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Clinical Evaluation of the Terumo Capiox® FX05 Hollow Fiber Oxygenator with Integrated Arterial Line Filter

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Abstract: Perfusion techniques and equipment in pediatric open heart surgery have continued to focus on decreasing prime volumes and lowering surface areas of the cardiopulmonary bypass circuit. While this has improved drastically over the last 20 years, greater demand is being placed on the perfusionist to reduce the deleterious effects of bypass without compromising safety or efficiency. Specifically, manufacturers of disposable perfusion equipment have focused on providing pediatric perfusionists with oxygenators that provide the smallest prime and surface area possible while attempting to maximize performance. Recently, Terumo Cardiovascular has introduced the Capiox® FX05, a neonatal hollow fiber oxygenator that includes an integrated arterial line filter. The FX05 provides a blood flow range of 0.1–1.5 L/min and a low priming volume of 43 mL. Additionally, it is coated with X Coating™, a biocompatible, hydrophilic polymer surface coating that reduces platelet adhesion and protein denaturation. The purpose of this study was to test the FX05 for gas transfer, blood path resistance, and blood handling characteristics in a standardized clinical setting. Heat exchange coefficients were also calculated during the cooling and warming period. Other data analyzed includes bypass circuit prime volumes and initial patient hematocrit along with the total operative homologous blood donor exposures. In summary, the FX05 offers good gas exchange capabilities and a low pressure drop during normal cardiopulmonary bypass parameters along with the safety of an integrated arterial line filter. Furthermore, the FX05 with integrated filter allows a reduction in overall bypass prime volume and surface area while promoting the reduction of homologous blood transfusions, optimizing hemostasis.
Keywords: oxygenator, cardiopulmonary bypass, gas exchange, heat exchange, arterial line filter. *JECT. 2009;41:220–225*

Neonatal and pediatric cardiac surgery have seen significant advancements in perfusion technology including lower prime and smaller surface area disposables, all tailored to small patient sizes. Reducing the cardiopulmonary bypass (CPB) surface area and subsequent prime volume is especially important in neonatal patients where the volume from the CPB circuit can be the major determinant in the patient's metabolic response to the cardiac operation (1). This is due not only to the profound difference in the patient's size with respect to the CPB prime volume but also from the deleterious effects of CPB on their immature organ function (2). Additionally, shifts in hemodilution from the CPB prime can result in multiple blood product exposures, all of which have been shown to further increase the morbidity of CPB (3). Thus, attempts by perfusionists to decrease the circuit prime volume by even a few milliliters can result in a reduction of exogenous blood products (4,5).

Perfusionists have continuously looked at methods to further reduce CPB prime volumes and often find themselves balancing this goal while maintaining safety. The use of arterial line filter (ALF) technology, one that is almost always used in adult cardiac surgery, is often debated in neonatal surgery (6). Although the majority of pediatric centers use an ALF, many have found that the use of this technology is at the expense of an increased prime volume and subsequent banked blood exposures (4,7).

The Terumo Capiox® FX05 oxygenator with integrated ALF was developed to be a high performance, low prime oxygenator without sacrificing the safety of the arterial filter. The design of the oxygenator is identical to the Terumo Capiox® RX05 with the only modification being the ALF integrated into the design. The two devices use the same integrated oxygenator/heat exchanger module that provides for gas transfer and blood temperature

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control. The FX05 oxygenator is made from polypropylene fibers (Surface Area = .5 m^2) with a stainless steel heat exchanger (Surface Area = .035 m^2) and a priming volume of 43 cc. With respect to the design of the ALF, the filter is a 32 micron polyethylene terephalate (PET) mesh material that is wrapped around the outer circumference of the oxygenator bundle. This filtration is designed to remove particulate matter and emboli prior to the blood leaving the device. Air removal is accomplished by entrapment followed by permeation of the air into the hollow fibers of the oxygenator bundle; subsequently, it is exhausted, along with carbon dioxide, via the gas outlet port. This design has allowed the safety and convenience of an integrated arterial line filter without an increase in prime volume.

Under the manufacturers in vitro conditions (bovine blood, 37°C, hemoglobin (Hgb) 12 g/dL, pH 7.4, venous saturation (SvO_2) of 65%, venous carbon dioxide ($PvCO_2$) 45 mmHg, base excess (BE) 0 mEq/L), the reported oxygen transfer rate at 100% fraction of inspired oxygen (FiO_2), a temperature of 37°C and ventilation to blood flow ration (V/Q Ratio) of 1 is 70 mL/min at 1.0 L/min blood flow and 100 mL/min at 1.5 L/min blood flow (8). Under the same conditions the reported CO_2 transfer is 50 mL/min at 1.0 L/min blood flow and 70 mL/min at 1.5 L/min blood flow. The reported pressure drop across the oxygenator is 60 mmHg at 1.0 L/min blood flow and 90 mmHg at 1.5 L/min blood flow. The reported heat exchange is .74 at 1.0 L/min blood flow and .63 at 1.5 L/min blood flow.

The purpose of this study was to evaluate the hemodynamics, gas transfer, heat exchange efficiency, and performance of the FX05 under varying clinical conditions of neonatal CPB compared to the manufacturers in vitro conditions. In addition, CPB prime volumes and resultant patient blood transfusion rates were analyzed.

METHODOLOGY

In November of 2008, we changed our perfusion circuit for patients under 10 kg to include the Terumo Baby FX05 Oxygenator with integrated ALF from the Terumo Baby RX05 Oxygenator. From November 2008 to February 2009, we undertook this study to evaluate this change retrospectively matching this group against patients operated on from June 2008 to October 2008 where we used the Baby RX with an external ALF. These populations were further broken down into two smaller groups; patients weighing less than 4 kg and patients weighing more than 4 kg. This weight was selected as this is our cutoff for the use of our 1/8 inch arterial line with 3/16 inch venous line, AV loop. Also, in the Baby RX05 population, this was the cutoff for the use of the Sorin D130 ALF (Arvada, CO). In the patient population of 4–10 kg, a 3/16 arterial line and a 1/4 inch venous line, AV loop, was used along with the Medtronic Pediatric Affinity ALF (Minneapolis, MN) in the Baby RX05 Group. All patients received the use of the Terumo HCO5S hemofilter as well as the Sorin CSC 14, 4:1 Blood Cardioplegia Device as part of our standard bypass circuit. All patients also received Tranexamic Acid at 100 mg/kg load and 100 mg/kg pump prime dose.

A total of 29 Baby FX05 circuits were compared to 33 Baby RX05 circuits. Patients were evaluated for case type, weight, total CPB prime volume (hemofilter and cardioplegia device included), CPB time, cross clamp time, average blood flow, initial bypass hematocrit (HCT), oxygen transfer, carbon dioxide transfer, heat exchange coefficient, and total operating room blood donor exposures (packed red blood cells (PRBC), platelets, fresh frozen plasma, and cryoprecipitate). Patients in the Baby FX05 group were also evaluated for pressure drop across the membrane by measuring the pre- and post- oxygenator pressures. There were no exclusion criteria for our study. As our perfusion practice does not routinely include measuring pre-oxygenator pressures, we were not able to retrospectively analyze the Baby RX05 group for transmembrane pressure drop (TMP). Post-oxygenator bubble detection was analyzed using Sorin's 1/4 inch tubing ultrasonic bubble detector set for 3.5 micron bubble detection.

Our routine bypass procedure includes flushing the circuit with carbon dioxide before crystalloid priming with PlasmaLyte A (Baxter Healthcare, Deerfield, IL). Oxygen transfer was calculated using a modified Fick Equation ([{Arterial − Venous Saturation} × 1.34 × actual hemoglobin × blood flow]/100/FiO_2) and carbon dioxide transfer was calculated using ([$PaCO_2$ × gas flow rate]/0.863) (9). Heat exchange coefficient was calculated using [(Temperature of blood entering heat exchanger) − (Temperature of blood exiting heat exchanger)/(Temperature of blood entering heat exchanger) − (Temperature of water entering heat exchanger)]. There were no changes to our perfusion practice during this period and all cases were conducted using the Sorin SIII or SV Perfusion System and roller pumps. CPB temperature was maintained at moderate hypothermia (greater than 32 degrees centigrade) or normothermia (36 degrees centigrade) using the Jostra HCU30 Heater/Cooler (Maquet, Bridgewater, NJ).

All patients received 1 unit of PRBC in the prime after being washed with the Fresenius CATS (Terumo Cardiovascular) autotransfusion device. This was added to the CPB prime along with 25% albumin with the excess volume hemofiltrated off. Heparin was added to the prime consisting of 500–750 units dependent on patient weight as per our perfusion protocols. The CPB prime was made physiologically normal by buffering with sodium bicarbonate and verified using a prime blood gas. In preparation for CPB all patients received a loading dose of 300 units/kg of heparin by anesthesia just before insertion of the arterial cannula. The patient's activated clotting time

(ACT) was maintained above 400 seconds during the operative procedure and verified using the Hemochron Junior Signature Plus (International Technodyne, Edison, NJ). Patient demographics for the four groups can be found in Table 1. Pre- and post-oxygenator pressure measurements were made each time a blood gas was obtained from the CPB circuit to calculate the TMP of the Baby FX05 groups. Data for the hematologic study was obtained with the first arterial and venous blood gas simultaneously drawn from the CPB circuit within the first 15 minutes of being on CPB as per our perfusion protocols in all study groups.

STATISTICS

Statistics were completed using Microsoft Excel 2003 statistical analysis. Values are expressed as mean plus or minus standard deviation. All statically significant values were ascertained using two-tailed Student's *t*-test assuming equal and unequal variances. A *p*-value of ≤ .05 was considered statically significant for all data groups.

RESULTS

The average weight for the less than 4 kg FX05 group was slightly lower than the same RX05 group yet was statistically significant (FX 2.8 kg ± .6 vs. RX 3.3 kg ±.5; $p = .01$). There were no other significant differences seen in any other demographic data: CPB time, cross clamp (XC) time, or average pump flow rates (Table 1). Average prime volumes for the four groups can be found in Figure 1. Statistical significance was seen in both groups favoring the prime reduction of the FX05 oxygenator (<4 kg FX 222 mL ± 21 vs. RX 330 mL ± 42; $p < .01$ AND >4 kg FX 236 mL ± 37 vs. 360 mL ± 39; $p < .01$). This resulted in a statistical significance seen in the initial CPB HCT for the <4 kg group favoring the FX05 (FX05 38% ± 4 vs. RX05 32% ± 5; $p < .01$) but no significance was seen in the >4 kg group (FX05 32% ± 4 vs. RX05 31% ± 4) (Figure 2). There was no statistical significance in oxygenator performance comparing the FiO_2, oxygen transfer, carbon dioxide transfer, gas to blood flow ratio, or heat exchange coefficient (Table 2). Statistical significance was seen in the >4 kg total operating room blood donor unit exposure, favoring the FX05 (FX05 of 3 ± 2 vs. RX05 of 5 ± 2; $p < .01$) and trended toward significance in the <4 kg group favoring the FX05 group (FX05 of 4 ± 2 vs. RX05 of 5 ± 2; $p = .08$) (Figure 3). The average calculated pressure drop for the FX05 was 47 mmHg ± 46 at an average flow rate of 864 ± 488 mL/min (Figure 4).

DISCUSSION

This review demonstrated that the oxygenator performance of the FX05 was comparable to the RX05 oxygenator in terms of pressure drop, heat exchange coefficient, and gas exchange. One of the greatest benefits of the FX05 is in the reduction of CPB prime by eliminating an external arterial line filter and the associated filter bypass loop and extra tubing needed to encompass the use of an ALF. The elimination of an external ALF has not only reduced the overall CPB surface area but has also allowed us to decrease our overall prime volumes (Figure 1). This has been accomplished through a reduction in static prime volume and also by allowing placement of the oxygenator closer to the patient. The results of this were most apparent

Table 1. Demographic data patient weight.

Number of FX < 4 kg	Number of RX < 4 kg	Procedure	Number of FX > 4 kg	Number of RX > 4 kg
4	3	ARCH/VSD		1
3		Norwood/Sano		
2		BT Shunt		
2	2	AVR/Septectomy/PA B		
2	1	ASD/VSD	5	4
	3	TOF	4	3
3	4	Switch	1	
	2	TAPVR		
	2	CAVSD	2	
		TVR	1	1
		RVOTO/LVOTO		2
		BDCPA		5
2.8 (±.6)*	3.2 (±.5)	Average weight (kg)	5.7 (±1.3)	5.6 (±1.0)
105 (±76)	125 (±43)	Average CPB time (min)	96 (±37)	111 (±34)
50 (±37)	62 (±29)	Average XC time (min)	62 (±28)	59 (±23)
.5 (±.2)	0.6 (±.1)	Average flow (L/min)	.81 (±.2)	.81 (±.1)
16	17	Total cases	13	16

*FX 2.8 kg ± .6 vs. RX 3.3 kg ± .5; $p = .01$.
ARCH, aortic arch repair; VSD, ventricular septal defect; BT, Blalock Taussig shunt; AVR, aortic valve repair; PA B, pulmonary artery band; ASD, atrial septal defect; TOF, tetralogy of fallot; TAPVR, total anomalous pulmonary venous repair; CAVSD, complete atrial ventricular septal defect; TVR, tricuspid valve repair; RVOTO, right ventricular outflow tract obstruction; LVOTO, left ventricular outflow tract obstruction; BDCPA, bidirectional caval pulmonary anastomosis.

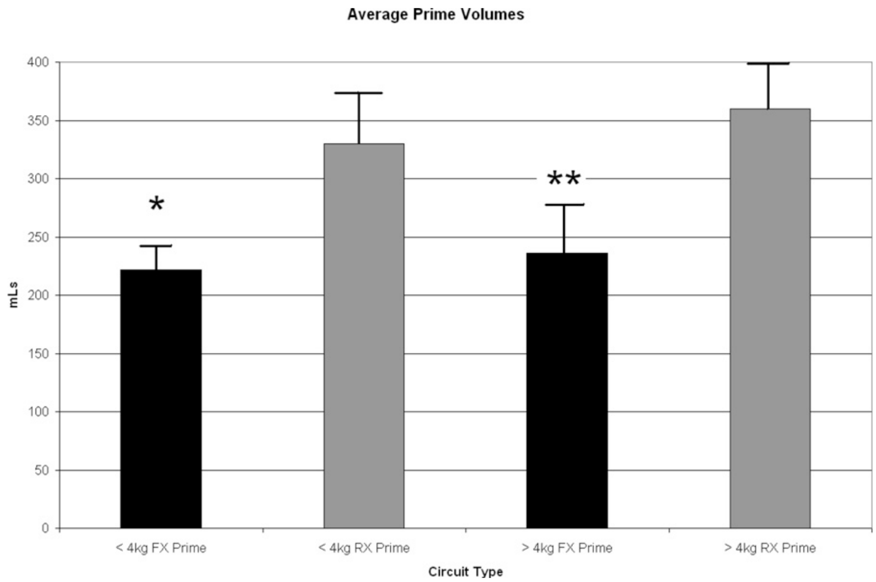

Figure 1. Average prime volumes. *<4 kg FX 222 mL ± 21 vs. RX 330 mL ± 42; $p < .01$ **>4 kg FX 236 mL ± 37 vs. 360 mL ± 39; $p < .01$.

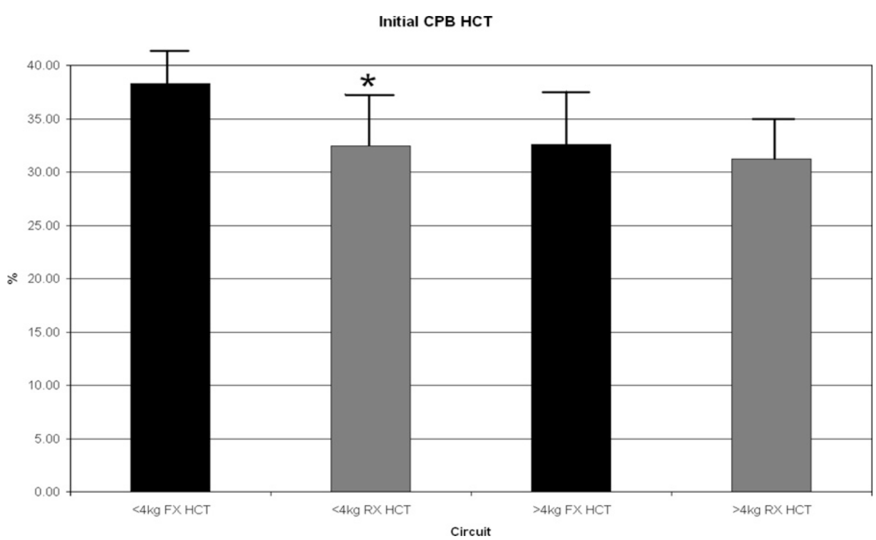

Figure 2. Initial CPB HCT. *<4 kg FX05 38% ± 4 vs. RX05 32% ± 5; $p < .01$.

in our initial CPB HCT for the <4 kg FX05 group (Figure 2). This translated into a clinically significant reduction in donor exposure for all FX05 patients, reaching statistical significance in the >4 kg group (Figure 3).

Performing CPB without an external ALF does add a few circuit modifications. Where we once measured circuit pressures from the top of the ALF, we now use the lured port on the outlet of the oxygenator. In our previous circuit with an ALF, we left our purge for the ALF open, shunted through our CDI 500 Arterial Sensor (Terumo), to our drug manifold and back to our reservoir. Now the CDI 500 and drug manifold run from the second lured port on the outlet FX05. We have continued with one connector distal to the oxygenator for blood removal for cardioplegia solution (CPS) and hemofiltration. Due to this, we have modified placement of our bubble detector to ensure no air can enter the circuit distal to this connector. These circuit modifications have, in fact, made the overall CPB setup simpler and faster. This is especially valuable in an emergent situation. Overall, the integrated ALF is extremely easy to prime and de-air in contrast to our previous practice of using a bypass loop to retrograde prime the external ALF.

Recognizing that there are concerns over failure of the integrated ALF or oxygenator, which would result in a complex component change during CPB, is not a valid reason

Table 2. Oxygenator performance.

	<4 kg FX05	<4 kg RX05	*p*-value	>4 kg FX05	>4 kg RX05	*p*-value
FiO_2 (%)	46 ± 5	47 ± 8	NS	58 ± 10	56 ± 11	NS
O_2 transfer (mL/min/FiO_2)	37 ± 14	42 ± 18	NS	44 ± 13	49 ± 12	NS
CO_2 transfer (mL/min)	11 ± 6	9 ± 5	NS	19 ± 7	20 ± 11	NS
Gas/blood flow ratio	.38 ± .15	.33 ± .1	NS	.47 ± .2	.45 ± .2	NS
Heat exchange coefficient	.56 ± .25	.43 ± .33	NS	.39 ± .16	.5 ± .29	NS

CO_2, carbon dioxide; FiO_2, fraction of inspired oxygen; kg, kilograms; min, minute; mL, milliliters; O_2, oxygen; NS, not significant.

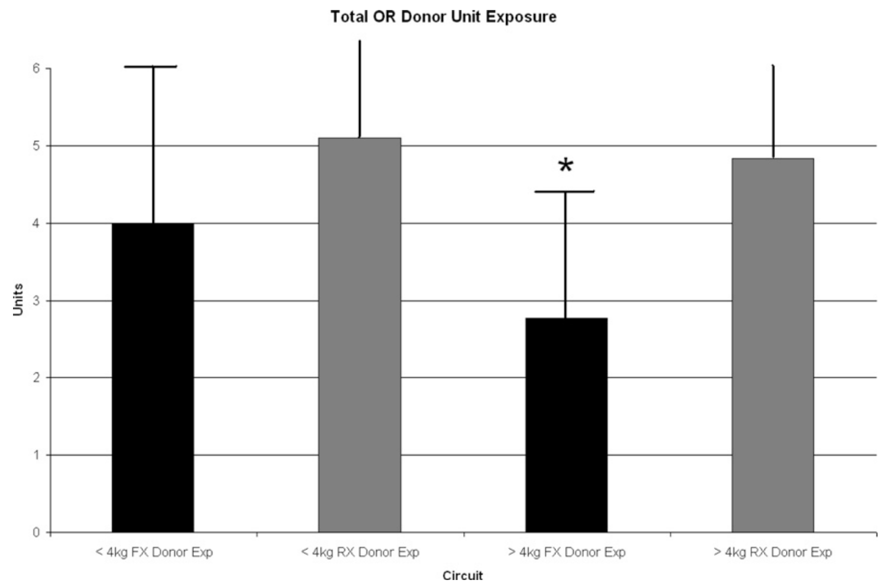

Figure 3. Total OR blood donor unit exposure. OR, Operating room. *>4 kg FX05 of 3 ± 2 vs. RX05 of 5 ± 2; $p < .01$.

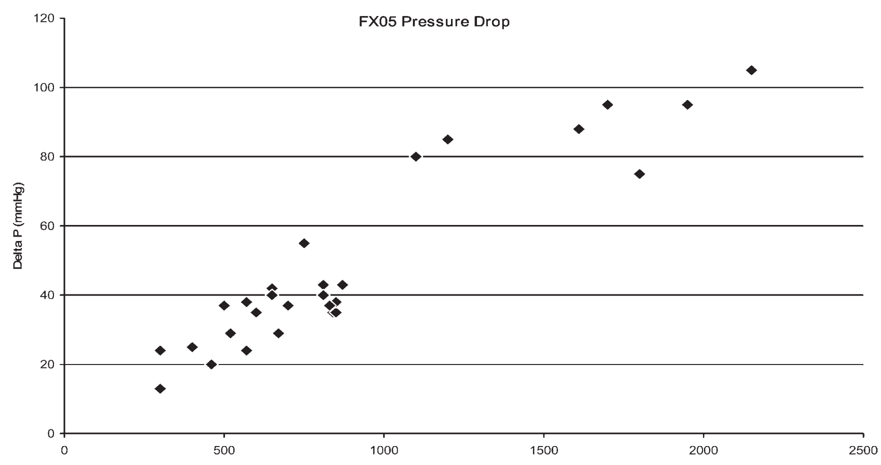

Figure 4. Pressure drop across FX05 oxygenator. P, Pressure; mL, milliliters; min, minute; mmHg, millimeters of mercury.

to avoid the FX05. Our previous CPB setup required the use of a bypass line in case of failure of the arterial line filter whether by accidental de-airing or thrombus formation, suggesting that simply clamping the filter out would result in the ability to remain on CPB without embolic complications. However, the reality is that the opening of the bypass line of the ALF may still result in emboli being sent to the patient.

Additionally, the FX05 oxygenator comes exclusively with Terumo's X Coating™ on the polypropylene fibers. X Coating™ is a 2nd generation amphiphilic organic polymer biocoating made of Poly (2-methoxyethylacrylate). The coating has hydrophobic/hydrophilic groups where water in blood collects at hydrophilic interface and the coating swells creating a molecular mesh. The formed elements of blood are therefore exposed to a "friendlier" surface. X Coating™ has been reported to reduce protein denaturization, reduce platelet adhesion to foreign surfaces, preserve platelet count and function, reduce blood loss, reduce inflammatory markers, reduce transfusion requirements, and reduce hospital stay (10,11).

After recognizing the benefits seen with the FX05, we promptly reviewed our blood transfusion practices in the operating room. By controlling the deleterious effects of CPB, limiting the use of cell saver suction, and maintaining mild or moderate hypothermia we have been able to tailor our approach to hemostasis in the operating room for each patient. Laboratory fibrinogen and platelet counts, along with clinical observation of hemostasis help to further dictate our transfusion requirements.

CONCLUSION

In conclusion, incorporating the Terumo Baby FX05 into our perfusion practice for patients <10 kg has allowed us to significantly reduce our CPB prime volumes and surface area while reducing our blood donor exposure, all without compromising patient safety. The FX05 is similar to the Baby RX05 in oxygenator performance, pressure drop, and heat exchanger performance. While there is a slight learning curve to running CPB without an external ALF, there is no sacrifice in safety by doing so. Incorporating an integrated arterial line filter allows for an improved CPB circuit; it primes rapidly, is easier to manage, and results in an overall improvement in patient management.

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