
Comparison of Terumo Hollow Fiber Membrane and Harvey 1500 Bubble Oxygenators Using Red Cell Microrheology Analysis during Cardiopulmonary Bypass

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Abstract

(*J. Extra-Corpor. Technol.* 19[2] p. 209-215, Summer 1987, 47 refs.) Seventy-three patients undergoing cardiopulmonary bypass (CPB) were prospectively randomized into two groups to compare the effect of membrane (Terumo hollow-fiber [MO]); versus bubble (Harvey 1500 [BO]) oxygenation on red blood cell (RBC) deformability. Comparison of blood trauma was done by measuring the red cell filtration rate (RFR) which reflects changes in RBC deformability. In patients with a high (>30 ul/sec) RFR before CPB, the MO-1 subgroup showed significantly ($p<0.05$) lower reductions of RFR during CPB compared to the BO-1 subgroup. In patients with a low (<30 ul/sec) RFR before CPB, the MO-2 subgroup showed a significantly ($p<0.01$) lower loss of RFR compared to the BO-2 subgroup. The use of blood gas-estimations also revealed that hyperoxia was more frequent in the BO group. The frequency of normal pO_2 levels (75-97 mmHg) at 30 min., 60 min. and 90 min. of CPB in the MO group was 65%, 43% and 77% compared to 22%, 11% and 11% ($p<0.01$) respectively in the BO group. The earliest significant RFR differences between the MO and BO groups could be detected at 30 minutes of CPB; differences in plasma hemoglobin reached significance after one hour of CPB. This study demonstrates a greater deleterious effect on red blood cells when a BO is used for CPB.

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Introduction

The use of extracorporeal circulation during open heart surgery is damaging to blood.¹⁻¹¹ Blood damage is reflected in both the cellular and humoral components,¹ and limits the use of cardiopulmonary bypass.² Damage to red blood cells (RBC) due to extracorporeal circulation is associated with abnormalities in metabolic, functional, and morphological properties, of these cells.¹²⁻¹⁵ As a result of this damage, the RBC's ability to actively deform in artificial capillaries (microfilters) is reduced.¹⁶⁻¹⁹ The red cell filtration rate (RFR) measures cell deformability and has been previously described for assessing red cell damage.¹⁷ The present study uses this technique as an estimate of red cell damage to compare the effects of two types of oxygenators, a bubbler and a membrane, on red cell deformability.

Patients

Seventy-three adults participated in this prospective, randomized study; 37 underwent coronary artery bypass graft surgery (GABG), and 36 underwent valve replacement surgery (VR) (30 aortic; 5 mitral; 1 double valve). Patients were randomized into two groups: Terumo hollow-fiber membrane oxygenator [N=37](MO), and the Harvey 1500 bubble oxygenator [N=36](BO). The general patient-data is presented in Table 1.

Cardiopulmonary Bypass Technique

The same standard technique for CPB was employed

Table 1
Data of patient groups

	All patients		RFR > 30 ul/sec.		RFR < 30 ul/sec.	
Oxygenator type	MO (n=37)	BO (n=36)	MO-1 (n=28)	BO-1 (n=27)	MO-2 (n=9)	BO-2 (n=9)
Sex						
male	22	24	15	18	7	6
female	15	12	13	9	2	3
Age(yr)(o)	61.5 ± 10.4	56.2 ± 10.7	62.4 ± 13	59.4 ± 10.9	60.4 ± 7.5	53.5 ± 10.5
Weight(kg)(o)	77.8 ± 15.6	77.5 ± 15.7	74.0 ± 22.4	72.6 ± 13.6	82.0 ± 7.2	83.0 ± 17.8
Body surface(m ²)(o)	1.88 ± 0.22	1.89 ± 0.23	1.80 ± 0.23	1.80 ± .20	1.98 ± 0.18	2.0 ± 0.24

MO= Terumo hollow fiber membrane oxygenator, BO= Harvey 1500 bubble oxygenator, MO-1 and BO-1 = patients with RFR > 30 ul/sec., MO-2 and BO-2 = patients with RFR < 30 ul/sec., (o)= values expressed as mean ± 1 standard deviation (SD).

Table 2
Perfusion Data

	All patients		RFR > 30 ul/sec.		RFR < 30 ul/sec.	
Oxygenator type	MO (n=37)	BO (n=36)	MO-1 (n=28)	BO-1 (n=27)	MO-2 (n=9)	BO-2 (n=9)
Perfusion time(min.)	106 ± 30	106 ± 30	90 ± 34	100 ± 28	123 ± 26	113 ± 34
Duration of aortic occlusion (min.)	70 ± 24	71 ± 20	66 ± 25	69 ± 16	75 ± 23	70 ± 34
Blood flow(l/min.)	4.5 ± 0.5	4.5 ± 0.6	4.3 ± 0.6	4.3 ± 0.5	4.7 ± 0.4	4.8 ± 0.6
Total cardioplegia during CPB(l)	2.1 ± 0.7	1.9 ± 0.5	2.2 ± 0.8	2.0 ± 0.4	2.1 ± 0.6	1.9 ± 0.6
Heparin(5000 IU/ml) during CPB(ml)	6.2 ± 0.9	6.2 ± 1.0	6.0 ± 0.9	5.9 ± 0.8	6.4 ± 0.5	6.5 ± 1.0
Protamine at end of CPB(mg)	324 ± 66	334 ± 100	284 ± 62	325 ± 75	365 ± 68	334 ± 53
Mean nasopharyngeal temperature(°C)	28.1 ± 0.6	28.0 ± 0.4	28.0 ± 0.9	28.1 ± 0.5	28.0 ± 0.2	28.1 ± 0.2
Priming volume(l)	2	2	2	2	2	2

MO= Terumo hollow-fiber membrane oxygenator, BO= Harvey 1500 bubble oxygenator, MO-1 and BO-1 = patients with RFR > 30 ul/sec., MO-2 and BO-2 = patients with RFR < 30 ul/sec. All values expressed as mean ± standard deviation (SD).

for all patients. The extracorporeal circuit (ECC) was primed with 2 liters of Ringerdex^a. A modified St. Thomas solution^a at 4°C was used to achieve cardioplegia. Heparin (7500 IU) was added to the prime and the activated coagulation time (ACT)^b was maintained around 450 seconds during CPB. A number 24 Blue Line^c aortic canula was used in the arterial line. A Sarns^d double lumen cava-canula was used in the venous line in CABG patients while a Polystan^e no. 9 in the cava superior and a no. 10 in the cava inferior was used in the VR patients.

The blood flow rate at 37°C and during rewarming was 2.4 l/min./m² and 2 l/min./m² during hypothermia at 28°C. See Table 2. The gas flow-blood flow ratio was started at 1:1. The gas flow was then reduced according to the bloodgases where a pO₂ of 75-113 mmHg and a pCO₂ of 30-45 mmHg was aimed for. Indicus of oxygenated blood flow rates were calculated using the following formulae:

Oxygen flow rate index (OFRI)

$$= \frac{\text{total oxygen volume (l) passing through the oxygenator}}{\text{total CPB time (min.)} \times \text{body surface (m}^2\text{)}}$$

Blood flow rate index (BFRI)

$$= \frac{\text{total blood flow (l) pumped by the heart-lung machine}}{\text{total CPB time (min.)} \times \text{body surface (m}^2\text{)}}$$

Drugs used for lowering perfusion pressures were Sodium nitroprusside. No other drugs (anesthetic gases or antibiotics) were added to the prime or perfusion fluid. The hematocrit varied from 17 to 30% and no patient received blood during perfusion.

Blood Sampling

Plasma hemoglobin (P-HB) was taken at the beginning of CPB, every 30 min. thereafter and soon after CPB was terminated. Total hemoglobin (HGB), white cell counts (WCC), and platelets counts (PC) were done on postoperative days 1, 2, and 3. OFRI, BFRI, and hematological data was compared between the MO and BO groups.

RFR Measurement Technique

Blood samples for the microfiltration studies were

a Pharmacia, Uppsala, Sweden

b International Technidyne Corp, Edison, NJ 08820

c Argyle, St. Louis, MO 63166

d Stöckert, Munich, W. Germany

e Polystan, Ballerup, Denmark

taken preoperatively, one day before surgery, every 30 minutes during CPB; and after termination of CPB. The 10 ml. samples were centrifuged immediately 4000 rpm for 5 min., and the supernatant and buffy coat were discarded. The red cells were washed twice in normal saline at room temperature (22°C), and suspended in saline in an amount giving a 20% red cell suspension. The red cell suspension was then filtered by a standard microfiltration method previously described,¹⁶ the only variation being that microfilters used were standardized with normal saline instead of buffered glucose solution.¹⁶ The RFR was calculated by the standard formula.¹⁶ The effect of MO or BO was compared in patients with RFR > 30 ul/sec. [MO-1=28 pts.; BO-1=27 pts.]; and patients with RFR < 30 ul/sec. [MO-2=9 pts.; BO-2=9 pts.].

The normal reference value in our lab is 60 ul/sec. (± SD, 10) for healthy individuals between 40 and 70 years of age (same range as MO and BO pts.). Since it is known that a reduced RFR is a reflector of chronic cardiovascular disease²⁰ like hypertension and diabetes we empirically divided the patients into a low risk group (MO-1, BO-1) and a higher risk group (MO-2, BO-2). This was done in order to see if CPB affected RFR to a greater extent in the higher risk group.

Statistics

Comparisons of two means was achieved by using appropriate students t-tests or by the modified t-test described by Swinscow.²¹ Comparisons of proportions were performed by the X²-test and percentages were compared by the method described by Swinscow.²¹ All data was expressed as mean (± one standard deviation [SD]). The median was calculated when data showed wide biological variation.²¹

Results

There were no significant differences in the mean values for perfusion time, duration of aortic occlusion, blood flow rates and other parameters during CPB for all groups.

Red Cell Deformability

The RFR in both MO and BO groups showed reductions during CPB but was greater in the BO group. In the MO group the significance of change was first noted at 60 min. while this was seen after 30 min. in the BO group. A significant difference when comparing MO and BO reductions was first seen after 30 min. (p < 0.05) (Table 3).

The mean preoperative RFR values for the MO-1 and

Table 3
Changes in red cell deformability expressed as red cell filtration rate (RFR) ul/sec.

	P	S	30 min.	60 min.	90 min.	120 min.	End
MO(n=37)	36.6	33.0(10)	33.2(9) *	30.5(16) **	30.0(17) **	29.0(19) **	28.4(20) **
BO(n=36)	37.0	34.0(8)	28.5(23)	25.2(32)	23.0(38)	22.2(40)	19.3(48)
MO-1(n=28)	44.0	42.6(3)	41.8(5) *	40.0(9) *	36.0(18) **	33.9(23) **	37.8(14) *
BO-2(n=27)	44.6	41.8(6)	37.9(15)	36.1(19)	27.7(38)	24.5(45)	33.5(25)
MO-2(n=9)	29.0	25.8(11)	24.4(16) **	22.4(23) *	19.7(32) **	—	23.2(20) **
BO-2(n=9)	29.4	26.5(10)	19.2(35)	17.7(40)	9.7(67)	—	10.8(62)

MO=Terumo hollow-fiber oxygenator, BO=Harvey 1500 bubble oxygenator, MO-1 and BO-1 = patients with RFR > 30 ul/sec., MO-2 and BO-2 = patients with RFR < 30 ul/sec.. Values expressed as mean, () = %RFR reduction, P=preoperative, S = start of CPB, End=end of CPB, * = p < 0.05, ** = p < 0.01.

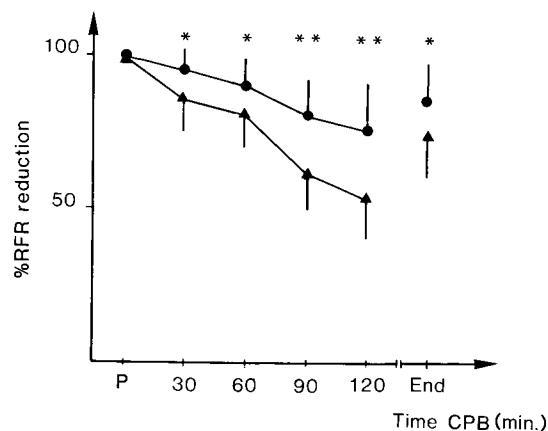


Figure 1: Mean red cell filtration rate (RFR) reduction in percent (%) during cardiopulmonary bypass (CPB) in patients with preoperative (P) values of RFR > 30 ul/sec. End = end of CPB, ● = Terumo hollow-fiber membrane oxygenator (MO-1, n=28), ▲ = Harvey 1500 bubble oxygenator (BO-1, n=27), I = Standard deviation, * = p < 0.05, ** = p < 0.01.

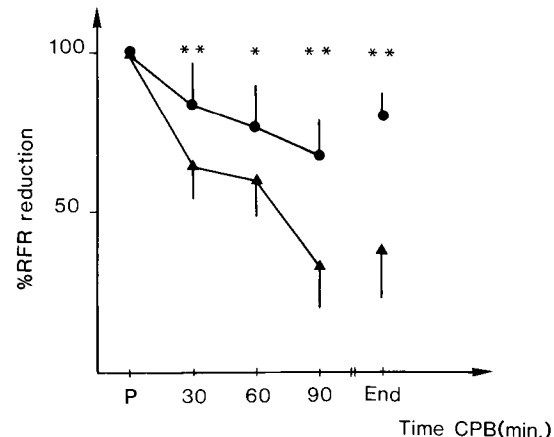


Figure 2: Median RFR reduction in percent during CPB in patients with preoperative (P) values of RFR > 30 ul/sec. End = end of CPB, ● = Terumo hollow-fiber membrane oxygenator (MO-2, n=9), ▲ = Harvey 1500 bubble oxygenator (BO-2, n=9), I = Standard deviation, * = p < 0.05, ** = p < 0.01.

BO-1 groups were 44 ul/sec and 44.6 ul/sec respectively. The mean RFR values fell during CPB in both MO-1 and BO-1 groups. At 30 minutes the MO-1 fell by 5% compared to 15% (p < 0.05) in the BO-1 group. The differences in RFR values remained statistically significant throughout CPB and at the end of CPB the MO-1 group had a reduction by 14% compared to 25% in the BO-1 group (p < 0.05) (Figure

1). The MO-2 and the BO-2 groups had preoperative RFR values which were 33% less compared to the other groups. These patients had a median reduction of RFR by 20% and 62% (p < 0.01) at the end of CPB respectively. Significant differences in percentage RFR reductions were noted in the respective groups as early as 30 minutes of CPB (15% and 35%, p < 0.01) (Figure 2).

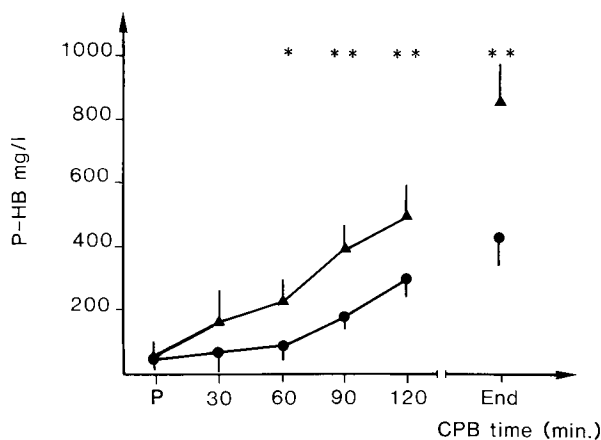


Figure 3: Mean plasma hemoglobin (P-HB) levels CPB. P = preoperative, End = end of CPB, ●—● = Terumo hollow-fiber membrane oxygenator (MO, n=37), ▲—▲ = Harvey 1500 bubble oxygenator (BO, n=36), I = Standard deviation, * = $p < 0.05$, ** = $p < 0.01$.

Plasma Hemoglobin (P-HB)

The mean P-HB increased with the duration of CPB but to a significantly lower extent in the MO group and the earliest significant difference was noted at 60 minutes (MO 95 ± 66 (SD) mg/l, BO 230 ± 90 (SD) mg/l, $p < 0.05$) (Figure 3).

Oxygenation during CPB

The effect of oxygenation was noted in the MO and BO groups. Hyperoxia (>98 mmHg) was noted with both oxygenators, but lower levels were seen with the MO type during CPB. In the BO group the hyperoxia tended to increase during the first 90 minutes while it fell in the MO group. The distribution of mean pO_2 during CPB showed that 65%, 43% and 77% of MO patients had normal values (75-98 mmHg) during 30, 60 and 90 minutes respectively compared to 22%, 11%, and 11% in the BO patients for comparative times ($p < 0.01$). In the pO_2 range of 98-150 mmHg there was a dominance of BO patients at 30 and 60 minutes. In the pO_2 values of more than 150 mmHg there were 27%, 21%, and 16% of MO patients compared to 33%, 56%, and 89% of BO patients at 30, 60, and 90 minutes (Figure 4). The mean OFRI in the MO group was 0.48 ± 0.26 l/min $\times$ m² and significantly higher when compared to 0.21 ± 0.12 l/min $\times$ m² in BO group ($p < 0.05$).

Other Hematological Parameters

Following CPB the hematological changes were

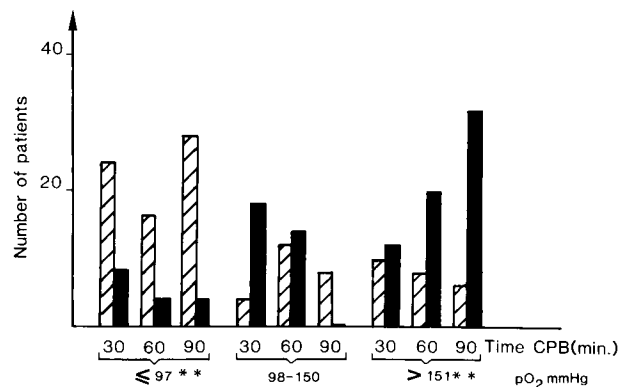


Figure 4: Distribution of patients at different pO_2 ranges during CPB. ●—● = Terumo hollow-fiber membrane oxygenator (MO, n=37), ▲—▲ = Harvey 1500 bubble oxygenator (BO, n=36), ** = $p < 0.01$.

comparable in the MO and BO groups. The postoperative total blood hemoglobin and platelet count fell while the white cell count showed a leukocytosis. The anemia persisted while the white cell and platelet counts began to normalize on the fourth postoperative day. All patients had uneventful postoperative courses and were discharged from the hospital.

Discussion

The damaging effects of CPB on blood results from contact with artificial surfaces in the extracorporeal circuit;³⁷ shear stresses induced by the oxygenators and blood suction; and the toxic effects of blood exposed to other surfaces in the surgical field.^{6,24} Many complications during CPB have been related to blood component damage.¹⁻¹¹ Hemolysis,^{3,8,9,11} thrombocytopenia,⁴ leukopenia,⁵ complement activation,^{6,7} platelet damage,^{22,23,25-30} postoperative blood loss,^{7,9} and anemia¹⁰ occur as a result of extracorporeal blood oxygenation. Reduced blood damage, in the form of less hemolysis, has been previously reported using the membrane oxygenator.^{8,31}

Use of the membrane oxygenator has shown advantages in the form of less blood damage, especially for long term support.^{38,45} It is generally assumed that using a bubble oxygenator for routine perfusions of less than two hours is simple and less expensive, and that the morbidity and mortality are acceptable low.³²⁻³⁴ A recent study on the effects of CPB on blood components showed no significant differences between membrane and bubble oxygenators regarding leukopenia, leukocytosis, and complement activation;

however, the amount of hemolysis and platelet damage was less with the membrane oxygenator.⁷

In this study red cell deformability was examined as an early indicator of blood cell damage on CPB. The red cell is damaged both mechanically and chemically during CPB.⁴⁶ We have shown that within the first 30 minutes of CPB, the red cell membrane is altered. This effect is more significantly pronounced when a bubble oxygenator is used. In patients whose RFR was reduced before CPB, the further decrease in RFR was even more severe. The direct blood-gas interface in bubble oxygenation and a tendency of bubble oxygenators to hyperoxygenate is a potential source of blood damage.

The comparable BFRI in both MO and BO groups exclude the possibility that different blood flow rates might have contributed to the difference in the RFR. Higher BFRI values have been shown to reduce RFR in a previous study.¹⁶ Hematological studies confirmed the usual postoperative leukocytosis,^{7,31} thrombocytopenia,^{7,31} and anemia¹⁰ which occurred in both groups.

This study has shown that the MO is less damaging in terms of effects on red cell deformability when compared to the BO. Using red cell deformability analyses by the microfiltration method, RFR, it is possible to detect red cell damage as 30 minutes after the initiation of CPB. This is apparently more sensitive than red cell survival studies used for the same purpose.⁴⁶ Furthermore, it has already been established that a reduction in RFR correlates well with reduced red cell survival.⁴⁷ Although the membrane oxygenator was shown to be better than the bubble oxygenator in terms of effects on red cell membranes, the clinical significance of this must be established. However, from a point of view of CPB related blood damage, a greater use of the MO can be recommended even for short perfusions.

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