Quantitative Gas Transfer of an Intravascular Oxygenator

Martin Tönz, MD, Ludwig K. von Segesser, MD, Boris Leskosek, BA, and Marko I. Turina, MD

Clinic for Cardiovascular Surgery and Research Division, Department of Surgery, University Hospital, Zurich, Switzerland

The intravascular oxygenator is a newly developed device for intracaval gas exchange in critically ill patients with respiratory failure. In an experimental ex vivo model, performance characteristics of the intravascular oxygenator/carbon dioxide removal device were studied. With a mean hemoglobin concentration of 6.2 ± 1.9 g/dL (mean ± standard deviation), total O_2 transfer was 21.8 ± 4.8 mL/min at a blood flow of 1 L/min, 37.0 ± 12.6 mL/min at 2 L/min, and 47.5 ± 16.7 mL/min at 3 L/min. Total CO_2 transfer was 27.3 ± 6.6 mL/min at a blood flow of 1 L/min, 38.6 ± 8.9 mL/min at 2 L/min, and 40.4 ± 9.3 mL/min at 3 L/min. In contrast to total gas transfer, O_2/CO_2 transfer rates (mL/L) diminished significantly with increasing blood flow. In addition, there was a negative correlation between O_2 transfer rate and venous O_2 partial pressure ($r = -0.73$; $p < 0.0001$), a positive correlation between CO_2 transfer rate and venous CO_2 partial pressure ($r = 0.65$; $p < 0.0001$), and a positive correlation between O_2 and CO_2 transfer rates and blood hemoglobin level ($r = 0.57$ [$p < 0.01$] and $r = 0.70$ [$p < 0.01$], respectively). These results demonstrate that the behavior of the intravascular hollow-fiber oxygenator is similar to that of the classic membrane oxygenator used for cardiopulmonary bypass: total gas transfer correlates directly with blood flow and venous CO_2 partial pressure and indirectly with venous O_2 partial pressure. The O_2 and CO_2 transfer rates increase significantly with increasing hemoglobin content of the blood.

(Ann Thorac Surg 1994;57:146–50)

Despite continuous efforts to develop and evaluate new methods for ventilatory support, adult respiratory failure remains a challenge in modern intensive care medicine. Even though extracorporeal membrane oxygenation has proved to be of some benefit in the treatment of the critically ill patient with compromised pulmonary function [1], it remains a cumbersome procedure requiring blood pumps, oxygenators, heat exchangers, tubing, and a highly specialized team throughout the procedure, which may last for weeks. To circumvent the problems of extracorporeal oxygenation and circulation, an intravascular oxygenator/carbon dioxide removal device has been developed [2]. Inserted in the superior and inferior venae cavae through the femoral vein, it provides respiratory assistance for patients with severe, potentially reversible, acute respiratory failure [3]. To evaluate the quantitative gas transfer and the performance characteristics of the oxygenator, we used an ex vivo animal model based on "reversible" hypoventilation.

Material and Methods

The intravascular oxygenator used (IVOX No. 10; CardioPulmonics, Salt Lake City, UT) is a hollow-fiber gas exchange device consisting of multiple siloxane-coated microporous polypropylene hollow fibers coated with heparin (total outer surface area, 0.52 m^2). The hollow fibers are connected to a dual-lumen gas conduit and joined at the distal end through a potted manifold to the inner lumen and at the proximal end through another manifold to the outer lumen. A vacuum pump attached to the outer lumen draws oxygen into the multiple hollow fibers from an oxygen source and exhausts the oxygen not transferred to the patient as well as the removed carbon dioxide.

All animals received humane care in compliance with the federal animal protection law (Federal Law 1978, revised 1991) and guidelines (Federal Guidelines 1981, revised 1991). In four bovine experiments (body weight, 60 to 80 kg), after premedication, anesthesia was induced with phenobarbital and maintained with volatile anesthetics. With the use of positive-pressure endotracheal ventilation, a right thoracotomy was performed with exposure of the heart. After systemic heparinization (Liquemin; 300 IU/kg body weight, F. Hoffmann-La Roche & Co, Basel, Switzerland), cannulas were placed into the pulmonary artery and the right atrium and connected to a right heart bypass system including a gas exchange chamber. The latter was a Plexiglas tube with an inner diameter of 26 mm containing the intravascular oxygenator (Fig 1) positioned at the side of the animal. By this arrangement, blood pressure in the chamber was kept equivalent to the central venous pressure. Gas flow through the intravascular oxygenator (3.3 ± 0.14 L/min; range, 3.1 to 3.4 L/min; gas outlet pressure, 50 kPa) and inlet gas oxygen concentration (100%) were held constant over the time of the experiment.

Accepted for publication Feb 24, 1993.

Address reprint requests to Dr Tönz, Clinic for Cardiovascular Surgery, University Hospital, 8091 Zurich, Switzerland.

0003-4975/94/$7.00

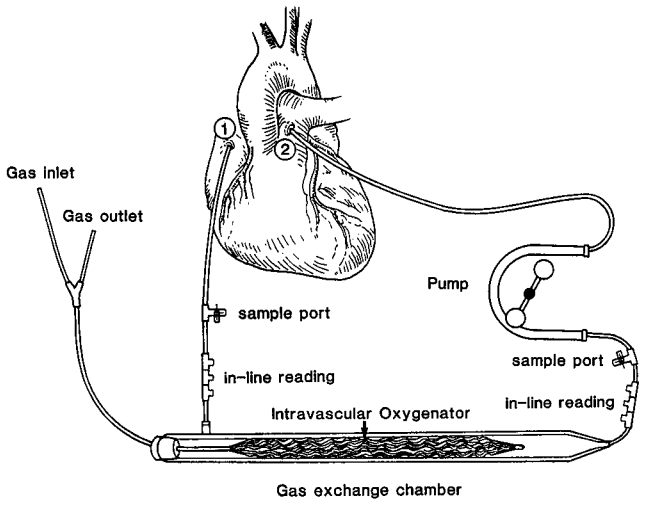

Fig 1. Schematic diagram of the right heart bypass with incorporated gas exchange chamber. (1 = right atrium; 2 = pulmonary artery).

Gas transfer was systematically measured with varying blood flows of 1, 2, and 3 L/min during normoventilation, during several grades of hypoventilation (oxygen partial pressures at the inlet of the gas exchange chamber [PvO_2], 1.0 to 4.0 kPa; carbon dioxide partial pressures at the inlet of the gas exchange chamber [$PvCO_2$], 3.9 to 7.9 kPa), and at the end with stepwise decreasing hemoglobin concentrations (range, 3.4 to 9.2 g/dL). Blood flow was controlled with the pump of the right heart bypass, PvO_2 and $PvCO_2$ by "reversible" hypoventilation of the animal (as described previously [4]: minute ventilation, 6.5 to 9 L/min; fractional inspired concentration of oxygen, 0.21 to 0.33), and hemoglobin concentrations by administration of Ringer's lactate. Blood samples were analyzed on-line at the inlet and outlet of the gas exchange chamber with a Cardiomet 4000 blood gas analyser (Biomedical Sensors; Shiley, Irvine, CA) and intermittently with a BGElectrolyte Analyzer (Instrumentation Laboratory Spa, Milan, Italy). Expired gas CO_2 content of the oxygenator was measured in-line with a modified capnograph (Accucap; Datascope, Paramus, NJ; modified for continuous gas flow). Oxygen and carbon dioxide transfer rates were calculated by the following formula (Association for the Advancement of Medical Instrumentation standard for blood/gas exchange devices): total O_2 transfer ($\dot{V}O_2$) = $(\Delta[O_2]_{a-v}) \cdot Qb$ (mL/min); total CO_2 transfer ($\dot{V}CO_2$) = $CO_2\% \cdot Qg$ (mL/min); O_2 transfer rate (transfer per unit blood flow) = $\dot{V}O_2/Qb$ (mL/L); and CO_2 transfer rate = $\dot{V}CO_2/Qb$ (mL/L) ($\Delta[O_2]_{a-v}$ = difference in oxygen content of the inlet and outlet blood, $CO_2\%$ = oxygenator expired gas CO_2 content, Qg = gas flow rate, and Qb = blood flow rate).

Data were analyzed with StatView II and Cricket Graph on an Apple Macintosh IICi. Paired and unpaired Student's *t* tests were employed where applicable for comparison of data. Differences were considered significant at a probability level of less than 0.05. Data are expressed as mean ± standard deviation.

Results

Table 1 summarizes the gas transfers for the respective blood flows based on blood hemoglobin content of 6.2 ± 1.9 g/dL, PvO_2 of 2.57 ± 0.38 kPa, $PvCO_2$ of 5.31 ± 1.01 kPa, pH of 7.35 ± 0.12, and blood temperature of 36°C. Total O_2 and CO_2 transfers at various blood flow are shown in Figure 2. Curve fitting resulted in a logarithmic function with a correlation coefficient of 0.99 and 0.97, respectively. There was a significantly higher total O_2 and CO_2 transfer at a blood flow of 3 L/min (47.5 ± 16.7 mL/min and 40.4 ± 9.3 mL/min, respectively) as compared with 1 L/min (21.8 ± 4.8 mL/min [$p < 0.001$] and 27.3 ± 6.6 mL/min [$p < 0.001$], respectively). The corresponding O_2 and CO_2 transfer rates are depicted in Figure 3. The O_2 and CO_2 transfer rates decreased significantly with augmentation of blood flow from 1 to 3 L/min (21.3 ± 4.5 versus 14.1 ± 3.4 mL/L [$p < 0.01$] and 25.9 ± 7.3 versus 16.4 ± 5.3 mL/L [$p < 0.001$], respectively). In addition, there is a strong correlation between gas transfer rates and gas partial pressures of the venous blood. The O_2 transfer rate is negatively correlated with the venous O_2 partial pressure (Fig 4) ($r = -0.73$; $p < 0.0001$); CO_2 transfer rate is positively correlated with the venous CO_2 partial pressure (see Fig 4) ($r = 0.65$; $p < 0.0001$). Gas transfer rates with various blood hemoglobin contents are shown in Figure 5. They are based on measurements with a blood flow within 2 to 3 L/min (2.58 ± 0.5 L/min), a PvO_2 within 2.0 to 3.0 kPa (2.65 ± 0.45 kPa), and a $PvCO_2$ within 3.9 to 7.6 kPa (5.31 ± 1.01 kPa). The O_2 and CO_2 transfer rates increased significantly ($p < 0.01$ for each) with increasing blood hemoglobin content.

Comment

Our results demonstrate that the behavior of the intravascular hollow-fiber oxygenator is similar to that of a classic membrane oxygenator used for cardiopulmonary bypass: (1) total O_2 and CO_2 transfer increase with increasing blood flow with a concurrent decrease in the transfer rates (see Figs 2, 3); (2) O_2 transfer rate is indirectly propor-

Table 1. Oxygen and Carbon Dioxide Transfer With Various Blood Flow Rates[a]

Variable	Blood Flow 1 L/min (n = 22)	Blood Flow 2 L/min (n = 30)	Blood Flow 3 L/min (n = 24)
Total O_2 transfer (mL/min)	21.8 ± 4.8[b]	37.0 ± 12.6	47.5 ± 16.7[c]
Total CO_2 transfer (mL/min)	27.3 ± 6.6[b]	38.6 ± 8.9	40.4 ± 9.3[c]
O_2 transfer rate (mL/L)	21.3 ± 4.5	19.4 ± 6.1	14.1 ± 3.4[c]
CO_2 transfer rate (mL/L)	25.9 ± 7.3[b]	19.6 ± 4.9[d]	16.4 ± 5.3[c]

[a] Blood hemoglobin content, 6.2 ± 1.9 g/dL; inlet oxygen partial pressure = 2.57 ± 0.38 kPa; inlet carbon dioxide partial pressure = 5.31 ± 1.01 kPa; pH, 7.35 ± 0.12; blood temperature, 36°C. [b] $p < 0.05$ versus 2 L/min. [c] $p < 0.05$ versus 1 L/min. [d] $p < 0.05$ versus 3 L/min.

tional to the venous O_2 partial pressure and CO_2 transfer rate is directly proportional to the venous CO_2 partial pressure (see Fig 4); and (3) O_2 and CO_2 transfer rates increase significantly with increasing hemoglobin content of the blood (see Fig 5).

Some characteristics of the intravascular oxygenator have been previously described by various authors in ex vivo and in vivo preparations [2, 4–7]. However, concerning O_2 and CO_2 transfer, the reported results are difficult to compare for the following reasons: (1) the large differences in venous O_2/CO_2 content and the various blood flow rates along the vena cava do not allow exact measurement of gas transfer by the intravascular oxygenator

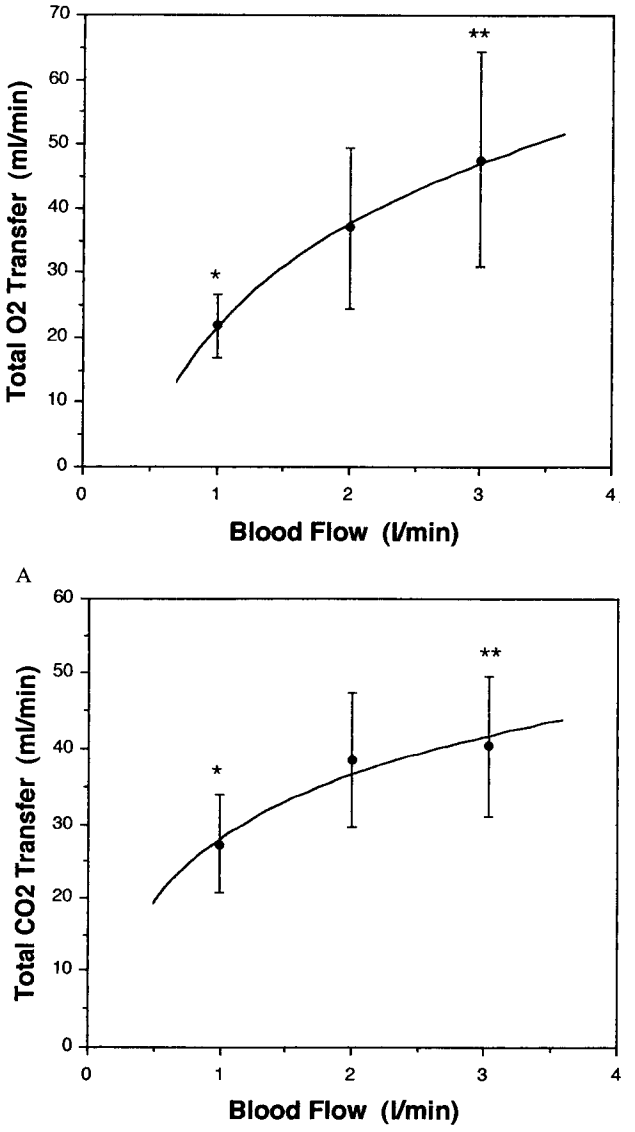

Fig 2. Total oxygen (A) and carbon dioxide transfer (B) with various blood flow rates (hemoglobin level = 6.2 ± 1.9 g/dL; inlet oxygen partial pressure = 2.57 ± 0.38 kPa; inlet carbon dioxide partial pressure = 5.31 ± 1.01 kPa; pH = 7.35 ± 0.12; blood temperature = 36°C). (p < 0.05 1 versus 2 L/min; ** p < 0.05 1 versus 3 L/min.)*

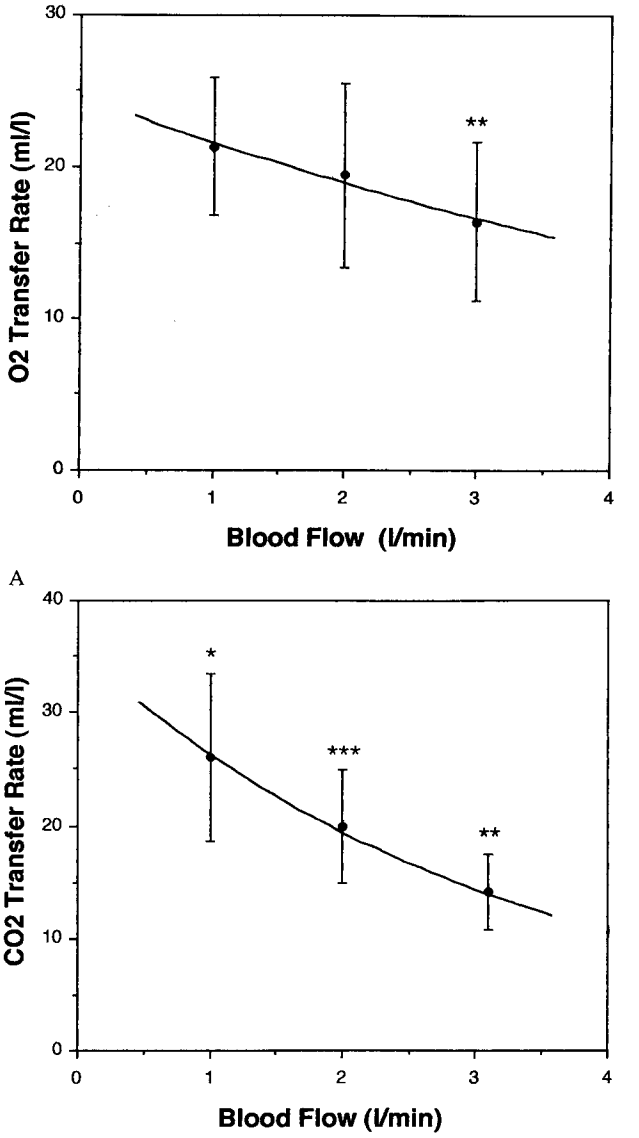

*Fig 3. Oxygen (A) and carbon dioxide transfer rates (B) with various blood flow rates (hemoglobin level = 6.2 ± 1.9 g/dL; inlet oxygen partial pressure = 2.57 ± 0.38 kPa; inlet carbon dioxide partial pressure = 5.31 ± 1.01 kPa; pH = 7.35 ± 0.12; blood temperature = 36°C). * p < 0.05 1 versus 2 L/min; ** p < 0.05 1 versus 3 L/min; *** p < 0.05 2 versus 3 L/min.)*

in vivo. Therefore, pulmonary blood gas analyses with the oxygenator turned on and off were used to estimate O_2 transfer. This technique, although the most convenient in vivo, is not very reliable because consecutively changing hemodynamic and ventilatory parameters between the on and off periods may heavily influence gas transfer rates. (2) The values of the ex vivo preparations are difficult to appreciate because the calculated gas transfers are expressed as total O_2 and CO_2 transfer, without correlation with hemodynamic parameters. This probably accounts for the big differences (up to 250%) in total gas exchange between ex vivo and in vivo preparations re-

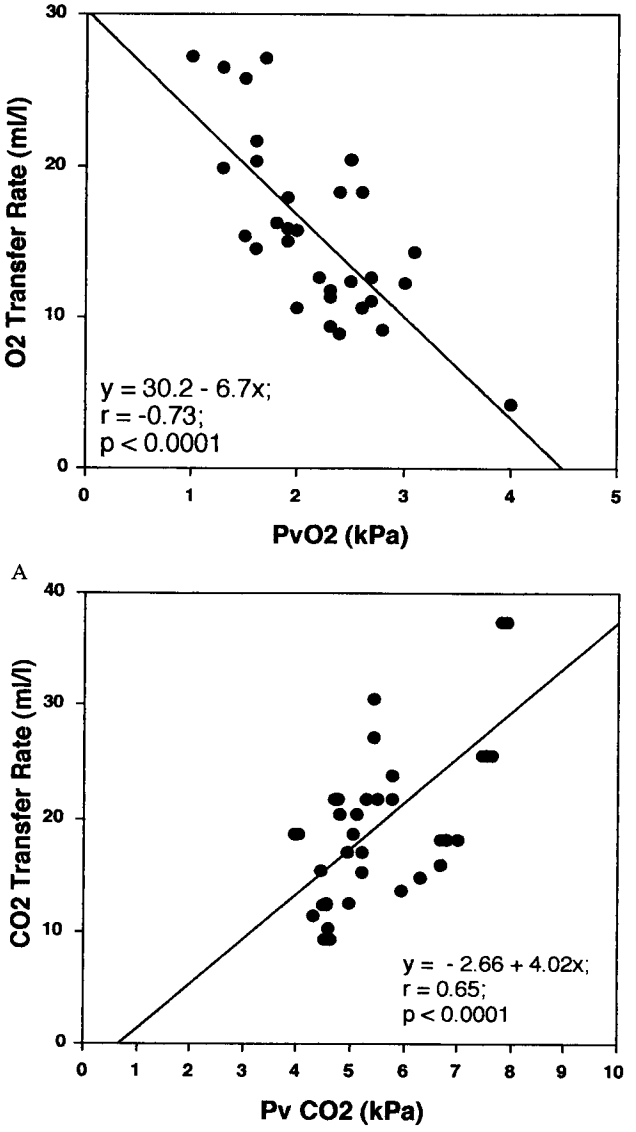

Fig 4. Oxygen (A) and carbon dioxide transfer rates (B) versus inlet oxygen partial pressure (Pv O2) *and inlet carbon dioxide partial pressure* (Pv CO2), *respectively (hemoglobin level = 6.2 ± 1.9 g/dL; blood flow = 2.58 ± 0.5 L/min; blood temperature = 36°C).*

ported in the literature [6]. In addition, the influence of various parameters such as blood flow, blood hemoglobin content, and venous O_2 and CO_2 partial pressures on quantitative gas transfer have not been shown.

To evaluate gas transfer rates and performance characteristics of the intravascular oxygenator in a reproducible manner, we therefore used an ex vivo model with an external gas exchange chamber integrated in a right heart bypass system. With this setting we were able to vary the significant parameters in standardized fashion: blood flow with the roller pump, PvO_2 and $PvCO_2$ with serial changes of the ventilatory parameters, and hemoglobin content with progressive hemodilution of the animal. Analogous to clinical use, we did not vary gas flow; it was held constant at a maximal level. Although this ex vivo model gives the most precise information about performance of the intravascular oxygenator, there are some limitations in clinical application of observed data: (1) the walls of the ex vivo gas exchange chamber are not compliant as is the vena cava. There is some evidence that quantitative gas transfer is influenced by changing vascular diameters. (2) Blood flow along the vena cava varies significantly (blood flow in the infrarenal vena cava is only a small part of the flow in the right atrium) and is bidirectional (ie, gas flow is partly concurrent and partly countercurrent to blood flow). At the moment we are not able to quantify the effect of these factors on gas transfer.

In spite of these limitations, we can draw the following

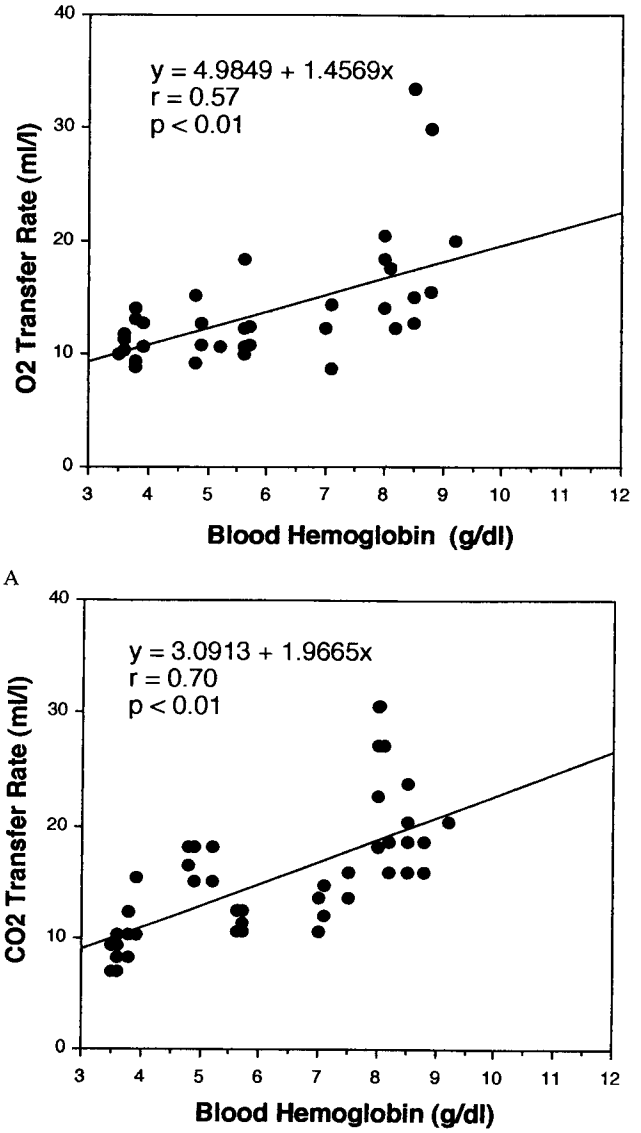

Fig 5. Oxygen (A) and carbon dioxide transfer rates (B) versus blood hemoglobin content (inlet oxygen partial pressure = 2.65 ± 0.45 kPa; inlet carbon dioxide partial pressure = 5.31 ± 1.01 kPa; blood flow = 2.58 ± 0.5 L/min; blood temperature = 36°C).

conclusion for clinical use of the intravascular oxygenator: optimal performance of the device can be obtained with high blood flow, high hemoglobin content, high $PvCO_2$, and low PvO_2. In situations with low cardiac output, the benefit of the system is limited. Because of the low blood hemoglobin concentration of the laboratory animals, the above-mentioned gas transfer rates are to be settled at the lower performance limit of the intravascular oxygenator. In clinical application, O_2 and CO_2 gas exchange will be superior because of the higher hemoglobin concentration of the patients. Therefore the intravascular oxygenator can provide significant support to the critically ill patient with respiratory failure. First clinical experiences up to 29 days are encouraging [3, 7, 8].

References

1. Anderson HL, Delius RE, Sinard JM, et al. Early experience with adult extracorporeal membrane oxygenation in the modern era. Ann Thorac Surg 1992;53:553–63.
2. Mortensen JD, Berry G. Conceptual and design features of a practical, clinically effective intravenous mechanical blood oxygen/carbon dioxide exchange device (Ivox). Int J Artif Organs 1989;12:384–9.
3. Kallis P, Al-Saady NM, Bennett D, Treasure T. Clinical use of intravascular oxygenation. Lancet 1991;337:549.
4. Von Segesser LK, Weiss BM, Pasic M, Friedel HP, Leskosek B, Turina MI. Temporary lung support using a intravascular gas exchanger. Thorac Cardiovasc Surg 1992;40:121–5.
5. Cox CS, Zwischenberger JB, Traber LD, Traber DL, Herndon DN. Use of an intravascular oxygen/carbon dioxide removal device in an ovine smoke inhalation injury model. ASAIO Trans 1991;37:M411–3.
6. Bagley B, Bagley A, Henrie J, et al. Quantitative gas transfer into and out of circulating venous blood by means of an intravenacaval oxygenator. ASAIO Trans 1991;37:M413–5.
7. Zwischenberger JB, Cox CS, Graves D, Bidani A. Intravascular membrane oxygenation and carbon dioxide removal—a new application for permissive hypercapnia? Thorac Cardiovasc Surg 1992;40:115–20.
8. Von Segesser LK, Schaffner A, Stocker R, et al. Extended (29 days) use of intravascular gas exchanger. Lancet 1992;339: 1536.