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Clinical evaluation of the Admiral 1.35m² hollow-fibre membrane oxygenator

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This prospective study was designed to evaluate the fundamental clinical performance of a new, small surface area oxygenator. Data were collected from twenty patients undergoing first-time coronary artery bypass grafting using this device. This study focuses on how the reduction of surface area and prime volume affects the essential function of the oxygenator in terms of oxygenation efficiency, heat transference, membrane pressure drops, haemolysis and safety. Oxygenation efficiency was deemed to be well within acceptable margins, even at high flows, over a temperature range of 32-36°C. Heat-exchanger performance was assessed by recording the heater/chiller water temperature compared to retrospective data from a current standard oxygenator. Heater/chiller water temperatures were on average 0.3°C higher with the small surface oxygenator than the standard data. The air handling of the device was excellent and extremely safe. Haemolysis, measured as plasma free haemoglobin, did not increase during bypass (p>0.05). This new oxygenator offers a reduced surface area and priming volume while still ensuring an acceptable safety reserve and performance. *Perfusion* (2008) **23,** 33–38.

Key words:

Introduction

Historically, the evolution of membrane oxygenators and heat-exchangers has focussed on increasing efficiency. This has largely been achieved by an increase in surface area and priming volumes. However, activation of inflammatory markers and pro-coagulation factors occurs when blood comes into contact with foreign surfaces. The bigger this foreign surface, the greater the activation of pro-coagulant factors. More recently, oxygenator development has been driven by a move towards a reduction in priming volume and membrane surface area in order to minimise haemodilution and the area of foreign surface in contact with the blood without significantly reducing gas transfer or increasing blood flow resistance. Predominantly, new oxygenators available are variations on an existing design and it is rare that an oxygenator is designed *de novo* with the requirements for modern cardiopulmonary bypass (CPB). The new ideal for a membrane oxygenator is to have a reduced contact surface area whilst still providing the same oxygenation and heat transference efficiency as larger oxygenators. The low surface area of the Admiral 1.35m² oxygenator combines a reduced membrane surface area with a low prime volume of 190ml. The accompanying hard-shell reservoir allows the separation of suction blood from the circulating volume. Unlike many current systems, this reservoir allows the sep-

aration of extra-cavity or dirty blood from vented or closed cavity blood that has not been exposed to air or injured (cut) vessels, ensuring the main cause of plasma free haemoglobin (FHb) is prevented from passively re-entering the circulation.[1,2]

The aim of this study was to determine whether this new design affects other fundamental functions and safety of CPB. In particular, the study investigated the efficiency of the oxygenator over the cooling and rewarming phases of CPB. The reduction in the surface area and priming volume of the Admiral oxygenator is achieved by a tighter fibre bundle. It has yet to be determined whether, in the clinical setting, this modification causes an increase in the pressure drop across the oxygenator or how it affects the handling of air in the event of gross air entrainment. The system was also assessed to ensure the new design did not create an unacceptable level of haemolysis.

Methods

Patients
The study group consisted of twenty patients undergoing elective coronary artery bypass grafting (CABG) with the Admiral oxygenator and hard-shell reservoir. Exclusion factors included previous cardiac surgery, known haematological disorder or gross haemodynamic instability.

Anaesthesia
All patients were anaesthetised using a standard technique. Briefly, induction was achieved with

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2-4mg midazolam, 2-3µg/kg remifentanil, 50mg propofol and 0.1mg/kg pancuronium for neuromuscular blockade. Anaesthesia was maintained with an infusion of 0.3-0.4µg/kg/min remifentanil and 3-4mg/kg/hr propofol. Upon chest wiring, remifentanil was ceased and propofol continued with morphine. Anticoagulation was maintained at an activated clotting time (ACT) of >480 s after an initial bolus of 300 IU/kg heparin. Heparin was reversed with 3 mg/kg protamine sulphate, following the termination of bypass.

Cardiopulmonary bypass

The Admiral circuit consisted of a reduced-volume, reduced-surface area oxygenator (Admiral Oxygenator Eurosets s.r.l. Medolla, Italy), with a hard-shell reservoir split into two sections, allowing for separation of extra-cavity and cavity blood. All cavity blood was kept in the separate cardiotomy reservoir unless needed for circulating volume, when it would be sent to the cell-saver for washing before re-introduction into the circulation. The S3 (Stöckert, Sorin Group GmbH, Munich, Germany) heart-lung machine was used with a 3T heater/chiller, (Stöckert, Sorin Group). The base prime consisted of 1.4L of Hartmann's solution (Baxter, United Kingdom) containing 10KIU heparin (Leo Laboratories Limited, Princes Risborough, United Kingdom). All patients were systemically cooled to a nasopharyngeal temperature of 32°C and myocardial protection was achieved with 1L of cold blood cardioplegia containing 20mmol of St Thomas's Solution (Martindale Pharmaceuticals, Romford, United Kingdom). Hammersmith temperature protocol[3] was performed using a maximum gradient of 8°C between the nasopharyngeal temperature probe and heater/chiller settings during re-warming (arterial blood temperature no greater than 37.5°C) until a maximum nasopharyngeal temperature of 37.5°C was achieved. Heat-exchanger performance was judged on the temperature required on the heater/chiller to maintain the oxygenator arterial blood temperature at 37.5°C and a nasopharyngeal temperature of 37-37.5°C before termination of bypass.

Oxygenator efficiency

Patients were retrospectively separated into 4 groups based on different cardiac outputs; 3.8-4.2L/min, 4.2-4.5L/min, 4.5-5.2L/min and over 5.2L/min. The patient's O_2 tension (PaO_2) was maintained at 25kPa using in-line monitoring (CDI100, Terumo, Leuven, Belgium), observing a consistent temperature regime, recording the necessary fraction of inspired oxygen (FiO_2) at 1°C intervals and using alpha-stat blood gas management.

Pressure drops

Pre- and post-membrane pressures were measured at 3 time points; 5 minutes on CPB, 30 minutes on CPB and 5 minutes after removal of the cross-clamp.

Air handling

The Admiral air handling abilities were judged upon the complete re-prime of a blood-coated oxygenator. Once CPB had been terminated and the patient had left the operating theatre, the used oxygenator was completely de-primed. A timed re-prime at 5L/min flow through the tangential re-circulation line using Gelofusin was commenced until complete air removal had occurred. Satisfactory re-prime was defined as the removal of all visible gross air from the oxygenator housing.

Haemolysis

Free plasma haemoglobin (FHb) was measured as an indicator of haemolysis. Pre-bypass samples were taken in the anaesthetic room whilst post-bypass samples were taken once bypass had been terminated and heparin reversal had been completed.

Results

The patient and operation characteristics are shown in Table 1.

Gas exchange

Maintenance of PaO_2 at 25kPa was attained within the 4 study groups using in-line monitoring (CDI500, Terumo). Whilst lower blood flow allowed for reduced FiO_2 to be used, the difference between 3.8L/min and 5.2L/min groups never exceeded 10%. We did find that the FiO_2 percentages required for maintaining a PaO_2 of 25kPa was greater than our standard bypass circuits by approximately 7% on average, but this was not to an extent as to cause concern. Upon re-warming, even in the highest flow group, the maximum FiO_2 needed to reach and maintain a 25kPa PaO_2 at 37.5°C was 67% (Figure 1).

Table 1 Patient and operation characteristics

Variable	
Age (y)	66.7 ± 7.9
Sex (M/F)	14/6
Height (cm)	167.3 ± 10.7
Weight (kg)	74.7 ± 14.9
Number of anastomoses	3.4 ± 0.7
Cardiopulmonary Bypass Time (min)	74.9 ± 19.4
X-Clamp Time (min)	39 ± 9.63

Data are presented as mean ± standard deviation.
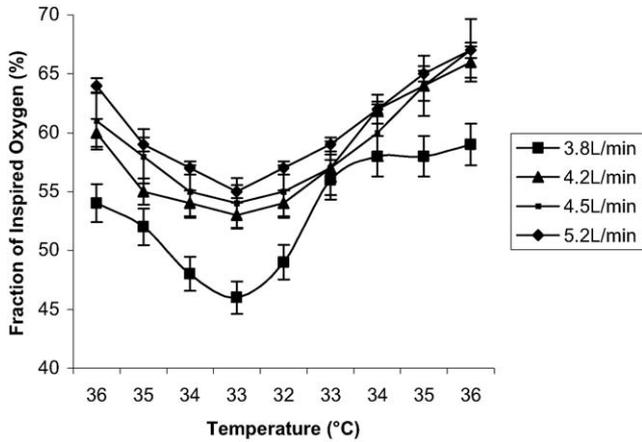
Figure 1 Mean FiO_2 levels required to maintain a PaO_2 of 25 kPa over the cooling and re-warming phases of bypass. Data are expressed as mean with standard deviation.

Oxygenator pressure drops

The average pressure drop found in the Admiral was 27.2mmHg/L/min (Figures 2A-C and 3). Pressure drop increased with cardiac output.

In vivo heat exchanger efficiency

The average heater/chiller water temperature required to achieve an oxygenator arterial blood temperature of 37.5°C was 0.3°C higher than in our standard circuits. For the Admiral oxygenator, an average heater/chiller water temperature of 38.8°C was required compared to 38.5°C for the Avant D903 (Dideco, Sorin Group, Milan, Italy).

Haemolysis

Baseline FHb levels were 8.45±7.92mg/dL compared to 9.2±5.31mg/dL (Figure 4). Although a slight increase could be seen after bypass, statistical analysis using the Student T-test showed the increase to be statistically insignificant ($p > 0.05$).

In vitro re-prime

Four different perfusionists undertook a complete re-prime in a blood-covered circuit through the internal re-circulation line only (Figure 5b). The average time for satisfactory re-prime was twelve seconds.

Discussion

In our study, we evaluated the basic clinical performance of the Admiral hollow-fibre membrane oxygenator. This was designed to investigate whether new reduced surface oxygenator designs affect the other fundamental functions and safety of cardiopulmonary bypass. The study did not look at the clinical impact of reduced surface area or prime volume as these advantages have been well documented.[4–6]
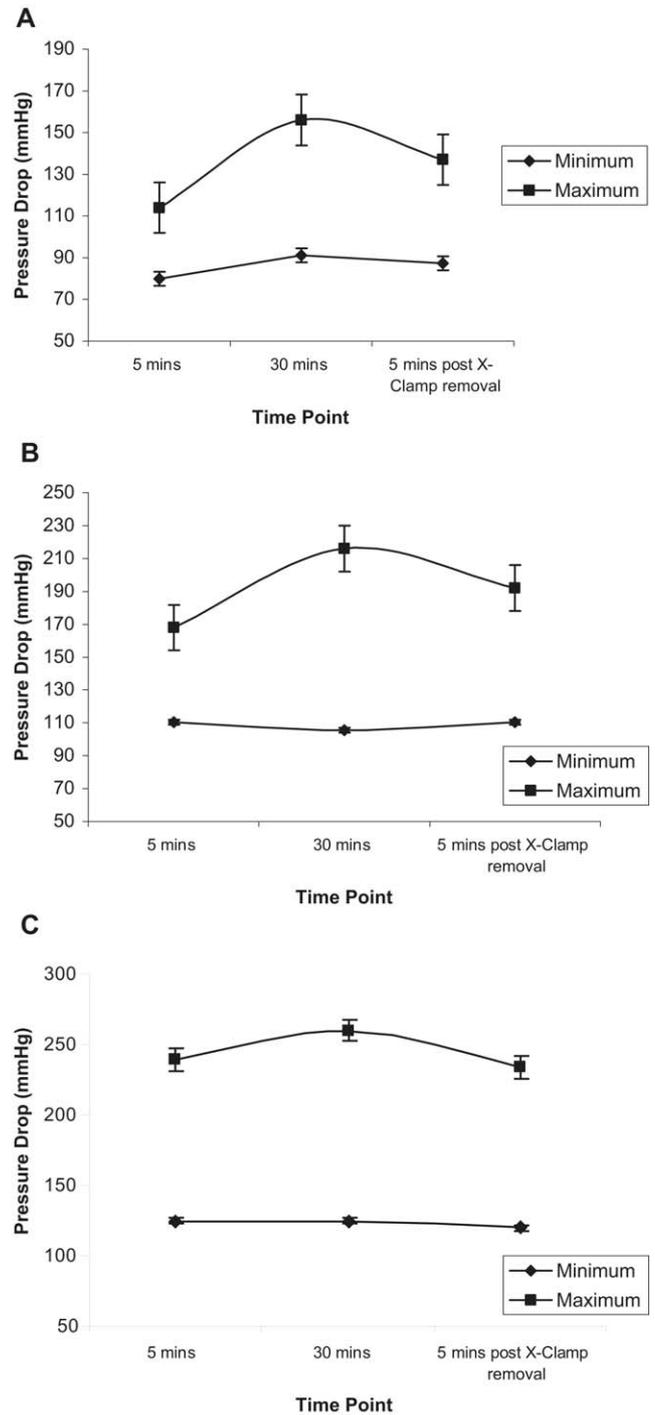

Figure 2 A) Minimum and maximum oxygenator pressure drops at time points during bypass at a flow rate of 3.8 L/min. Data are expressed as mean with standard deviation. B) Minimum and maximum oxygenator pressure drops at time points during bypass at a flow rate of 4.8 L/min. Data are expressed as mean with standard deviation. C) Minimum and maximum oxygenator pressure drops at time points during bypass at 5.2 L/min. Data are expressed as mean with standard deviation.

Admiral efficiency

Reducing the surface contact area of cardiopulmonary bypass has been shown to have a multitude of benefits to the patient. Haemodilution-associated
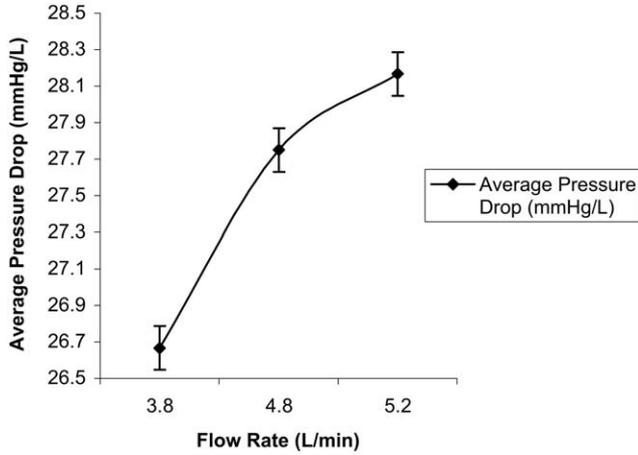
Figure 3 Average pressure drop at 3.8, 4.8 and 5.2 L/min flow rates. Data are expressed as mean with standard deviation.
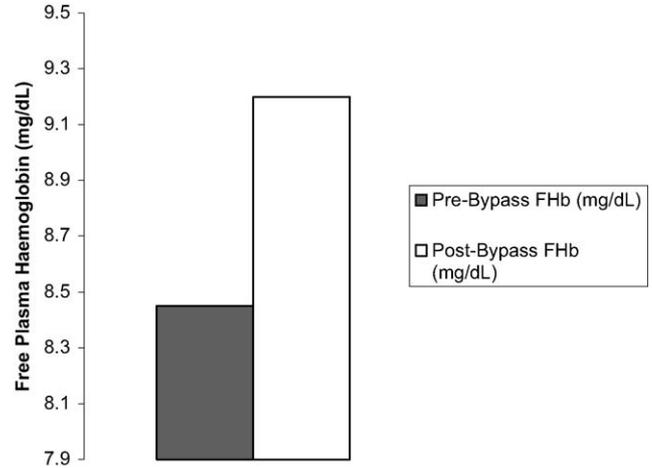
Figure 4 Average plasma levels of free haemoglobin in patients undergoing CABG surgery. Data are presented as mean.

low haematocrits are linked with higher morbidity and mortality rates.[4] Reduction in haemodilution is also associated with improved gas exchange efficiency[5] and a diminished inflammatory response.[6] With a static prime volume of 190ml, the Admiral offers a reduction in prime volume and surface contact area compared with a number of commercially available oxygenators (Table 2). Our study has shown that maintaining a PaO₂ of 25kPa throughout CPB can easily be accomplished with a smaller oxygenator at adequate flows for patients requiring cardiac outputs up to 5.2L/min, with sufficient reserve not to compromise patient safety.

The pressure drops measured across the Admiral averaged 27.2mmHg/L, which is comparable with other oxygenators, even though many of these are of a greater surface area.[7] This suggests that the wrapping of fibre bundles and fibre casing does not require increased pressure to move blood through the oxygenator. However, it should be noted that the conditions under which the pressure drop data were collected was not in agreement with the International Organisation for Standardisation[8] guidelines. Whereas other oxygenators are tested at 37°C with an Hb of 12mg/dL and at 4L flow, the Admiral
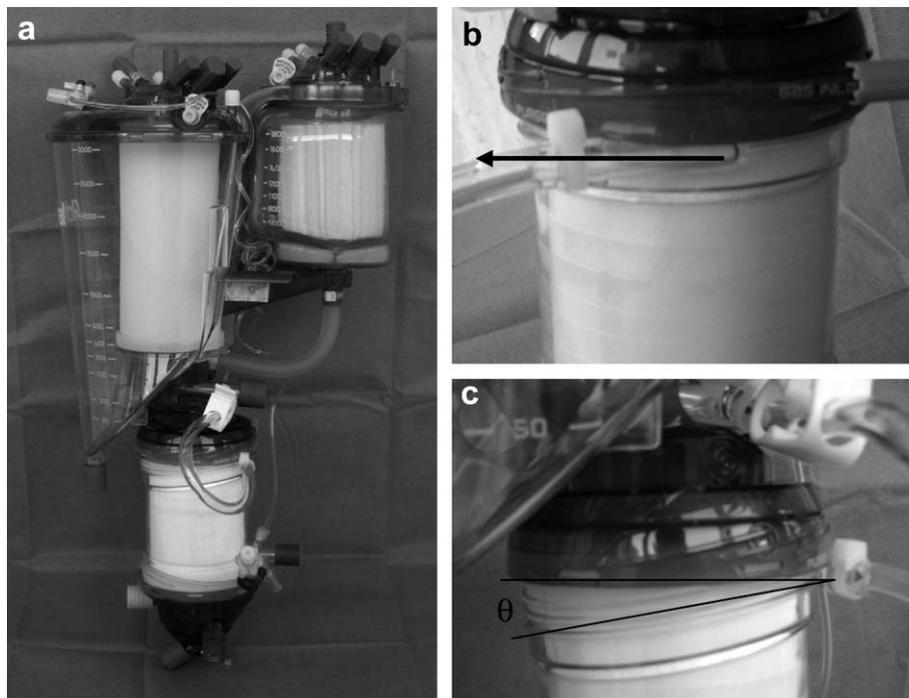
Figure 5 The Admiral oxygenator: a – separate cardiotomy reservoir; b – tangential re-circulation line, c – angled oxygenator potting.

Table 2 Data for 4 different oxygenaors, the Admiral (Eurosets), Quadrox (Maquet), Capiox RX25 (Terumo) and Affinity (Medtronic)

	Admiral	Quadrox	Capiox	Affinity
Static Prime Volume (mls)	190	250	250	270
Surface Area (m²)	1.35	2.4	1.7	2.5
H.E Performance	0.64	0.83	0.68	0.56
Average Pressure Drop (mmHg/L)	27.2[†]	42*	40*	40*

[†]Figure given at 37°C, 4L flow rate and haemoglobin of 9 g/dL.
*Figure estimated from oxygenator data sheet supplied by the manufacturer under standard conditions.

pressure data were recorded at 37°C with an Hb of 9mg/dL and at 4L flow and, therefore, is understandably lower.

Upon the re-warming phase of CPB, we noted that a 0.3°C increase on our heater/chiller water settings was required to obtain an oxygenator arterial blood temperature of 37.5°C. Whilst this would suggest that the heat-exchanger is less efficient, an increase from 38.5-38.8°C is something the authors consider to be negligible as the heater-chillers can reach a water temperature of 41°C. When considering the reduced priming volume and, therefore, the added benefits that this reduction entails, the increase is insignificant.

During CPB, the most important feature must be safety. In order to determine whether the smaller oxygenator (fibre bundles and casing), could be re-primed quickly in the event of air entrainment, a blood-coated oxygenator was completely de-primed, mimicking an emergency situation. Four different perfusionists then undertook a complete re-prime under timed conditions, using only the internal recirculation line (Figure 5b). At 5L/min, the average time was 12 seconds for a macro air-free re-prime. The air handling of the oxygenator is good because the potting (Figure 5c) at the top of the oxygenator is angled towards a tangential (rather than the more commonly used perpendicular) internal re-circulation line. This is a clever design modification.

Haemolysis
In order to determine the direct effect of the oxygenator on the haemolysis encountered during CPB, the closed cavity blood was separated from the extra-cavity and circulating blood to remove the major source of FHb.[2] In agreement with both Pierangeli[9] and Hansbro[2] groups, we saw a small, but statistically insignificant, increase in the levels of circulating FHb, even though both other groups used significantly larger oxygenators. This suggests that design changes implemented to reduce the oxygenator surface area do not increase haemolysis during CPB. Pierangeli and colleagues[9] have previously shown that, by managing suction blood separately, a significant reduction is seen in the circulating levels of plasma free haemoglobin. However, with the split reservoir system (Figure 5a), the suction blood can be divided into two distinct groups; the first being from the plural space, giving rise to cavity blood, and vented blood from within the chambers of the heart. The latter group has not come into contact with cut surfaces, therefore, is regarded as "clean", showing significantly less FHb than cavity blood, which can be returned to the circulation. The effect of this feature was not investigated in this study as it has been described by other workers,[2,9] but the authors believe this to be of great potential benefit in cases where large volumes of vented blood occur.

Conclusion

Reduced surface area oxygenators offer many benefits over the existing larger oxygenators. Here, we have shown that these benefits come without the loss of fundamental functions of CPB and provide good gas exchange efficiency and safety. In conclusion, the Admiral is a safe, competitive oxygenator that offers a reduced surface area and priming volume without compromising the other established functions of cardiopulmonary bypass.

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