Original Article

Impact of Hollow-Fiber Membrane Surface Area on Oxygenator Performance: Dideco D903 Avant Versus a Prototype with Larger Surface Area

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ABSTRACT

This study compares the gas transfer capacity, the blood trauma, and the blood path resistance of the hollow-fiber membrane oxygenator Dideco D 903 with a surface area of 1.7 m^2 (oxygenator 1.7) versus a prototype built on the same principles but with a surface area of 2 m^2 (oxygenator 2).

Six calves (mean body weight: 68.2 ± 3.2 kg) were connected to cardiopulmonary bypass (CPB) by jugular venous and carotid arterial cannulation, with a mean flow rate of 4l/min for 6 h. They were randomly assigned to oxygenator 1.7 ($N = 3$) or 2 ($N = 3$). After 7 days, the animals were sacrificed. A standard battery of blood samples was taken before the bypass, throughout the bypass, and 24 h, 48 h, and 7 days after the bypass.

The oxygenator 2 group showed significantly better total oxygen and carbon dioxide transfer values throughout the perfusion ($p < .001$ for both comparison). Hemolytic parameters (lactate dehydrogenase and free plasma hemoglobin) exhibited a slight but significant increase after 5 h of bypass in the oxygenator 1.7 group. The pressure drop through the oxygenator was low in both groups (range, 43–74 mmHg).

With this type of hollow-fiber membrane oxygenator, an increased surface of gas exchange from 1.7m^2 to 2 m^2 improves gas transfer, with a limited impact on blood trauma and no increase of blood path resistance.

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INTRODUCTION

The design objectives of the "ideal" oxygenator described in 1962 by Galetti and Brecher (1) are still valid. This oxygenator should provide oxygenation of venous blood, carbon dioxide elimination, minimum trauma to the blood, small priming volume, and safety. With the advent of membrane oxygenators, modification in their design have consistently aimed toward these design objectives. Reductions in surface area to minimize blood contact with foreign surface has been one of the mainstays of research. However, this design feature may decrease gas transfer and increase blood path resistance as well as blood trauma. On the other hand, larger surface area for gas exchange might be beneficial for patients with a high body mass index.

Dideco Inc. (Mirandola, Italy) has recently added the D903 Avant membrane oxygenator to its cardiopulmonary product line with further reduction of the surface area (1.7 m^2). The present study was designed to compare the gas transfer capacity of this oxygenator (oxygenator 1.7) with a prototype built on the same principles but with a surface area of 2 m^2 (oxygenator 2). The impact of the surface area on blood trauma and blood path resistance were studied as well.

METHOD

The protocols described herein were reviewed and approved by the Committee on Animal Care, Office Vé terinaire Cantonal, Lausanne. All animals received care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication No. 80-23, revised 1985).

ANIMALS

This study was conducted on six calves with a mean body weight of 68.2 ± 3.2 kg (standard deviation). All the animals were premedicated with xylazine (0.15 mg/kg, given intramuscularly). General anesthesia was started with thiopentone sodium (10 mg/kg, given intravenously) and maintained thereafter with volatile anesthetics (N_2O and halothane) mixed with oxygen-enriched air. The animals were equipped with a jugular central venous catheter and a femoral arterial catheter for hemodynamic monitoring.

OXYGENATOR

The D903 Avant 1.7[a] is an integrated hollow-fiber membrane oxygenator containing an open hard shell reservoir, a heat exchanger, and the oxygenating compartment. The latter contains microporous hollow fibers (380 μm outer diameter and 100 μm wall thickness) made from polypropylene for separation of the gaseous phase from the blood with a total outer surface of 1.7 m^2. The ventilating gas goes through the hollow fibers; whereas, the blood circulates outside the hollow fibers mounted in a polycarbonate shell. This set-up is known for a low pressure drop between inlet and outlet of the oxygenating compartment (2). The pump loop and the roller pump are installed between the venous reservoir on one side and the heat exchanger and oxygenating compartment on the other. Thus, the blood is pushed through the space outside the hollow fibers.

The innovation of the D903 Avant 1.7 oxygenator lies in the configuration of the inner design of the oxygenating compartment. The hollow fibers are inserted in a cylinder fashion into a polycarbonate housing. The inner surfaces of the inside and outside walls of the housing are wavy. Blood enters at the top of the housing on the inner side. The blood is then forced between the fibers and follows the wavy way between the inside and the outside walls of the housing. This wavy pattern is intended to diminish the blood streamlining (direct flow through the oxygenator without gas exchange) and, therefore, to increase gas exchange efficiency. Arterial blood is collected at the bottom of the oxygenator. The prototype studied for comparison has the same design except for the larger total outer surface of 2 m^2.

EQUIPMENT

A primary calibrated roller pump model 10.10.00, Stö ckert,[b] custom 1/2 and 3/8 polyvinylchloride (PVC) tubing packs, and a gas blender[c] were used on all cases. Closed chest perfusion was selected for this study. For this purpose, the right atrium was cannulated through a jugular vein for venous drainage; whereas, a carotid artery was used for the arterial return. Before cannulation, heparin (Liquemin[d]), 300 U/kg body weight, was given systemically and the activated clotting time (ACT[e]) was kept above 400 sec throughout perfusion. The cardiopulmonary bypass circuit was connected after being primed with 1500 cc of crystalloid only. Blood flow rate was maintained by a roller pump at 4l/min. Arterial pH was between 7.4–7.5, and mean femoral arterial pressure was kept between 60–80 mmHg. Temperature was maintained at 36°C. Oxygen flow was supplied to the oxygenator with the gas blender at a flow rate equal to the blood flow rate.

After perfusion, the animals were weaned and decannulated. Then the animals were weaned from the ventilator and extubated. After 7 days survival, the animals were electively sacrificed with a lethal dose of sodium pentobarbital. A necropsy was performed for macroscopic analyses of the lungs, the heart, the liver, the spleen and the kidneys, with special atten-

[a] Dideco, Inc., Mirandola, Italy

[b] Sorin Biomedical, Irvine, CA
[c] Sechrist Industries, Inc., Anaheim, CA
[d] F. Hoffman La Roche & Co., Basle, Switzerland
[e] Hemochron, International Technidyne Corp., Edison, NJ

tion being paid to the latter to detect any focal necrosis suggestive of emboli (3).

MEASUREMENTS

ECG, central venous pressure, femoral artery pressure, arterial line pressure, pump flow, and inlet and outlet pressures of the oxygenator were recorded continuously. A standard battery of blood samples was taken for arterial and venous blood gas analyses, hematology (hematocrit, white blood count, thrombocytes), and chemistry (LDH, free plasma hemoglobin) before bypass after mixing (10 min bypass), after 1, 2, 5, and 6 h of perfusion. Blood gas samples were taken again 30 min after bypass (spontaneous breathing) and 60 min after bypass (after extubation). Furthermore, hematology and chemistry samples were taken 24 h after bypass, 48 h after bypass, and 7 days after bypass.

DATA ANALYSES

Mean and standard deviation were derived for each parameter analyzed. Student's *t*-test and analysis of variance (ANOVA) for repeated measures were used where applicable for determination of statistical significance ($p < .05$).

RESULTS

The six animals were perfused for 6 h according to the protocol. All the animals were weaned from perfusion and extubated. Survival after perfusion was 7 days for all calves when they were killed electively for postmortem studies.

In both groups, mean pH varied between 7.40 and 7.50 throughout the runs. Mean oxygen saturation (SaO_2) could be maintained above 99.27% in the oxygenator 1.7 group and above 99.53% in the oxygenator 2 group (Table 1). Mean venous oxygen saturation (SvO_2) could be maintained above 60% throughout the 6-h runs with both models. Mean SvO_2 values varied between 64.57 and 70.97 for the oxygenator 1.7, and between 62.63 and 71.70 for the oxygenator 2 (Table 2).

Table 1: Arterial oxygen saturation (%). There was no significant difference between both groups

	1.7	2
prebypass	99.83 ± 0.12	99.46 ± 0.58
mixing	99.83 ± 0.12	99.90 ± 0.00
1h	99.67 ± 0.06	99.80 ± 0.10
2h	99.27 ± 0.32	99.53 ± 0.32
3h	99.57 ± 0.12	98.96 ± 0.76
4h	99.70 ± 0.10	99.60 ± 0.34
5h	99.70 ± 0.20	99.69 ± 0.10
6h	99.57 ± 0.15	99.76 ± 0.15
30′ postbypass	99.20 ± 0.26	99.80 ± 0.36
60′ postbypass	95.63 ± 0.41	99.10 ± 0.20

Table 2: Venous oxygen saturation (%). There was no significant difference between both groups

	1.7	2
prebypass	69.10 ± 4.40	67.76 ± 5.68
mixing	66.30 ± 3.44	67.83 ± 8.92
1h	64.57 ± 6.02	71.70 ± 6.51
2h	66.13 ± 7.09	66.76 ± 9.13
3h	66.60 ± 3.81	63.36 ± 8.29
4h	68.67 ± 7.85	62.63 ± 7.87
5h	70.97 ± 6.52	64.60 ± 6.67
6h	69.87 ± 6.42	66.03 ± 10.56
30′ postbypass	64.90 ± 4.37	63.33 ± 11.37
60′ postbypass	72.03 ± 2.89	63.66 ± 9.60

Oxygenator type was not found to have any significant influence on either SaO_2 or SvO_2.

Oxygen transfer rates during bypass are shown in Figure 1. Oxygen transfer rates in the oxygenator 1.7 group were 273 ± 4 mL/min after 1 h of bypass and 255 ± 7mL/min after 6 h; whereas, those in the oxygenator 2 group were 280 ± 5 mL/min and 270 ± 6 mL/min, respectively. The difference of O_2 transfer rates between the two oxygenator types was significant ($p < .001$).

Carbon dioxide transfer rates during bypass are shown on Figure 2. Carbon dioxide transfer rates in the oxygenator 1.7 group were 208 ± 4 mL/min after 1 h of bypass and 194 ± mL/min after 6 h; whereas, those in the oxygenator 2 group were 225 ± 4 mL/min and 212 ± mL/min, respectively. The difference of CO_2 transfer rates between the two oxygenator types was significant ($p < .001$).

Post bypass blood gas analyses showed physiologic values and no evidence of major lung trauma or pulmonary edema in relation to the 6 h bypass.

Figures 3 and 4 show the thrombocyte and the white blood cell counts, corrected by hematocrit and normalized by prebypass values. Thrombocytes exhibited a drop that was maximal after 6 h of bypass. However, the values were not significantly different from baseline. White blood cells peaked after 5 h of bypass. The difference with baseline value was significant with

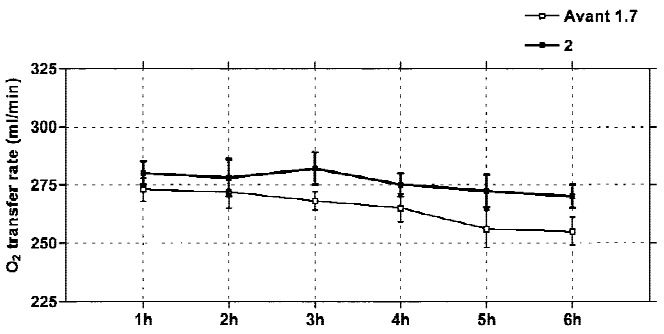

Figure 1: O_2 transfer rate; —□—= oxygenator 1.7 m ^{2}; —■—= oxygenator 2 m^2

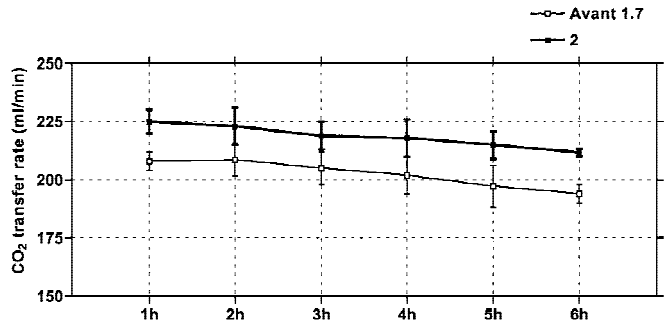

Figure 2: CO_2 transfer rate; —□—= oxygenator 1.7 m ^{2}; —■— = oxygenator 2 m^2

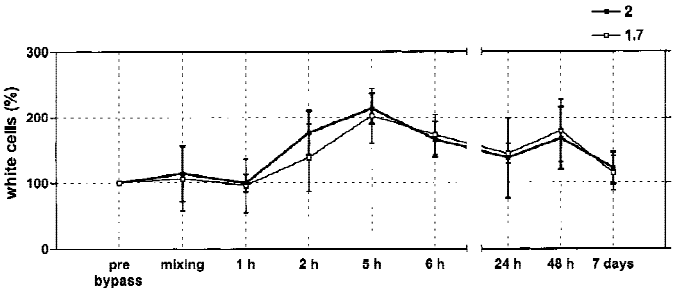

Figure 3: White blood cell count. The values are corrected by hematocrit (Table 3) and normalized by prebypass values; —□— = oxygenator 1.7 m^2; —■—= oxygenator 2 m ^{2}

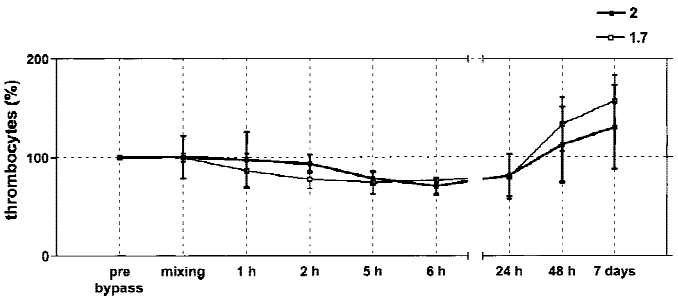

Figure 4: Thrombocyte count. The values are corrected by hematocrit (Table 3) and normalized by prebypass values; —□—= oxygenator 1.7 m^2; —■—= oxygenator 2 m ^{2}

a *p* value of .001 for oxygenator 2, and .01 for oxygenator 1.7. None of the hematological values exhibited any statistical significance between groups at any time interval. Mean free plasma hemoglobin and LDH are shown in Figures 5 and 6, respectively. Both had a peak at 24 h, which was significantly different from baseline for oxygenator 1.7 only (p = .02 for both plasma hemoglobin and LDH).

The pressure drop through the oxygenator was similarly low in both groups. The values varied between 43 and 54 mmHg for the oxygenator 1.7 and between 59 and 74 mmHg for oxygenator 2 (Figure 7). None of the pressure drop values for both groups differed significantly at any time interval.

Postmortem studies of the five major organs (lung, heart,

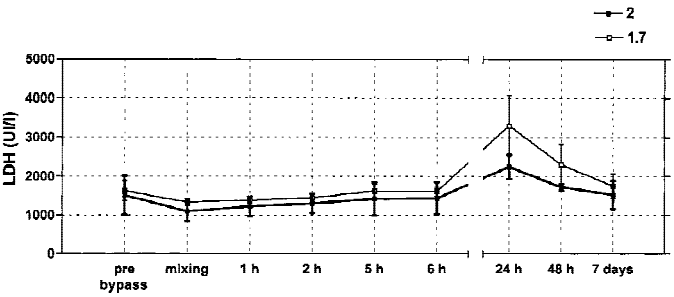

Figure 5: Lactate deshydrogenase (LDH); —□—= oxygenator 1.7 m^2; —■—= oxygenator 2 m ^{2}

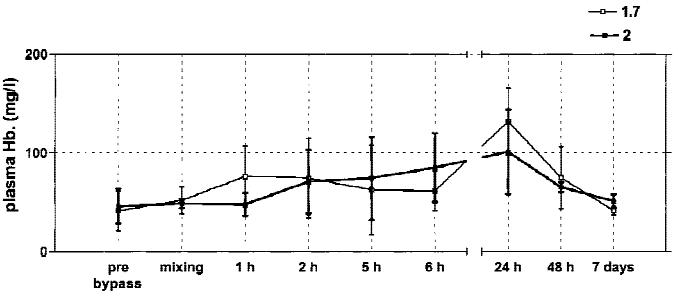

Figure 6: Free plasma hemoglobin (free Hb); —□—= oxygenator 1.7 m^2; —■—= oxygenator 2 m ^{2}

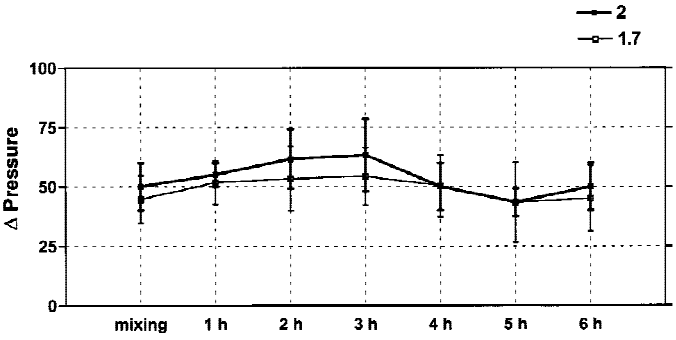

Figure 7: Pressure drop (Δ Pressure) through the oxygenator; —□—= oxygenator 1.7 m ^{2}; —■—= oxygenator 2 m ^{2}

liver, spleen, and kidney) did not demonstrate any macroscopic lesions. No macroscopic defects, such as rupture of hollow fibers, cracking of external housing, or deposit of clots, were observed after gentle rinsing of the devices with clear water.

DISCUSSION

In the membrane oxygenator, a gas-permeable membrane physically separates the blood from the gas in a manner analogous to the natural lung. The superiority of membrane oxygenators during cardiac surgery with cardiopulmonary bypass has been firmly established and has led to their widespread use despite their more elevated cost (4, 5). Their main advantages lie in their predictability of gas exchange and their improved

blood handling. The trend has been toward surface area reduction to reduce blood contact with foreign surfaces. However, larger surface area with increased potential of gas exchange might be beneficial for large patients.

Oxygen transfer in the membrane oxygenator obeys Fick's law of diffusion and varies directly with the total surface area of the membrane, the oxygen gradient developed across the membrane, and the permeability of the membrane material to oxygen (6, 7). In our experimental set-up, variation of surface area from 1.7 to 2 m^2 has made a significant impact on both oxygen and carbon dioxide transfers. Therefore, such an increase in membrane surface in this type of oxygenator might be useful for clinical application when larger oxygen transfer rates are needed.

Hemolysis during cardiopulmonary bypass is known to be mainly associated with roller or centrifugal pumps and suctioning into the cardiotomy reservoir. Red cell injury has been shown to be a function of perfusion time rather than oxygenator employed (8, 9). However, shear stresses induced by flow through the oxygenator will impart some damage to red cells (10). In the present experiment, the profile of free plasma hemoglobin and LDH exhibit a similar trend. The values are stable during the 6 h of perfusion, with a peak at 24 h, which significantly differed from baseline in the oxygenator 1.7 group only, and a return toward baseline values at 48 h. However, the absolute value of this peak in the oxygenator 1.7 group is small (132 ± 34 mg/L). A similar profile was observed clinically in coronary artery bypass grafting (11–13), taking into account the difference that there was already a progressive elevation of hemolytic parameters during the bypass because of the effect of cardiotomy suction during the procedure.

Damage to thrombocytes occurs as a result of interaction of the blood with the membrane surface and shear stresses within the blood. As a consequence, the patients may experience an impairment in postoperative hemostasis following cardiopulmonary bypass. The profile of thrombocyte counts was not affected by the surface of the oxygenator in our experiment. The decrease of platelet counts is to be attributed partly to the aggregating effect of the first contact of blood with the extracorporeal circuit (14). Clinically, a similar profile was found with coronary artery bypass grafting (12) and aortic valve surgery (15).

The leukocyte profile is similar for both groups of oxygenators. Extracorporeal circulation usually produces a prompt leukopenia 30 min after the initiation of bypass (16, 17). This event may have been missed in our experiment, because the counts were measured at 10 min and 1 h. This leukopenia is known to be transient and is followed by a leukocytosis attributable to the mobilization of a large reserve capacity and the ability for rapid leukopoiesis (18). This leukocytosis is clearly demonstrated in our experiment and is not affected by the surface of the membrane.

Pressure drop exhibits parallel curves for both oxygenator types. The difference between the groups was never significant, suggesting that with this type of oxygenator, surface area does not significantly affect this variable. This feature is important for blood trauma, because high pressure drop may be associated with high shear stress (19).

This experimental study shows that with this type of hollow-fiber membrane oxygenator, an increased surface area for gas exchange improves gas transfer, with limited impact on blood trauma and no increase of blood path resistance.

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