes gas delivered through both the blood and gas pathways of the oxygenator and describes several indices that can be used to evaluate the gas transfer capabilities.

METHODS AND MATERIALS

Three hollow fiber oxygenators, the Medtronic Minimax Plus[a], the Terumo Capiox 320[b], and the Sorin Masterflo 34[c] (all with rated blood flows of 2 – 2.5 L/min), were tested and compared using gas on both sides of the hollow fiber.

In order to ascertain the timing required to accurately perform some of the gas exchange evaluations, the equilibration time between gas in the blood path and that in the gas path was determined. To do this, room air was initially passed through both the blood and gas paths at 1.5 L/min. Then, 3% CO_2 was quickly introduced to the gas path in such a way as to cause no change in the pressure or flow of the gas itself by switching between two gas mixtures using a pair of solenoids. A gas analyzer[d] was used to measure the CO_2 coming out of the blood path. This test demonstrated that complete equilibration occurred within 1 minute following a change in gas composition (Figure 1). As a result, a minimum of 2 minutes was allowed to elapse following a change of experimental conditions before a measurement was made.

a Medtronic, Inc. Anaheim, CA
b Terumo Medical Corp., Tokyo Japan
c Sorin Biomedical Inc., Irvine, CA
d Normocap 200, Datex Division of Instrumentation, Helsinki, Finland

Figure 1: Capnograph traces showing the time course of CO_2 changes in the "blood" outlet gas when CO_2 is suddenly introduced into the flow in the gas phase.

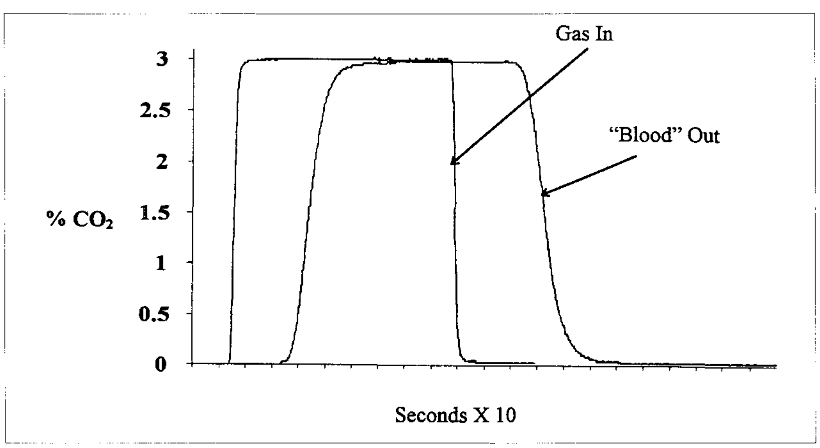
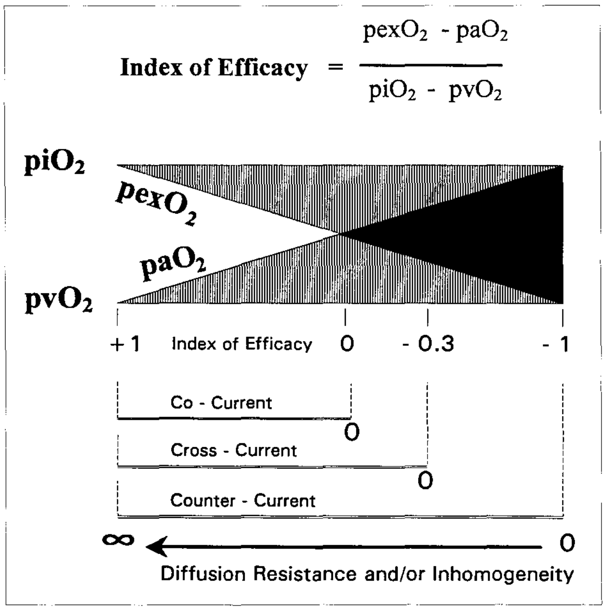


Figure 2: Index of efficacy used in the present study. As shown, the relationship between partial pressures in the outlet blood and gas approach input partial pressures as efficacy increases. Increasing diffusion resistance and "inhomogeneities" serve to reduce effectiveness, moving the relationships toward the left of the figure (From 5, 6).



Convective Flow Resistance:

The first test was designed to determine the membrane resistance to bulk O_2 flow through the pores and across the hollow fibers. For this evaluation, the blood outlet was blocked and O_2 was introduced to the blood inlet at various pressures ranging between 1.5 and 8 cmH_2O. The inlet pressure and the flow of the resultant O_2 into the blood side of the membrane were measured simultaneously using a water manometer and a spirometer[e] respectively.

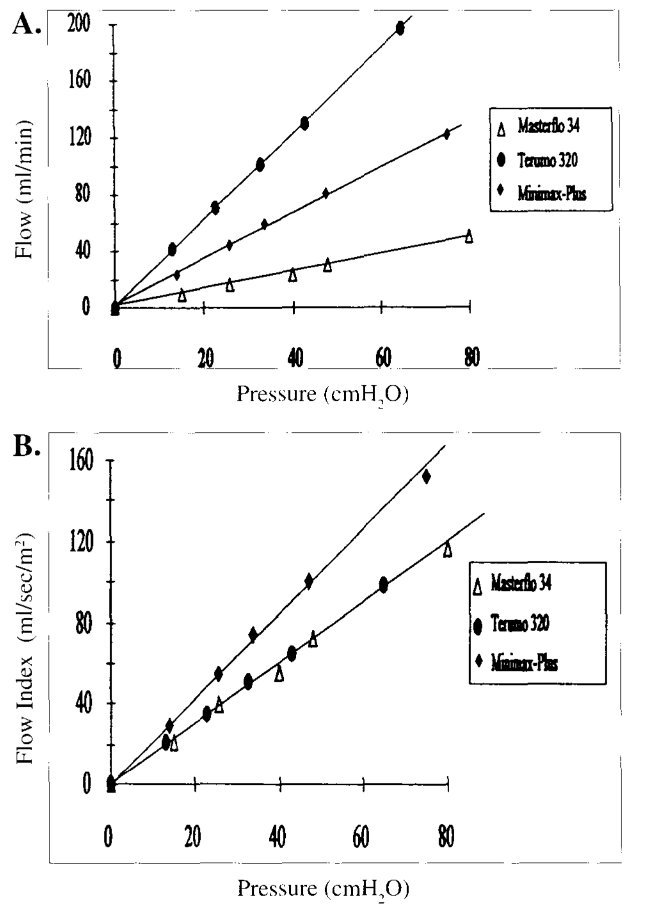
Rate of Gas Transfer and Exchange Efficacy:

Gas was directed into the blood and gas ports of the membrane lung and flows were measured with a pneumotacograph. A gas mixture of 6% CO_2, 8% O_2, and balance nitrogen (providing gases with partial pressures approximating venous blood) was forced through the blood inlet port and tested at flows of 0.5, 1,1.5, or 2 L/min. The gas inlet port of the membrane lung was connected to a supply of 40% O_2 tested at flows of 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 L/min. The recirculation lines on the Minimax Plus and Masterflo 34 were clamped.

A 16G angiocath was inserted into a 6 inch piece of tubing connected to the blood and gas outlet ports and advanced as far as possible into these ports to ensure that a pure, non-contaminated sample of exhaust gas was collected. Fractional composition of O_2 and CO_2 in the inlet and exhaust gases from both sides of the membrane were measured with a gas analyzer and partial pressures calculated.

e 13.5 L Spirometer, Warren E. Collins, Inc., Braintree, MA

Figure 3: A) Resistance to convective O_2 flow across the membrane, and B) Same data as in A, indexed for surface area



At every gas and "blood" flow setting, the outlet of the least resistant pathway was restricted with a Hoffman's clamp positioned on a small piece of tubing. This adjustment was made so that the resistance through both phases was equal, eliminating any pressure gradient and possible gas flow across the membrane. This was verified by ensuring equal flows into and out of both pathways.

Index of Gas Exchange Efficacy:

In order to evaluate the effectiveness of gas exchange, an index was used which was developed and applied in the field of comparative respiratory physiology by Drs. Johannes Piiper and Peter Scheid (6,7). This index is an expression of the ratio of the differences between the input partial pressures and the exit partial pressures (see Figure 2). An index value of 1 indicates no gas exchange between inlet "blood" and inlet gas. An index value of zero indicates gas and "blood" partial pressures are equal and a value of -1 results if outlet "blood" partial pressure equals

Figure 4: Rate of oxygen transfer ($\dot{V}O_2$) as a function of gas flow through the blood path (A). When indexed to surface area (B), the Masterflo 34 exhibits the highest rate of O_2 transfer.

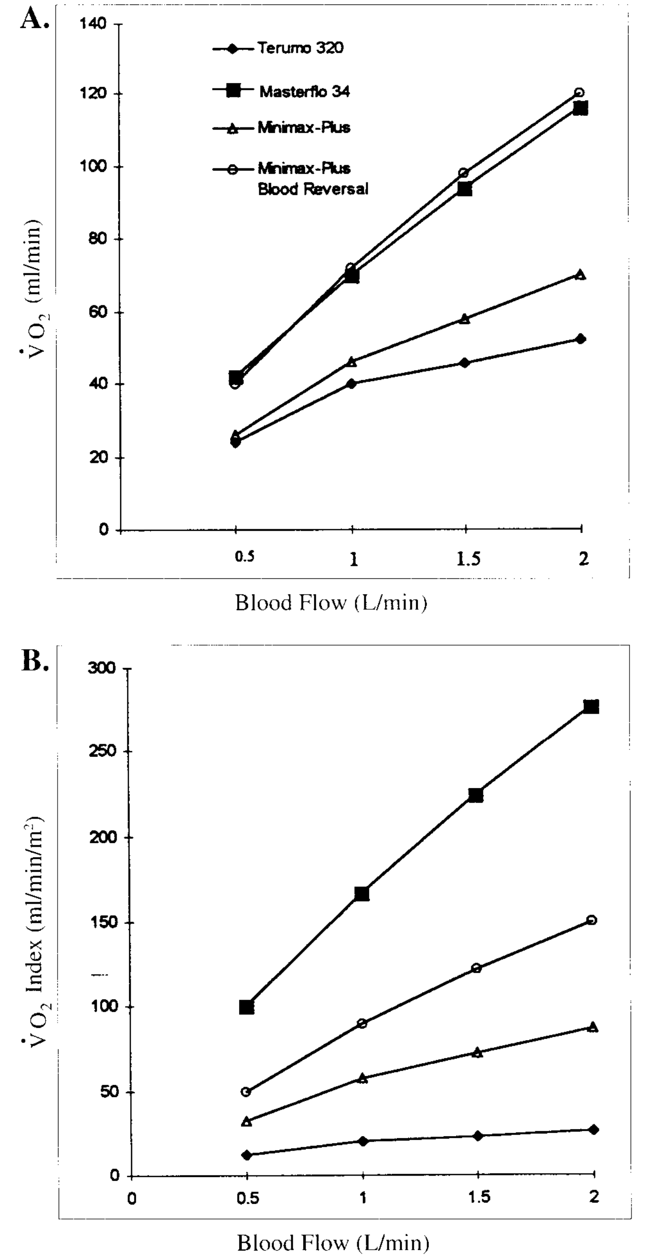
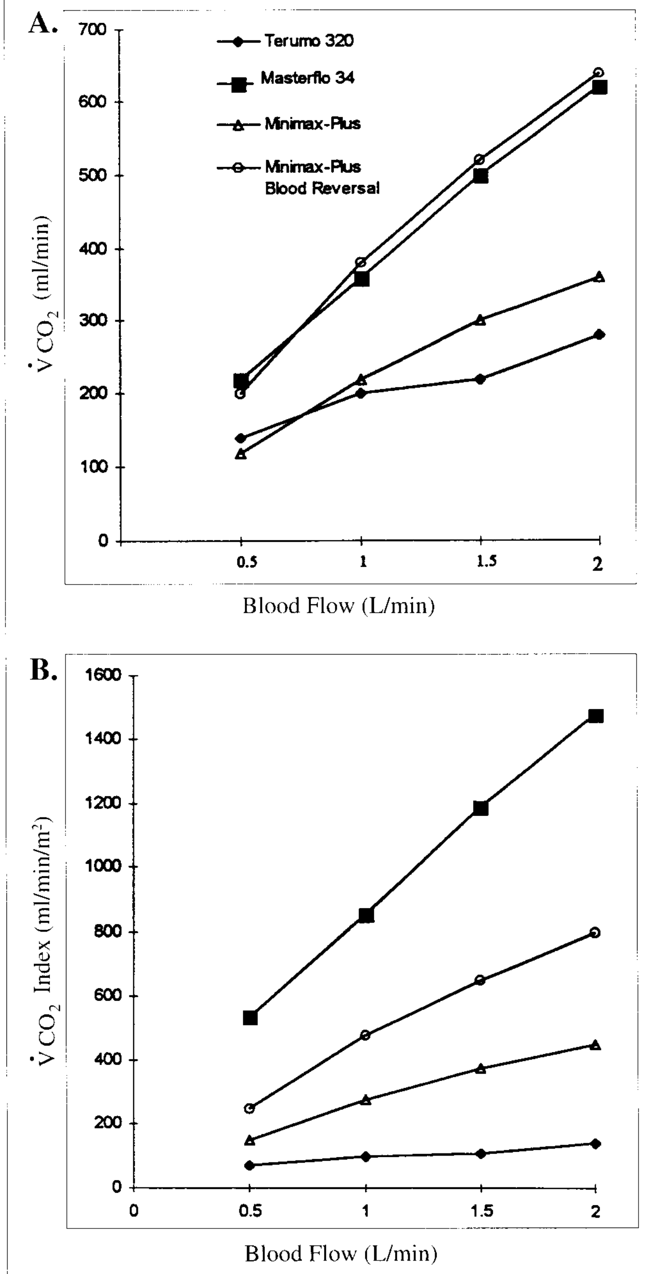


Figure 5: Rate of carbon dioxide transfer ($\dot{V}CO_2$) as a function of gas flow through the blood path (A). When indexed to surface area (B), the Masterflo 34 exhibits the highest rate of CO_2 transfer.



inlet gas partial pressure and vice versa.

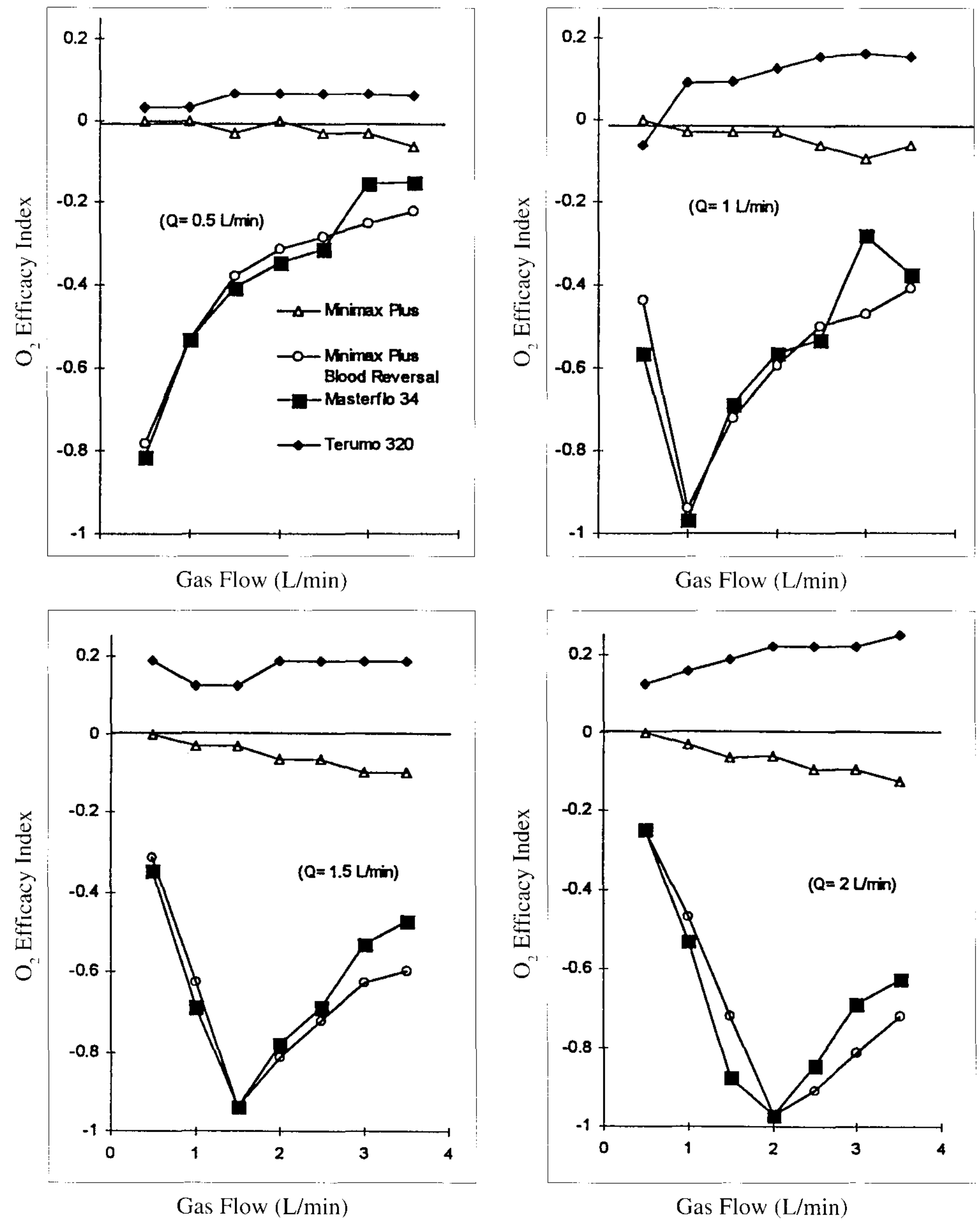
RESULTS

Figure 3 shows the "resistance" to bulk O_2 flow through the pores and across the membrane. As expected, the Capiox 320, having the largest surface area (2 m^2), also had the greatest convective flow across the membrane at any pressure. Next was the Minimax Plus (0.8 M^2), and the oxygenator with the smallest surface area, the Masterflo 34 (0.42 M^2) showed the highest flow resistance. When this data was indexed to account for surface area, the data from the oxygenators with the largest and smallest surface areas (Capiox 320, Terumo and Masterflo 34 respectively) fell along the same line. The Minimax Plus showed less resistance to bulk O_2 flow across the membrane.

Figure 4 shows the effect of "blood" flow on the rate of oxygen transfer with the gas flow held at 2 L/min. Increasing the "blood" flow resulted in an increase in the rate of O_2 transfer for all oxygenators. The Masterflo 34 had the highest rate of O_2 exchange at every blood flow followed by the Minimax Plus and the Capiox 320. Indexing these results to surface area only exaggerated the differences between these devices. Similar results were obtained with the rate of CO_2 transfer (Figure 5). Although less CO_2 than O_2 was transferred at all blood flows under these test conditions, the Masterflo 34 transferred CO_2 at the highest rate. Reversing the direction of gas flow through the blood phase of the Minimax Plus greatly increased the transfer rate of both oxygen and carbon dioxide.

The gas exchange effectiveness was calculated as a function of gas flow and the results are shown in Figures 6 and 7. At any blood flow rate, the Masterflo 34 was more effective as a gas exchanger followed by the Minimax Plus and the Terumo 320. Interestingly, reversing the blood flow through the Minimax Plus resulted in an increase in efficacy matching that of the Masterflo 34. Of particular interest is the fact that the cross-current exchangers (Masterflo and "reversed" Minimax Plus) showed the greatest gas exchange efficacy when the gas to "blood" flow ratio was one.

Figure 6: Index of exchange efficacy for O_2 as a function of gas flow at four blood flows

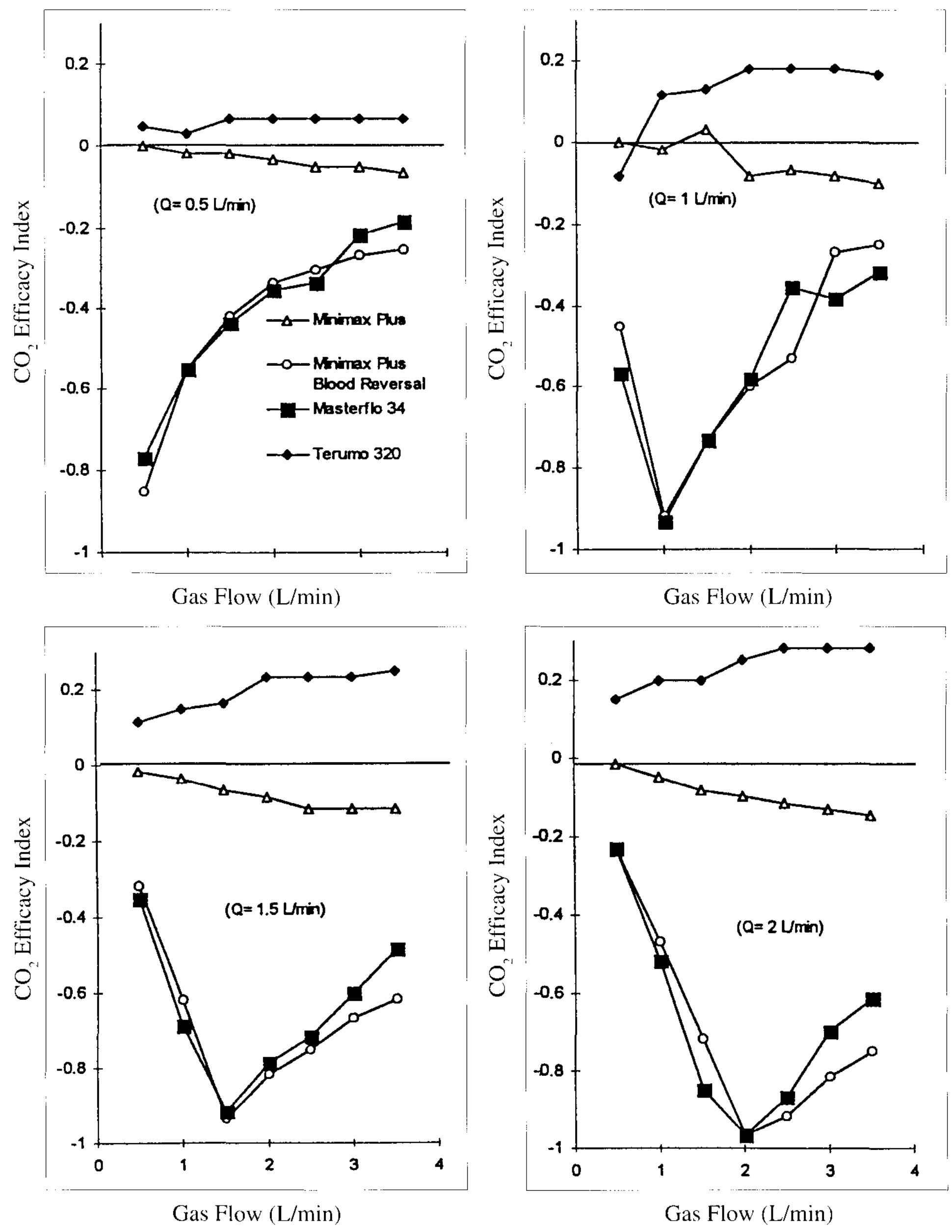


DISCUSSION

Unlike oxygenators that are tested with blood, oxygenators which are evaluated using gas on both sides of the membrane are very sensitive to blood and gas phase pressure differences. One phase having a higher resistance to flow will result in a pressure gradient which may force bulk flow across the membrane. For this reason, a clamp was used to equalize the resistance and thus the flow through both phases.

Although the tests described in this study can be easily and rapidly performed, they allow quantification of several important features of oxygenator design and function. The convective flow resistance is essentially a function of the porosity and average pore size of the membrane material used. A smaller average pore size will increase flow resistance whereas a larger porosity will serve to decrease the resistance. The Minimax Plus has a porosity of 40% and had a lower convective flow resistance than the other oxygenators tested which contain fibers having a porosity of 20%. This test could also easily distinguish

Figure 7: Index of exchange efficacy for CO_2 as a function of gas flow at four blood flows



between devices that may be defective with a significant number of plugged pores or fibers. Also, the presence of an open pathway or shunt between the two compartments could be determined if a particular unit had a lower than expected resistance.

Despite its smaller surface area, the Masterflo 34 was capable of transferring O_2 and CO_2 at a higher rate than the other two oxygenators. It was capable of doing so because it was operating much more effectively under these study conditions. Among the factors which affect gas exchange effectiveness are the geometric relationship between the gas flow and blood flow paths (i.e. co-current, cross-current or counter current flow). Figure 2 graphically depicts the effects of this flow relationship on the efficacy index and the partial pressure in the exhaust media. A countercurrent exchange device with no diffusion resistance could ideally have an index of -1. Adding diffusion resistance shifts the index toward the left. A cross-current device without diffusion resistance will have an index of -0.3 and a co-current device could only achieve an index of zero (6) The Masterflo 34 is a countercurrent exchanger and reached a maximum index of close to -1 indicating that there is very little diffusion resistance across the membranes (Figure 2). The maximum gas exchange effectiveness is seen when the gas to "blood" flow ratio was 1:1 (6). Although in the Masterflo 34 the fibers are wrapped radially, placing the gas and blood flows at right angles, the blood flows from the bottom to the top of the device and the gas flows from top to bottom. The Minimax-Plus places gas and blood flows at right angles but gas and blood ultimately flow from the top to the bottom of the oxygenator. The efficacy index of the Minimax-Plus extends below zero to a maximum of -0.1 showing how the radial design results in gas exchange exceeding that of a purely co-current exchanger. On the other hand, the "reverse" Minimax-Plus, with the intention to create a countercurrent flow, indeed matches the indices of a countercurrent device. The Capiox 320 is a co-current device, and its efficacy index clearly reflects this.

Other factors which serve to decrease the effectiveness of gas exchange are lumped together as "inhomogeneities". These include shunts (or low ventilation/perfusion ratios) and lack of chemical equilibrium (6,7,8). When blood is used as the medium in the blood phase, lower indices and exchange rates can be expected. This is due to a slower rate of diffusion through the plasma, (exaggerating any lack of complete equilibrium by excessive diffusion distance between fibers), much lower capacitance (ml/mmHg) of the blood for these gases and the lack of chemical equilibrium for CO_2 (7). For these reasons, a direct comparison of the results of the present study to those obtained when blood is used should be made with caution. The value of the present study lies in the ability to compare the gas exchange capabilities of the devices with many of these other variables either kept constant or eliminated from consideration. Thus, an evaluation can readily be made of the materials used and the physical relationships of the gas and blood pathways and the effect these considerations have on the exchange capabilities of the different oxygenators.

The results of this study demonstrate the usefulness of evaluations using gas on both sides of the membrane to distinguish various characteristics of membrane oxygenators. Since equilibrium between gases occurs relatively quickly, these tests can be easily run without contaminating new, unused units. These evaluations could therefore be readily used to assure quality during the manufacturing process. In order to conduct these tests of gas exchange effectiveness and rate of gas transfer, only the analyses of exhaust gas and "blood" outlet gas are required. Thus, introducing known gas mixtures at known flows provides the investigator with the only other variables needed to make these analyses.

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