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A clinical evaluation of the Maquet Quadrox-i Neonatal oxygenator with integrated arterial filter

RM Ginther Jr., R Gorney and R Cruz

Abstract

High-performance, low-prime-volume oxygenators for the pediatric patient population have become a growing market among manufacturers. In the summer of 2011, our institution clinically evaluated the performance of the newly released Maquet Quadrox-i Neonatal oxygenator with integrated arterial filter. The static priming volume, including the integrated arterial filter, is 40 ml and the maximum rated blood flow is 1.5 liters per minute (LPM). The device was used on seven pediatric patients, ranging from 3.2 to 14 kg, undergoing various congenital heart defect repairs. Data were collected to calculate gas transfer, trans-oxygenator pressure drop, and heat exchange performance. The mean cardiopulmonary bypass time was 85 minutes and the mean cross-clamp time was 56 minutes. The average oxygen transfer was 34.3 ± 22.8 ml/O_2/min and increased with both blood flow and FiO_2. The average carbon dioxide transfer was 22.3 ± 17.8 ml/min and increased with both blood flow and gas sweep to blood flow ratio. The average trans-oxygenator pressure drop per blood flow was 53.3 ± 15.5 mmHg/L/min and increased with flow. The average heat exchanger performance factor was 47.6 ± 11.6% and decreased with flow. The heat exchange performance factor at maximum observed clinical flow, 1.42 LPM, was 36.4%. During this evaluation, the Maquet Quadrox-i Neonatal oxygenator adequately performed within its operational flow in the clinical setting.

Keywords

cardiopulmonary bypass; pediatric oxygenator; Quadrox- i neonatal oxygenator; integrated arterial filter; low prime oxygenator

Introduction

In pediatric cardiopulmonary bypass surgery (CPB), circuit miniaturization has become a popular technique to reduce hemodilution, allogeneic blood transfusion and the systemic inflammatory response.[1] Clinicians are using smaller tubing sizes, augmenting venous drainage, decreasing tubing length and integrating or eliminating pump components such as arterial line filters.[2] Manufacturers have responded by developing high-performance, low-prime-volume oxygenators for the pediatric patient population. These low-prime-volume and surface area oxygenators allow the perfusionist to further attenuate the negative effects associated with CPB.[3] An emerging miniaturization trend that is gaining popularity is integrating the arterial filter with the oxygenator. As these miniaturized devices become clinically available, the perfusionist must evaluate the performance and safety risks among the target patient population.

In the summer of 2011, our institution clinically evaluated the performance of the newly released Maquet Quadrox-i Neonatal oxygenator with integrated arterial

Division of Pediatric Cardiothoracic Surgery, University of Texas Southwestern Medical Center and Children's Medical Center, Dallas, Texas, USA

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Corresponding author:
Richard M Ginther Jr. CCP
Division of Pediatric Cardiothoracic Surgery
Children's Medical Center of Dallas
1935 Medical District Drive
Suite C3211
Dallas, TX 75235, USA.
Email: Richard.ginther@utsouthwestern.edu

Table 1. Technical specifications of oxygenators with integrated filters.

	Quadrox-i Neonatal	Terumo FX05
Maximum blood flow rate	1.5 L/min	1.5 L/min
Static priming volume, including arterial filter	40 ml	43 ml
Filter pore size	33 µm	32 µm
Surface gas transfer fibers	0.38 m^2	0.5 m^2
Heat exchanger surface area	0.07 m^2	0.035 m^2
Microporous fiber material	Polypropylene	Polypropylene
Heat exchanger fiber material	Polyurethane	Stainless Steel

filter (Maquet, Hirrlingen, Germany). The static priming volume, including the integrated arterial filter, is 40 ml and the maximum rated blood flow is 1.5 liters per minute (Table 1; Figure 1). At 40 ml total priming volume, the Quadrox-i Neonatal is the smallest combination of oxygenator and arterial filter commercially available. The low oxygenator surface area, 0.38m^2, is achieved by unconventionally stacking single layers of polypropylene fiber mats perpendicular to each other rather than weaving and wrapping them in a bundle. The minimum overlapping, low contact area and constant fiber distance of this fiber design is advertised to provide optimal gas and heat transfer with a low pressure drop.

The purpose of this study was to evaluate the performance of this newly released oxygenator in the clinical setting, using performance characterizations outlined in the FDA's Guidance for Cardiopulmonary Bypass Oxygenators 510(k) Submissions.[4] These performance characterizations include oxygen and carbon dioxide gas transfer, trans-oxygenator pressure drop and heat exchanger performance. The clinical performance factors should appropriately function when compared to in vitro results reported by the manufacturer.

Methods

The Maquet Quadrox-i Neonatal was used on seven pediatric patients, ranging from 3.2 to 14 kg, undergoing various congenital heart defect repairs. Operative data was collected and used to report weight, height, body surface area (BSA), bypass time, cross-clamp time, procedure, lowest temperature and lowest hematocrit (Table 2).

To calculate gas transfer, arterial and venous line samples were collected every 15-20 minutes and analyzed with the i-STAT point of care analyzer (Abbott Laboratories, Abbott Park, IL). Oxygen transfer (ml/O_2/min) was calculated using the formula ([arterial oxygen content {C_aO_2} – venous oxygen content {C_vO_2}] x blood flow {LPM} x 10). Carbon dioxide transfer (ml/min) was calculated using the formula ([$PaCO_2$ x gas flow rate] / 0.863). Arterial, venous and water temperatures were captured every 60 seconds during the warming phase via the electronic record to calculate the heat exchange coefficient. The heat exchange coefficient (%) was calculated using the formula ([venous line temperature – arterial line temperature] / [venous line temperature – heater cooler water temperature]). Pre-oxygenator pressures measured at the pressure port on the inlet of the oxygenator and post-oxygenator pressures measured

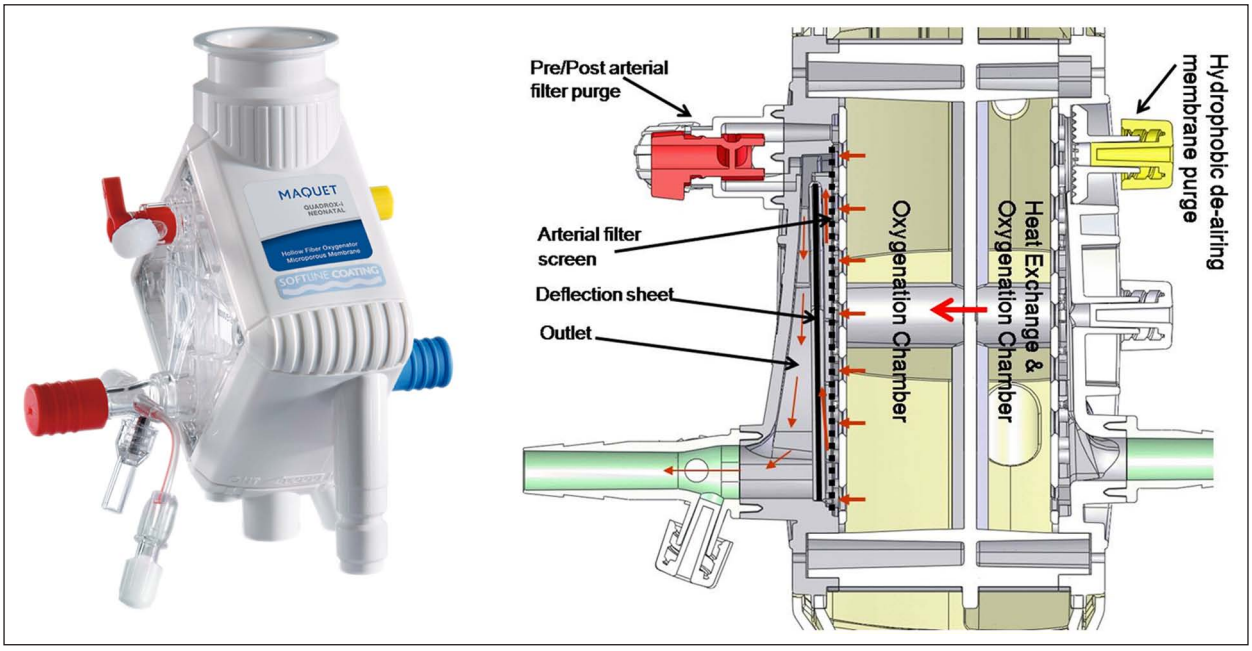

Figure 1. Picture and cross-sectional view of the Quadrox-i Neonatal oxygenator with integrated filter. Reproduced with permission from MAQUET Medical Systems, USA.

Table 2. Operative demographics.

Case	Weight (kg)	Height (cm)	BSA	CPB	Cross-clamp	Lowest Temp(C°)	Lowest Hct(%)	Procedure
1	3.2	47	0.19	133	70	20	35	Norwood
2	5.44	57	0.28	71	57	30	39	VSD, ASD, PDA
3	5.77	63	0.3	96	78	27	34	VSD, PFO, TVP
4	6.5	61	0.31	133	105	27	34	TOF w/ TA patch
5	8.8	80	0.44	22	16	35	36	ASD
6	9.5	71	0.43	39	0	32	38	BDG
7	14	96	0.61	99	64	27	32	RVOT patch
Mean	7.6	69	0.37	85	56	28.3	35.4	
Range	3.2–14	47–96	.19–.61	22–133	0–105	20–35	32–39	

BSA: body surface area; CPB: cardiopulmonary bypass; Hct: hematocrit; VSD: ventricular septal defect closure: ASD: atrial septal defect closure; PDA: patent ductus arteriosus ligation; PFO: patent foramen ovale closure; TVP: tricuspid valvuloplasty; TOF: tetralogy of Fallot repair; TA patch: transannular patch; BDG: bidirectional shunt; RVOT: right ventricular outflow tract.

at the pigtail on the oxygenator outlet were captured every 60 seconds via the electronic record to calculate the trans-membrane pressure drop. The trans-membrane pressure drop (mmHg) was calculated using the formula (pre-oxygenator pressure – post-oxygenator pressure). With the exception of measuring pre-oxygenator pressure, there were no changes to our perfusion practice during the evaluation. All procedures were conducted using the S5 System heart/lung machine, 3T 208volt Heater Cooler System, Data Management System, DHF0.2 hemoconcentrator (Sorin, Arvada, CO), the CDI 500 Blood Parameter Monitoring System (Terumo Cardiovascular Systems Corporation, Ann Arbor, MI), and the Medtronic HMS Plus Hemostasis Management System (Medtronic, Minneapolis, MN).

Our institutional protocol is to maintain a hematocrit of ≥30% and all patients received one unit of packed red blood cells in the prime. The prime consisted of heparin, calculated by the Medtronic HMS Plus, 30 mg/kg of solumedrol, 0.5 mg/kg of mannitol, 0.25 mg/kg furosemide, 30 ml of 25% albumin, and sodium bicarbonate to buffer the solution to approximately pH 7.4. Pre-bypass ultrafiltration with 300 ml of Plasmalyte A was used to wash the solution prior to initiating bypass. We use a 3/16" x 1/4" AV loop for patients up to 10 kg and a 1/4" x 1/4" AV loop for patients between 10 – 15 kg. We chose 15 kg as a maximum cutoff weight during this evaluation. pH stat blood gas management was used during all phases of bypass, with a gas flow : blood flow range of 0.1-1.2 : 1.0 LPM.

Results

The average weight and height were 7.6 kg (range 3.2 – 14 kg) and 69 cm (range 47 – 96 cm), respectively. The mean cardiopulmonary bypass time was 85 minutes and the mean cross-clamp time was 56 minutes. Full operative and patient demographics are shown in Table 2. A total of 26 blood gas samples from the seven study groups were used to calculate oxygen and carbon dioxide gas transfer. The average oxygen transfer was 34.3 ± 22.8 ml/O_2/min and increased with both blood flow and FiO_2 (Figures 2 and 3). The average carbon dioxide transfer was 22.3 ± 17.8 ml/min and increased with both blood flow and gas to blood flow ratio (Figures 4 and 5). The average trans-oxygenator pressure drop per blood flow was 53.3 ± 15.5 mmHg/L/min and increased with blood flow (Figure 6). The average heat exchanger performance factor was 47.6 ± 11.6% and decreased with blood flow. The heat exchange performance factor at maximum observed clinical flow, 1.42 LPM, was 36.4% (Figure 7). Potential failure modes, such as leaks, toxicity, loss of gas transfer efficiency, gas embolism, thromboembolism and blood damage were not clinically observed.

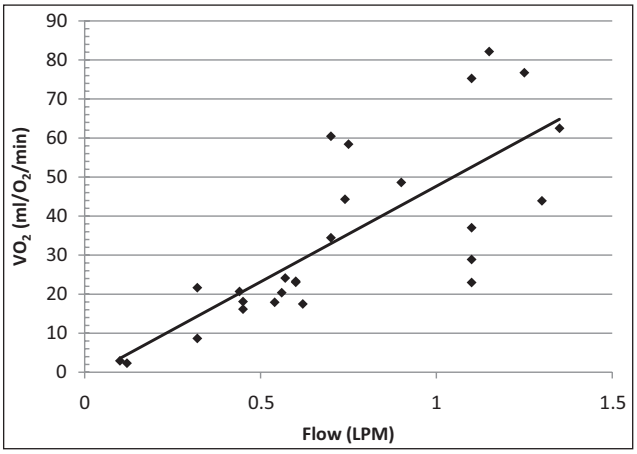

Figure 2. The average oxygen transfer was 34.3 ± 22.8 ml/O_2/min and increased with blood flow. The oxygen transfer at the highest reported flow, 1.4 LPM, was 62.5 ml/O_2/min.

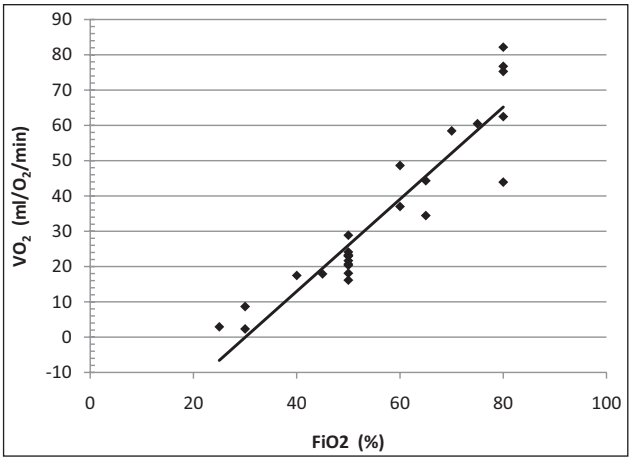

Figure 3. The oxygen transfer positively increased with FiO_2. The highest oxygen transfer at the maximum reported FiO_2, 80%, was 82.2 ml/O_2/min.

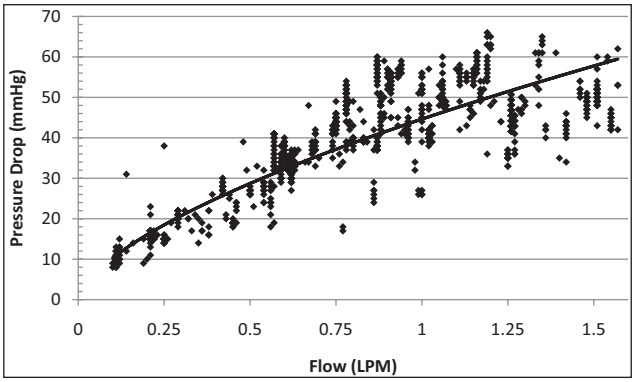

Figure 6. The average trans-oxygenator pressure drop per blood flow was 53.3 ± 15.5 mmHg/L/min and increased with flow. The minimum and maximum reported flow, 0.1 and 1.57 LPM, generated trans-oxygenator pressure drops of 8 and 62 mmHg, respectively.

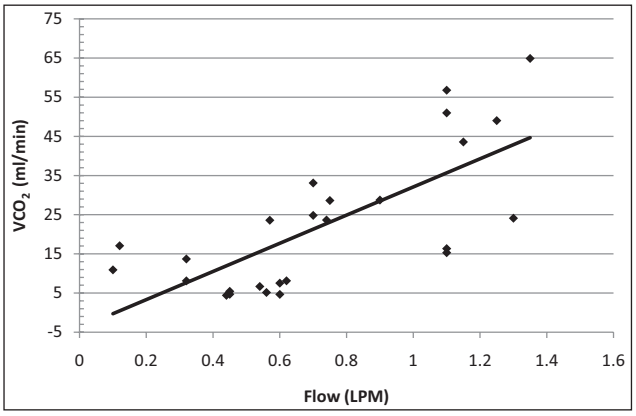

Figure 4. The average carbon dioxide transfer was 22.3 ± 17.8 ml/min and increased with blood flow. The carbon dioxide transfer at the highest reported flow, 1.4 LPM, was 64.9 ml/min.

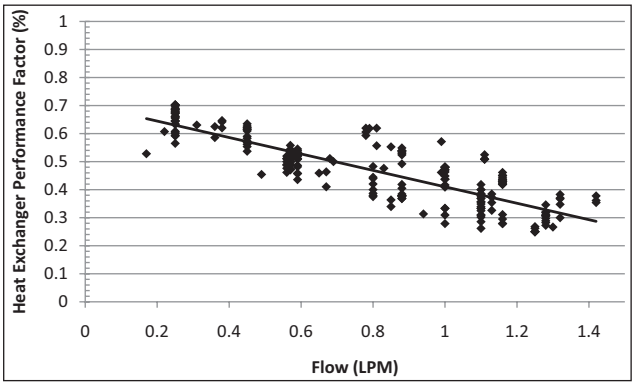

Figure 7. The average heat exchanger performance factor was 47.6 ± 11.6% and decreased with flow. The heat exchange performance factor at maximum observed clinical flow, 1.42 LPM, was 36.4%.

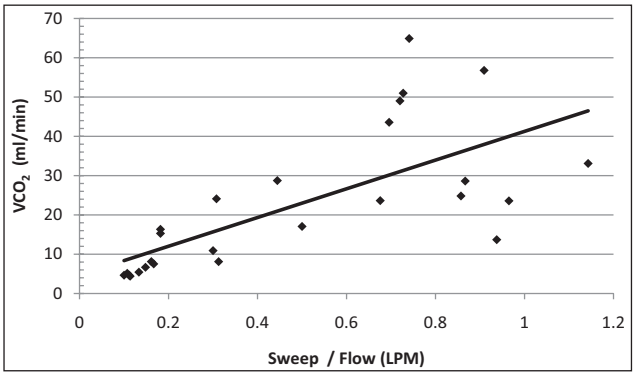

Figure 5. The carbon dioxide transfer positively increased with the gas sweep to blood flow ratio. The carbon dioxide transfer at the highest reported ratio, 0.8:0.7 or 1.14 LPM, was 33.1 ml/min.

Discussion

Maquet is widely known for its very popular Quadrox D line of oxygenators, used for extracorporeal membrane oxygenation (ECMO). Unlike the Quadrox-i, the hollow-fiber oxygenation membrane used within the Quadrox D is made of non-porous polymethylpentene (PMP) rather than microporous polypropylene. A PMP membrane is suitable for long-term ECMO support because the characteristics of a non-porous diffusion membrane are far superior at reducing plasma leaks and micro-air versus the polypropylene fibers. However, a limiting factor for using a PMP membrane during conventional CPB is that these membranes do not allow the transfer of volatile anesthetics and, therefore,

intravenous anesthetics must be employed. Maquet states that the utilization period of the Quadrox-i, a polypropylene oxygenator, is limited to 6 hours.

The unique design approach of stacking single layers of polypropylene fiber mats perpendicular to each other and integrating both heat exchange and arterial line filtration has resulted in the smallest prime volume and surface area device on the market. In vitro lab results performed by Maquet have shown the Quadrox-i Neonatal to perform adequately within conventional performance characteristics.[5] An in vitro evaluation offers a snapshot of performance data within a controlled environment, but does not account for the many uncontrollable variables within the clinical setting. This study used our institutional CPB policy and procedure to evaluate the clinical performance of the Quadrox-i Neonatal within its approved operational range of flows.

The performance data shows that the oxygenator and heat exchanger performed appropriately as flows approached the maximum rating of 1.5 LPM. Raw data in this type of evaluation are typically very subjective due to the multiple variations in institutional CPB policy and procedure. So, while it is difficult to interpret whether or not a reported performance value is adequate, the important interpretation is that the result changed respectively with the variable. This interpretation can be supported by comparing clinical performance trends with published in vitro results.

It is demonstrated that, as blood flow increases, the oxygen and carbon dioxide transfer also increase. This trend is consistent with the reported in vitro results from the manufacturer. Since FiO_2 is not constant during CPB, the oxygen transfer has been reported versus FiO_2 and shows a positive linear relationship (Figure 3). Our PaO_2 policy is to maintain values in the 200-300 mmHg range and our highest reported blood flow of 1.4 LPM required an FiO_2 of 80%. Also, the oxygenator was very efficient at removing CO_2, which is demonstrated by the low gas sweep required to maintain CO_2 with pH stat blood gas management (Figure 5).

Though the trans-oxygenator pressure drop paralleled the manufacturer's in vitro results, it is important to note that the pre-membrane pressure is not measured in the conventional fashion. Typically, this pressure can only be measured by placing a Luer connector proximal to the oxygenator and measuring pressure at that location. The Quadrox-i Neonatal has a pressure port located at the face of the pre-oxygenator housing and, because of its positioning, will report values less than if they were measured in the conventional fashion (personal communication with Quadrox-i Neonatal developer). We were not aware of this when designing the study, but this factor should be considered if conducting a comparative evaluation against a different oxygenator. The post-oxygenator pressure was measured from a pigtail port at the oxygenator outlet. A recent in vitro study by Salavitavar et al. showed that the Quadrox-i Neonatal had an extremely low pressure drop compared to previously published reports.[6] A similar in vitro study comparing the Quadrox-i and Terumo FX neonatal oxygenators reports slightly lower transmembrane pressure drops for the Quadrox-i in both the temperature and blood flow groups.[7]

Our heat exchange performance data does demonstrate the same negative linear relationship between the performance factor and blood flow reported by the manufacturer, but, at similar flow rates, the unit demonstrated a lower performance factor percentage. However, clinically measuring the heat exchange performance factor presents a particular challenge. The heater/cooler water temperature, venous line temperature, 10°C difference between water and venous line temperature and the blood flow rate are kept constant during laboratory testing. It is impossible to keep these variables constant during the warming phase of CPB. During CPB, as the venous line and arterial temperature approach the set water temperature, the heat exchange performance factor will approach zero. Clinically changing the controlled variables nullifies the equation for the heat exchange performance factor. Our best compromise was to only gather data at the onset of warming. We set the water temperature 10°C higher than the venous line temperature and collected data every 20 seconds for two minutes. We were then able to trend the performance factor versus blood flow and, most importantly, report clinical efficiency near maximum flows.

The oxygenator with integrated arterial filter primed easily and does not require CO_2 flushing. The integrated filter has a stopcock at the apex that can alternate between pre- and post-filter purging. It is not recommended to use the arterial filter purge for arterial line sampling or a manifold source as this blood is not an accurate arterial sample. Since it is recommended that the arterial filter purge be open during oxygenator use, this adds an additional shunt while on CPB. Salavitavar et al. observed that the pressure drop across the oxygenator was not affected by opening the arterial line purge.[6] We placed a large-bore, three-way stopcock on the female Luer on the oxygenator outlet and ran both the manifold and hemoconcentrator from this port.

The venous reservoir has a unique funnel shape and is designed to offer low-volume operation at high flows, with minimal eddies. We employ gravity venous drainage and place the reservoir low to the ground to assist drainage. We found that, because of the funnel shape and low placement, visualization of the volume level is cumbersome if the perfusionist is standing or looking down at the unit. The Neonatal reservoir has a volume capacity of 800 ml and we elected to not use this reservoir for patients larger than 10 kg because we were concerned

about exceeding this capacity in the event of needing to exsanguinate the patient for circulatory arrest. The typical circulating blood volume of a child is 70-80 ml/kg and, considering this calculation, patients larger than 10 kg would exceed the maximum capacity. To accommodate our concern, we asked Maquet to supply us with the Neonatal oxygenator and Pediatric reservoir (VHK 31000) separately so that we could use them together for the larger patients. The Pediatric reservoir has a volume capacity of 1700 ml and we felt this capacity would satisfy our 15 kg cutoff weight for the Neonatal oxygenator.

In the USA, the only other comparable oxygenator with an integrated arterial filter is the Terumo FX05 (Terumo Cardiovascular Systems Corporation, Ann Arbor, MI) (Table 1). Both the Maquet and Terumo oxygenators are rated at 1.5 liters per minute maximum flow, but both are designed quite differently. Rather than wrapping and bundling the oxygenator hollow fibers around a stainless steel heat exchanger core, Maquet stacks and integrates oxygenator hollow-fiber mats with perpendicular polyurethane heat exchange mats. Maquet's configuration allows for a smaller oxygenation surface area, but the less effective polyurethane heat exchanger requires a high surface area to increase efficiency. Terumo wraps a 32μ arterial screen filter around the oxygenator fibers and this technique does not add any prime volume. The filter is designed to entrap particulate emboli, but air emboli removal is accomplished by entrapment followed by permeation and exhaustion via the oxygenator's hollow fibers. This unconventional technique does not utilize a venting stopcock for air removal. Alternately, Maquet directly interfaces the oxygenator and 33μ arterial screen filter with blood flowing into, through and out of the integrated unit. The pre- and post-arterial filter compartments add 2 ml to the oxygenator prime volume and can be purged via the venting stopcock.

In conclusion, the Maquet Quadrox-i Neonatal oxygenator trended appropriately with the manufacturer's in vitro data and performed adequately in the clinical setting. The oxygenator was able to accommodate our largest patient at 14 kg, but we were not comfortable using the Neonatal reservoir for patients larger than 10 kg. The unit allowed us to achieve our institutional hematocrit protocol 30% without needing to exceed our current standard of 1 unit of packed red blood cells. Standard performance data, such as gas transfer, heat exchange performance and pressure drop, offer subjective data in the absence of benchmark industry values. In addition to comparing similar oxygenators side by side (with and without arterial filter integration), emerging performance data regarding the handling of gaseous microemboli and the benefits of low transmembrane pressure drop should be considered.

Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

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