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In Vitro Comparison of Two Neonatal ECMO Circuits Using a Roller or Centrifugal Pump With Three Different In-Line Hemoconcentrators for Maintaining Hemodynamic Energy Delivery to the Patient

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Abstract: The objective of this study was to compare three different hemoconcentrators (Hemocor HPH 400, Mini, and Junior) with two different neonatal ECMO circuits using a roller or a centrifugal pump at different pseudo-patient pressures and flow rates in terms of hemodynamic properties. This evidence-based research is necessary to optimize the ECMO circuitry for neonates. The circuits used a 300-mL soft-shell reservoir as a pseudo-patient approximating the blood volume of a 3 kg neonate, two blood pumps, and a Quadrox-iD Pediatric oxygenator with three different in-line hemoconcentrators (Hemocor HPH 400, Mini, and Junior). One circuit used a Maquet H20 roller pump and another circuit used a Maquet RotaFlow centrifugal pump. The circuit was primed with lactated Ringer's solution followed by heparinized packed red blood cells with a hematocrit of 40%. The pseudo-patient's pressure was manually maintained at 40, 60, or 80 mm Hg and the flow rate was maintained at 200, 400, or 600 mL/min with a circuit temperature of 36°C. Pressure and flow data was recorded using a custom-made data acquisition device. Mean pressures, diverted blood flow, pressure drops, and total hemodynamic energy (THE) were calculated for each experimental condition. The roller pump and centrifugal pump performed similarly for all hemodynamic properties with all experimental conditions. The Hemocor HPH Junior hemoconcentrator added the highest resistance to the circuit. The Hemocor HPH Junior provided the highest circuit pressures, lowest diverted blood flow, highest pressure drop across the circuit, and highest THE generated by the pump. The Hemocor HPH 400 added the least resistance to the circuit, providing the lowest circuit pressures, more diverted flow, lowest pressure drop, and the lowest THE generated by the pump. However, the THE delivered to the patient was the same for the three hemoconcentrators. While the three hemoconcentrators performed differently in terms of hemodynamic properties throughout the circuit, the THE transmitted to the patient was similar for all three hemoconcentrators due to the consistent pseudo-patient's pressure that was manually maintained for each trial. While the THE delivered to the patient indicates similar perfusion for these patients with any of the three hemoconcentrators, the differences in added resistance to the circuit may impact the decision of which hemoconcentrator is used. There was no clinically significant difference between the two circuits with the roller versus centrifugal pump in terms of hemodynamic properties in this study. Further in vivo research is warranted to confirm our findings. **Key Words:** Extracorporeal membrane oxygenation—Neonatal—Hemoconcentration—Roller pump—Centrifugal pump.

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Extracorporeal life support (ECLS) provides mechanical support in the setting of cardiovascular or respiratory failure. ECLS use has been significantly increasing since 2005 (1). This support can be life-saving, however, neonatal patients who require ECLS have increased morbidity and mortality, and it is associated with many multi-organ

complications (2). One of the most common requirements during neonatal ECLS is the use of hemofiltration (1). Hemofiltration is used to remove excessive fluid and inflammatory molecules from the extracorporeal membrane oxygenation (ECMO) system (2). In the last year it has been required in 23% of neonatal respiratory, 25% of pediatric respiratory, 26% of neonatal cardiac, and 24% of pediatric cardiac ECLS cases (1).

The need for hemofiltration during neonatal ECLS is most often due to acute kidney injury (AKI) and fluid overload (2). AKI can be due to altered renal perfusion or systemic inflammation which is caused by the underlying illnesses of the patients and the ECMO circuitry itself (3). The ECMO circuitry exposes the blood to artificial surfaces causing cytokine activation, fluid overload, and increased capillary permeability (3). The ECMO circuit must also be primed with a volume of fluid and often patients require blood and drug transfusions which further increase the fluid volume (4). This increased fluid volume is particularly significant in neonates. The added volume can lead to fluid overload, increased blood pressure, and electrolyte imbalances (4).

Using an in-line hemoconcentrator to remove ultrafiltrate from the patients while on ECMO can reduce AKI and prevent fluid overload (3). Ultrafiltration is a process in which water is removed by passive diffusion due to hydrostatic transmembrane pressure, so the amount of volume removed will depend on the pressure and the flow rate of the blood. The amount of ultrafiltrate removed and the amount of hemodynamic energy being delivered to the patient should be monitored to ensure appropriate oxygenation (5).

Evidence-based research has been used to evaluate many different circuit set-ups for neonatal ECMO patients at Penn State Children's Hospital (6–10). This study compares the use of three different in-line hemoconcentrators in two distinct ECMO circuits: The one used in the neonatal intensive care unit (NICU) at Penn State Children's Hospital, and the one used in the pediatric intensive care unit (PICU) at the same institution. The NICU circuit uses a roller pump, and the PICU circuit uses a nonocclusive centrifugal pump. The occlusive roller pump can overcome downstream resistance to maintain the same flow rate regardless of pressure changes (11). The nonocclusive centrifugal pump changes the flow rate depending on downstream resistance (11). Adding an in-line hemoconcentrator changes the resistance, which changes the flow rate of the nonocclusive centrifugal pump (11). We compared the hemoconcentrators in circuit with the different pumps at various pseudo-patient pressures (40, 60, 80 mm Hg) and flow rates (200, 400, 600 mL/min).

The three hemoconcentrators used were Hemocor HPH 400, Mini, and Junior. The Hemocor HPH 400 is the one used in the NICU at our institution. The Hemocor HPH Mini is a smaller concentrator with a low priming volume and is suggested for use in the smallest pediatric patient, including the neonate. The Hemocor HPH Junior is a new model with a similarly small priming volume to the Mini, but a larger ultrafiltration potential.

To our knowledge there is no data in the literature that evaluates these hemoconcentrators with human blood in any neonatal circuit. The objective of this study is to compare the hemoconcentrators with two circuits including a roller pump or a centrifugal pump in order to determine the clinically translatable significance of the use of these hemoconcentrators during ECMO in neonates.

MATERIALS AND METHODS

Experimental circuit

The simulated ECMO circuits mimic the clinical circuits used in the NICU and PICU at our institution and are shown in Fig. 1. A 300 mL soft-shell reservoir served as a 3 kg pseudo-patient approximating the blood volume of a term neonate. Both circuits used the same Quadrox-iD Pediatric diffusion membrane oxygenator (Maquet, Inc., Wayne, NJ, USA), 8-Fr Biomedicus arterial cannula (Medtronic Inc., Minneapolis, MN, USA), and 10-Fr Biomedicus venous cannula as shown in Fig. 1. The pediatric circuit includes the Maquet RotaFlow centrifugal pump head and console (Maquet, Inc., Wayne, NJ, USA). The pediatric circuit used 3 feet of 1/4 inch ID arterial and venous tubing. The neonatal circuit includes the Maquet H20 roller pump (Maquet, Inc., Wayne, NJ, USA) and a Better Bladder (BB) (Circulatory Technology Inc., Oyster Bay, NY, USA) inserted into the venous line. The neonatal circuit had 51 inches of 1/4 inch ID arterial tubing and 161 inches of 1/4 inch ID venous tubing. Each circuit had a purge line with 55 inches of 1/8 inch ID tubing and a COBE five-port manifold (Sorin Infant Perfusion Pack, Sorin Cardiovascular, Inc., Arvada, CO, USA) attached after the oxygenator and before the pump as shown in Fig. 1. A hemoconcentrator was attached to the manifold.

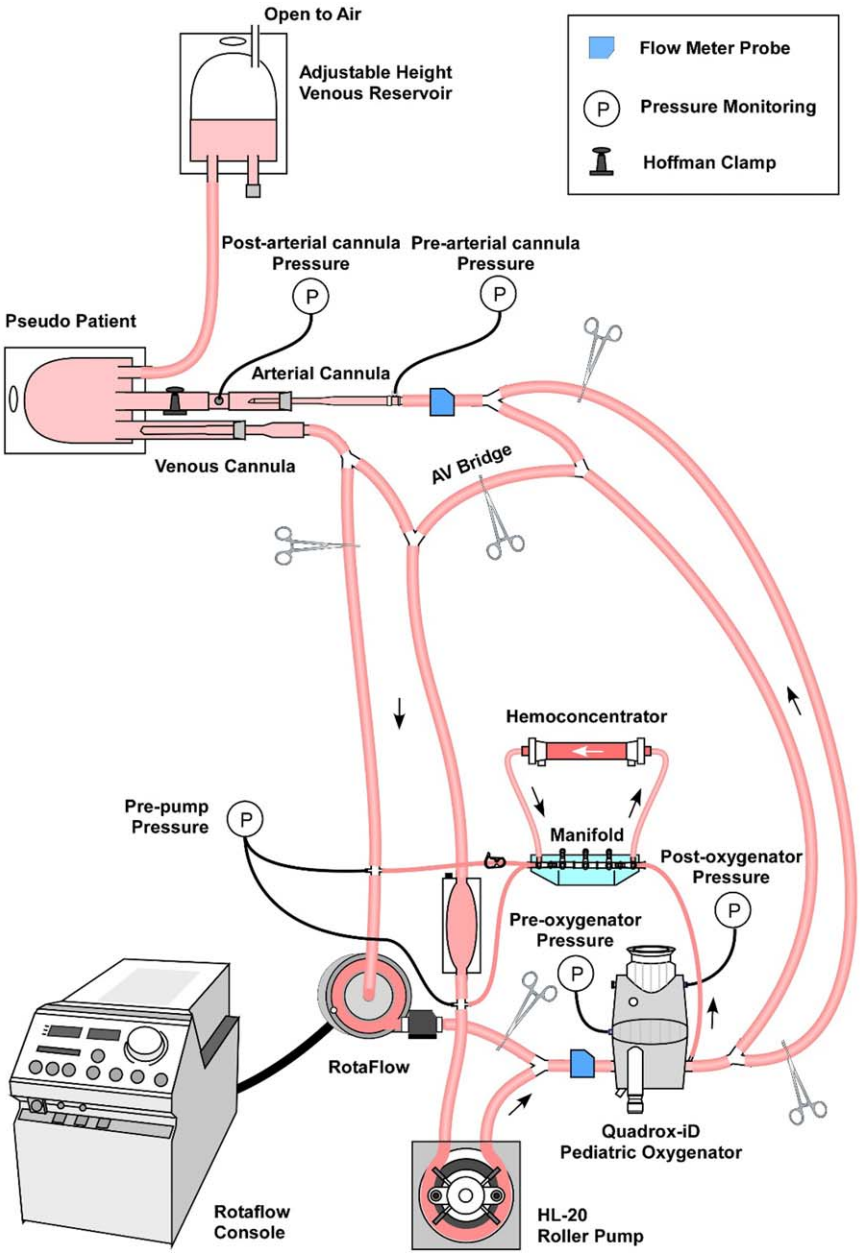

FIG. 1. Experimental circuit. [Color figure can be viewed at wileyonlinelibrary.com]

Three different hemoconcentrators were compared: Hemocor HPH 400, Hemocor HPH Mini, and Hemocor HPH Junior (Medivators Inc., Minneapolis, MN, USA). The hemoconcentrators had 46 inches of 1/4 inch ID tubing on either end. An AV bridge was attached with "Y" connectors between the arterial and venous lines in the neonatal circuit, and was kept closed with tubing clamp forceps for all experimental conditions. Temperature was maintained at 36°C with a Seabrook ECLS-Temp heater-cooler unit (Medical Systems Co., Cincinnati, OH, USA). Specifications of circuit components are detailed in Table 1.

Hemodynamic data acquisition

Pressure transducers (Argon Medical, Athens, TX, USA) were placed in the circuit to measure pressure at five sites: Prepump, preoxygenator, postoxygenator, prearterial cannula, postarterial cannula. Two transonic ultrasound flow probes (Transonic Systems Inc., Ithaca, NY, USA) were placed in the circuit to measure flow rate: Preoxygenator and prearterial cannula. Pressure transducers and flow probes were linked to a custom-made data acquisition device (NI USB-6521, National Instruments, Austin, TX, USA). Pressure and flow measurements were collected at 1000

TABLE 1. *The components of the experimental circuit*

Component	Hemoconcentrator		
	Hemocor HPH 400	**Hemocor HPH Mini**	**Hemocor HPH Junior**
Membrane surface area (m^2)	0.3	0.07	0.09
Priming volume (mL)	34	14	8
Pressure drop (mm Hg)	61	30	55
Internal unit diameter (cm)	3.0	2.5	2.5
Internal fiber diameter (microns)	200	620	200
	Pump		
	Maquet H20 Roller Pump	**Maquet RotaFlow Centrifugal Pump**	
Flow range (L/min)	0–10	0–10	
Maximum pressure (mm Hg)	997	750	
Rotational speed range	0–250 rpm	0–5000 rpm	
	Quadrox-iD Pediatric Oxygenator		
Blood flow range (L/min)	0.2–2.8		
Priming volume (mL)	81		
Gas exchange surface area (m^2)	0.8		

samples/s using LabView 7.1 Software for Windows (National Instruments, Austin, TX, USA).

Experimental design

Lactated Ringer's solution was used to prime the circuit. Heparinized human packed red blood cells were diluted to a hematocrit of 40% and added to the circuit. Tubing clamp forceps (Becton, Dickinson and Company, Franklin Lakes, NJ, USA) were used to direct blood flow through only the NICU (HL-20 Roller pump) or the PICU (RotaFlow Centrifugal pump) circuit. Pseudo-patient pressure was maintained at the postarterial cannula site with a Hoffman clamp. Flow rate was controlled by the RPMs of the given pump and monitored by the preoxygenator flow probe (Fig. 1).

Hemodynamic data included pressure and flow waveforms collected at 20 s intervals at all sites. Variables included two circuits with different pumps (NICU/HL-20 Roller pump, PICU/RotaFlow Centrifugal pump), three flow rates (200, 400, 600 mL/min), three pseudo-patient pressures (40, 60, 80 mm Hg), and three different hemoconcentrators (Hemocor HPH 400, Mini, Junior). Six trials were performed under each experimental condition.

Pressure drop calculation

The pressure drops across various parts of the circuit were calculated for each experimental condition. The pressure drops across the oxygenator, arterial tubing including the hemoconcentrator, and arterial cannula were calculated using the following equations:

$$\text{Oxygenator pressure drop (mm Hg)} = \text{preoxygenator pressure} - \text{postoxygenator pressure} \quad (1)$$

$$\text{Arterial tubing pressure drop (mm Hg)} = \text{postoxygenator pressure} - \text{precannula pressure} \quad (2)$$

$$\text{Cannula pressure drop (mm Hg)} = \text{precannula pressure} - \text{postcannula pressure} \quad (3)$$

$$\text{Circuit pressure drop (mm Hg)} = \text{preoxygenator pressure} - \text{postcannula pressure} \quad (4)$$

Diverted blood flow calculation

The blood flow diverted through the hemoconcentrator was calculated for each experimental condition using the following equation:

$$\text{Diverted flow (mL/min)} = \text{preoxygenator flow} - \text{precannula flow} \quad (5)$$

THE calculation

Total hemodynamic energy (THE) was calculated for each experimental condition. THE is derived from the energy equivalent pressure (EEP) to quantify pulsatility. EEP was calculated using Shepard's EEP formula (12). The blood flow (f) and pressure (p) values recorded by LabVIEW software (Eq. 6). THE was calculated by converting units of pressure to units of energy (Eq. 7).

$$\text{EEP} = \frac{\int fp\ dt}{\int f\ dt} \quad (6)$$

$$\text{THE}\ \left(\text{ergs/cm}^3\right) = 1332 \times \text{EEP} \quad (7)$$

Percent THE lost across various parts of the circuit were calculated with the following equation:

TABLE 2. *Mean pressures at preoxygenator and postarterial cannula sites*

Pump	Flow Rate (mL/min)	Pressure (mm Hg)	Preoxygenator MP (mm Hg) with different hemoconcentrators			Postarterial cannula MP (mm Hg) with different hemoconcentrators		
			400	Mini	JR	400	Mini	JR
Roller	**200**	**40**	$90.3 \pm 0.3^{\dagger\ddagger}$	$97.3 \pm 0.3^{\ddagger}$	$92.2 \pm 0.4^{*\ddagger}$	39.2 ± 0.1	41.4 ± 0.2	41.7 ± 0.4
		60	$109.7 \pm 0.2^{\dagger\ddagger}$	$116.8 \pm 0.3^{\ddagger}$	$112.0 \pm 0.6^{*\ddagger}$	60.4 ± 0.2	61.0 ± 0.2	61.3 ± 0.6
		80	$128.9 \pm 0.8^{\dagger\ddagger}$	$141.7 \pm 0.1^{\ddagger}$	$129.6 \pm 0.7^{*\ddagger}$	80.3 ± 0.5	81.0 ± 0.1	80.1 ± 0.7
	400	**40**	$127.9 \pm 0.2^{\dagger\ddagger}$	$131.1 \pm 0.6^{\ddagger}$	$139.4 \pm 0.3^{*\ddagger}$	40.4 ± 0.1	41.1 ± 0.5	42.0 ± 0.3
		60	$148.1 \pm 0.2^{\dagger\ddagger}$	150.1 ± 0.4	$158.4 \pm 0.5^{*\ddagger}$	61.0 ± 0.1	61.2 ± 0.4	61.2 ± 0.6
		80	$164.4 \pm 0.3^{\dagger\ddagger}$	168.7 ± 0.5	$178.1 \pm 0.4^{*}$	80.2 ± 0.1	80.2 ± 0.4	81.7 ± 0.3
	600	**40**	$181.1 \pm 0.2^{\dagger\ddagger}$	$184.0 \pm 0.2^{\ddagger}$	$194.2 \pm 0.2^{*\ddagger}$	41.1 ± 0.1	41.7 ± 0.2	39.4 ± 0.2
		60	$199.8 \pm 0.2^{\dagger\ddagger}$	$202.7 \pm 0.3^{\ddagger}$	$214.6 \pm 0.4^{*\ddagger}$	59.8 ± 0.2	61.4 ± 0.2	60.9 ± 0.3
		80	$216.3 \pm 0.3^{\dagger\ddagger}$	$221.2 \pm 0.7^{\ddagger}$	$234.6 \pm 0.7^{*\ddagger}$	79.5 ± 0.1	81.4 ± 1.0	81.8 ± 0.7
RotaFlow	**200**	**40**	$85.8 \pm 0.0^{\dagger}$	87.8 ± 0.0	$90.1 \pm 0.0^{*}$	40.7 ± 0.1	39.5 ± 0.2	40.8 ± 0.1
		60	108.2 ± 0.0	107.5 ± 0.0	$110.4 \pm 0.1^{*}$	61.2 ± 0.1	61.2 ± 0.0	60.7 ± 0.4
		80	$125.9 \pm 0.0^{\dagger}$	126.8 ± 0.0	127.7 ± 0.1	80.4 ± 0.0	81.2 ± 0.1	80.1 ± 0.3
	400	**40**	$125.0 \pm 0.0^{\dagger}$	133.0 ± 0.0	$137.1 \pm 0.1^{*}$	41.3 ± 0.0	39.9 ± 0.2	41.6 ± 0.1
		60	$146.1 \pm 0.0^{\dagger}$	150.5 ± 0.0	$156.7 \pm 0.0^{*}$	60.5 ± 0.1	60.1 ± 0.1	62.0 ± 0.0
		80	$161.9 \pm 0.0^{\dagger}$	169.5 ± 0.0	$178.0 \pm 0.1^{*}$	80.3 ± 0.0	80.1 ± 0.1	80.6 ± 0.2
	600	**40**	$179.3 \pm 0.0^{\dagger}$	187.2 ± 0.0	$199.5 \pm 0.0^{*}$	40.5 ± 0.1	40.4 ± 0.1	40.9 ± 0.2
		60	$199.4 \pm 0.0^{\dagger}$	206.9 ± 0.0	$218.1 \pm 0.1^{*}$	60.2 ± 0.1	59.3 ± 0.0	60.3 ± 0.2
		80	$219.8 \pm 0.0^{\dagger}$	226.2 ± 0.0	$238.2 \pm 0.1^{*}$	81.3 ± 0.1	79.7 ± 0.0	80.4 ± 0.4

$^{*}P < 0.0001$ Hemocor HPH Junior versus Others.
$^{\dagger}P < 0.0001$ Hemocor HPH 400 versus Mini.
$^{\ddagger}P < 0.0001$ HL20-Roller pump versus RotaFlow Centrifugal pump.

$$\text{THE loss oxygenator } (\%) = [(\text{preoxygenator THE} - \text{postoxygenator THE})/\text{preoxygenator THE}] \times 100 \quad (8)$$

$$\text{THE loss arterial tubing } (\%) = [(\text{postoxygenator THE} - \text{prearterial cannula THE})/\text{preoxygenator THE}] \times 100 \quad (9)$$

$$\text{THE loss cannula } (\%) = [(\text{prearterial cannula THE} - \text{postarterial cannula THE})/\text{preoxygenator THE}] \times 100 \quad (10)$$

$$\text{THE loss circuit } (\%) = [(\text{preoxygenator THE} - \text{postarterial cannula THE})/\text{preoxygenator THE}] \times 100 \quad (11)$$

Statistical analysis

An analysis of variance (ANOVA) model to compare pumps (Roller, RotaFlow), flow rates (200, 400, 600 mL/min), pressure (40, 60, 80 mm Hg), and hemoconcentrators (400, Mini, JR) with respect to the outcome of diverted flow. General linear models with correlated errors were fit to the continuous hemodynamic outcomes measured at multiple locations within the circuit (e.g., MP, THE, THE loss, pressure drop) to compare pumps, flow rates, pressures, hemoconcentrators, and locations (i.e., preoxygenator, postcannula, etc.) within the circuit (13). The general linear model with correlated errors is an extension of linear regression that accounts for the within-subject variability inherent in repeated measures designs. In this study, the repeated factor is the location in the circuit. For each outcome, P values were adjusted for multiple comparisons testing using the Tukey procedure. All hypotheses tests were two-sided and all analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Mean pressures

The postcannula mean pressure (MP) in the ECMO circuit was manually maintained constant at 40, 60, or 80 mm Hg as the pseudo-patient's pressure. The circuit pressure (preoxygenator MP) varied with experimental condition. The preoxygenator MP increased with increasing flow rates and increasing pseudo-patient pressures with all three hemoconcentrators and with both the roller and centrifugal pump (Table 2).

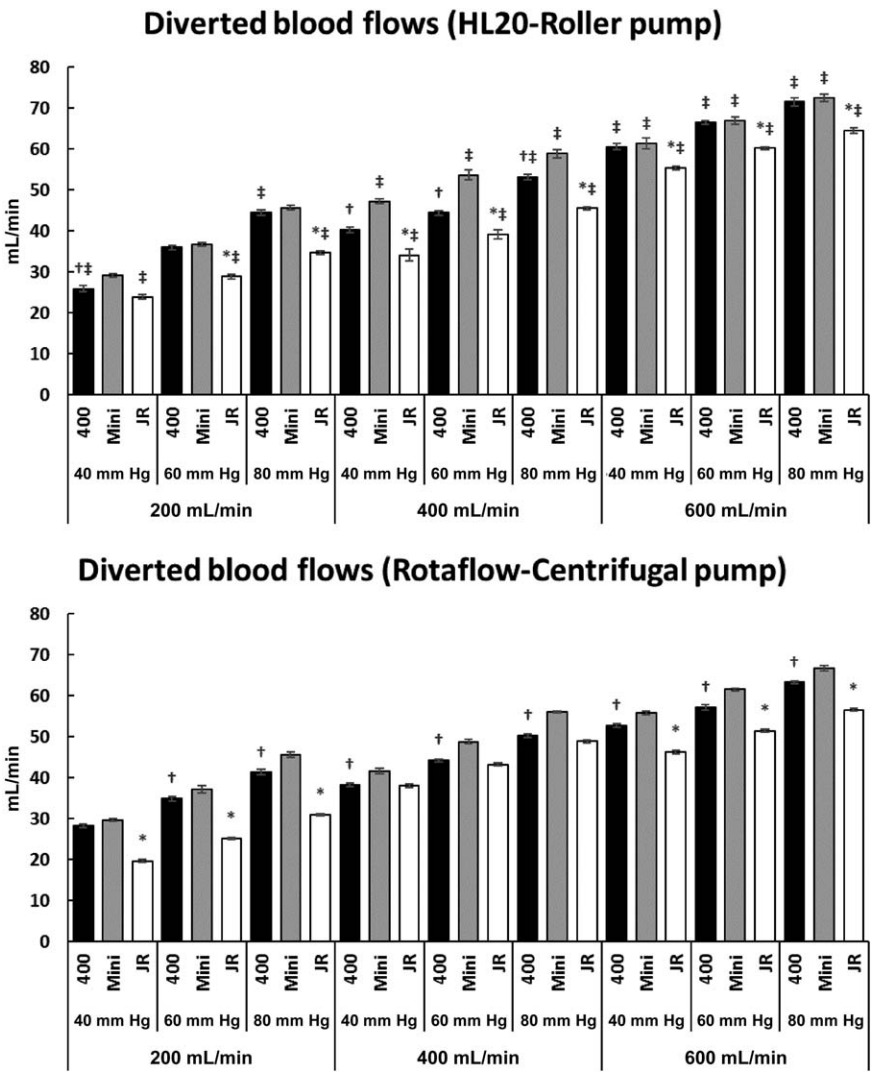

FIG. 2. Diverted blood flow from the recirculation line with different hemoconcentrators. *$P < 0.0001$ Hemocor HPH Junior versus Others. †$P < 0.0001$ Hemocor HPH 400 versus Mini. ‡$P < 0.0001$ HL20-Roller pump versus RotaFlow Centrifugal pump.

For the roller pump at 200 mL/min flow rate, the preoxygenator MP was similar for Hemocor HPH 400 and Junior, and highest with Mini. For all other flow rates with the roller pump and the centrifugal pump, the preoxygenator MP was the lowest with Hemocor HPH 400, higher with Mini, and highest with Junior (Table 2).

Diverted blood flow

The rate of blood flow diverted away from the patient through the hemofilter (mL/min) was calculated for each experimental condition. Diverted blood flow across the hemofilter was similar for both the roller and centrifugal pump (Fig. 2). The diverted blood flow increased with increasing pseudo-patient's pressure and increasing flow rate for each hemoconcentrator. With both pumps the diverted blood flow was the lowest with the Hemocor HPH Junior, and highest with the Mini (Fig. 2).

Pressure drop

Pressure drops were calculated across the oxygenator, arterial tubing, and arterial cannula, and the entire circuit (Fig. 3). In all conditions, the greatest pressure drop was across the arterial cannula. The pressure drops were similar for the roller and centrifugal pump. The pressure drop across the circuit increased with increasing flow rate. The pressure drop was not dependent on the pseudo-patient's pressure. The pressure drop across the circuit in all flow rates except 200 mL/min was the lowest with the Hemocor HPH 400, higher with the Mini, and highest with the Junior for both the roller and centrifugal pump (Fig. 3).

Total hemodynamic energy

THE levels were calculated using Eq. 7 for each experimental condition. THE levels for the roller pump were slightly higher than the THE levels for

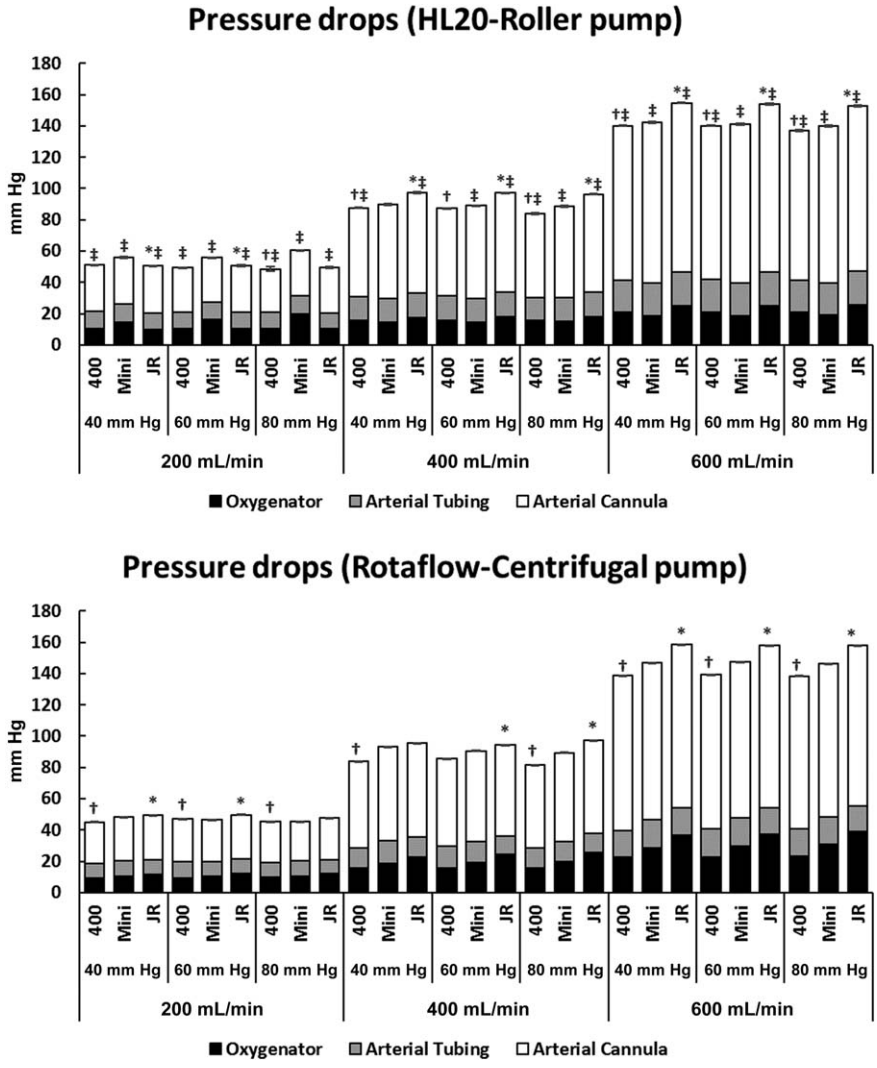

FIG. 3. Pressure drop across the components of ECLS circuit. *$P < 0.0001$ Hemocor HPH Junior versus Others. †$P < 0.0001$ Hemocor HPH 400 versus Mini. ‡$P < 0.0005$ HL20-Roller pump versus RotaFlow Centrifugal pump.

the centrifugal pump (Fig. 4). The preoxygenator THE increased with increasing pseudo-patient pressure and flow rate. The postarterial cannula THE increased with increasing pseudo-patient pressure and was similar across all flow rates (Fig. 4). With both pumps for all flow rates except 200 mL/min the preoxygenator THE was lower with Hemocor HPH 400, higher with Mini, and highest with Junior. The postarterial cannula THE was similar for all three hemoconcentrators with both pumps, and all pressures and flow rates (Fig. 4).

Percentage of THE loss across circuit components was calculated. The THE loss decreased with increasing pressure across all components and experimental conditions (Table 3). With the centrifugal pump, the percentage of THE lost across the oxygenator was highest with the Hemocor HPH Junior, lower with Mini, and lowest with 400. With the roller pump the percentage of THE lost across the oxygenator was similar for all hemoconcentrators (Table 3). The percentage of THE lost across the arterial tubing was lower with the centrifugal pump than the roller pump and was similar for each hemoconcentrator (Table 3).

The highest THE loss was across the cannula for all experimental conditions. The percentage of THE lost across the arterial cannula was similar with the roller pump and centrifugal pump and for each hemoconcentrator. The percentage of THE lost across the cannula varied the greatest with pressure increase (widest range from 33.4% at 80 mm Hg to 45.1% for 40 mm Hg) (Table 3). The percentage of THE lost across the entire circuit was similar with both pumps and similar across all three hemoconcentrators (Table 3).

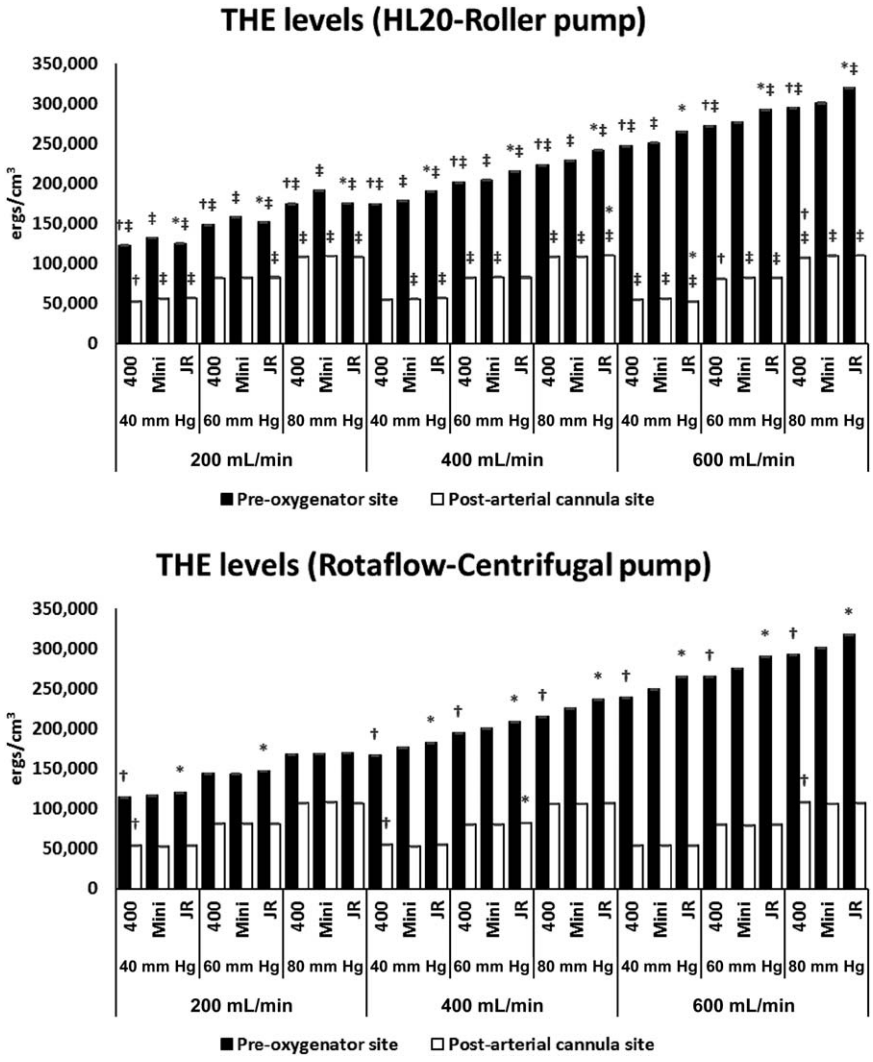

FIG. 4. THE levels at preoxygenator and postarterial cannula sites. *$P < 0.0001$ Hemocor HPH Junior versus Others. †$P < 0.0001$ Hemocor HPH 400 versus Mini. ‡$P < 0.0001$ HL20-Roller pump versus RotaFlow Centrifugal pump.

DISCUSSION

This study compared three in-line hemoconcentrators with two ECMO circuits including a roller pump or a centrifugal pump in terms of MP, diverted blood flow, pressure drop, and THE.

Mean circuit pressure was dependent on pseudo-patient's pressure and flow rate (Table 2). The circuit pressure was similar with both the roller pump and centrifugal pump. For both pumps at 400 and 600 mL/min flow rates, the Hemocor HPH Junior had the highest circuit pressures, and Hemocor HPH 400 had the lowest circuit pressures at all pseudo-patient pressures, suggesting the Hemocor HPH Junior has the highest resistance, and the Hemocor HPH 400 has the lowest resistance (Table 2). The Hemocor HPH Junior and Hemocor HPH 400 hemoconcentrators have the same internal fiber diameter (200 microns), but the Junior has a much smaller membrane surface area (0.09 M^2, compared to 0.3 M^2 for the 400) suggesting a smaller number of fibers, accounting for the higher resistance (Table 1).

The amount of blood flow diverted through the hemoconcentrator was dependent on pseudo-patient's pressure and flow rate (Fig. 2). Both the roller pump and centrifugal pump performed similarly in terms of diverted blood flow. For both pumps at 200, 400, and 600 mL/min flow rates and all pseudo-patient's pressures, the Hemocor HPH Junior had the lowest diverted flow. The diverted flow through the Hemocor HPH Mini was slightly higher than the Hemocor HPH 400, but the values were very similar and likely not clinically significant (average difference 3 mm Hg) (may be statistically significant) (Fig. 2). This lower diverted flow with the Hemocor HPH Junior is likely due to the

TABLE 3. *Percentages of the loss across the components of ECLS circuit*

Pump	Flow rate (mL/min)	Pseudo-patient's pressure (mm Hg)	Percentage (%) of THE loss across oxygenator with different hemoconcentrators			Percentage (%) of THE loss across arterial tubing with different hemoconcentrators			Percentage (%) of THE loss across arterial cannula with different hemoconcentrators		
			400	Mini	JR	400	Mini	JR	400	Mini	JR
Roller	**200**	**40**	$11.2 \pm 0.0^{\dagger\ddagger}$	$14.8 \pm 0.1^{\ddagger}$	$10.6 \pm 0.0^{*\ddagger}$	$12.6 \pm 0.1^{\dagger\ddagger}$	$12.1 \pm 0.1^{\ddagger}$	$11.4 \pm 0.1^{*\ddagger}$	$32.7 \pm 0.0^{\dagger\ddagger}$	$30.5 \pm 0.1^{\ddagger}$	$32.7 \pm 0.2^{\ddagger}$
		60	$9.4 \pm 0.0^{\dagger\ddagger}$	$13.8 \pm 0.1^{\ddagger}$	$9.2 \pm 0.0^{*\ddagger}$	$10.0 \pm 0.0^{\dagger\ddagger}$	$9.7 \pm 0.0^{\ddagger}$	$9.5 \pm 0.0^{*\ddagger}$	$25.6 \pm 0.0^{\dagger}$	$24.2 \pm 0.0^{\ddagger}$	$26.6 \pm 0.2^{*\ddagger}$
		80	$7.9 \pm 0.2^{\dagger}$	$13.8 \pm 0.1^{\ddagger}$	$8.0 \pm 0.0^{\ddagger}$	$8.7 \pm 0.1^{\ddagger}$	$8.8 \pm 0.0^{\ddagger}$	$8.1 \pm 0.1^{*\ddagger}$	$21.2 \pm 0.0^{\dagger\ddagger}$	20.3 ± 0.0	$22.2 \pm 0.1^{*\ddagger}$
	400	**40**	$12.2 \pm 0.0^{\dagger\ddagger}$	$10.9 \pm 0.0^{\ddagger}$	$12.4 \pm 0.1^{*\ddagger}$	$12.6 \pm 0.0^{\dagger\ddagger}$	$12.3 \pm 0.1^{\ddagger}$	$11.9 \pm 0.0^{*\ddagger}$	$43.8 \pm 0.0^{\dagger\ddagger}$	$45.6 \pm 0.2^{\ddagger}$	$45.8 \pm 0.1^{\ddagger}$
		60	$10.4 \pm 0.0^{\dagger\ddagger}$	$9.7 \pm 0.0^{\ddagger}$	$11.3 \pm 0.0^{*\ddagger}$	$11.2 \pm 0.0^{\dagger\ddagger}$	$10.6 \pm 0.0^{\ddagger}$	$10.4 \pm 0.0^{*\ddagger}$	$37.4 \pm 0.0^{\dagger\ddagger}$	$39.1 \pm 0.1^{\ddagger}$	$39.8 \pm 0.2^{*\ddagger}$
		80	$9.4 \pm 0.0^{\dagger\ddagger}$	$8.9 \pm 0.0^{\ddagger}$	$10.3 \pm 0.0^{*\ddagger}$	$9.6 \pm 0.0^{\ddagger}$	$9.6 \pm 0.0^{\ddagger}$	$9.3 \pm 0.0^{*\ddagger}$	$32.4 \pm 0.0^{\dagger\ddagger}$	$34.3 \pm 0.1^{\ddagger}$	$34.8 \pm 0.1^{*\ddagger}$
	600	**40**	$11.6 \pm 0.0^{\dagger\ddagger}$	$10.1 \pm 0.0^{\ddagger}$	$12.8 \pm 0.0^{*\ddagger}$	$12.2 \pm 0.0^{\dagger\ddagger}$	$12.4 \pm 0.0^{\ddagger}$	$12.1 \pm 0.0^{\ddagger}$	$53.7 \pm 0.0^{\dagger\ddagger}$	$55.2 \pm 0.1^{\ddagger}$	$55.0 \pm 0.1^{\ddagger}$
		60	$10.5 \pm 0.0^{\dagger\ddagger}$	$9.3 \pm 0.0^{\ddagger}$	$11.8 \pm 0.0^{*\ddagger}$	$11.4 \pm 0.0^{\dagger\ddagger}$	$11.2 \pm 0.0^{\ddagger}$	$10.9 \pm 0.0^{*\ddagger}$	$48.4 \pm 0.1^{\dagger\ddagger}$	$49.5 \pm 0.0^{\ddagger}$	$49.2 \pm 0.1^{\ddagger}$
		80	$9.8 \pm 0.0^{\dagger\ddagger}$	$8.7 \pm 0.0^{\ddagger}$	$11.0 \pm 0.0^{*\ddagger}$	$10.1 \pm 0.0^{\ddagger}$	$10.2 \pm 0.1^{\ddagger}$	$10.0 \pm 0.0^{*\ddagger}$	$43.7 \pm 0.0^{\dagger\ddagger}$	$44.7 \pm 0.3^{\ddagger}$	$44.5 \pm 0.1^{\ddagger}$
RotaFlow	**200**	**40**	$10.9 \pm 0.0^{\dagger}$	11.6 ± 0.0	$12.8 \pm 0.0^{*}$	$10.7 \pm 0.0^{\dagger}$	11.8 ± 0.1	$10.2 \pm 0.0^{*}$	$30.9 \pm 0.0^{\dagger}$	31.6 ± 0.1	31.6 ± 0.0
		60	$8.6 \pm 0.0^{\dagger}$	9.5 ± 0.0	$11.2 \pm 0.1^{*}$	$9.4 \pm 0.0^{\dagger}$	8.9 ± 0.0	$8.3 \pm 0.0^{*}$	$25.5 \pm 0.0^{\dagger}$	24.7 ± 0.0	25.6 ± 0.2
		80	$7.8 \pm 0.0^{\dagger}$	8.3 ± 0.0	$9.7 \pm 0.1^{*}$	7.6 ± 0.0	7.5 ± 0.0	$6.9 \pm 0.0^{*}$	$20.8 \pm 0.0^{\dagger}$	20.2 ± 0.0	20.7 ± 0.1
	400	**40**	$12.4 \pm 0.0^{\dagger}$	14.0 ± 0.0	$16.3 \pm 0.0^{*}$	$10.2 \pm 0.0^{\dagger}$	10.9 ± 0.1	$9.5 \pm 0.0^{*}$	$44.4 \pm 0.0^{\dagger}$	45.1 ± 0.1	$43.8 \pm 0.1^{*}$
		60	$10.8 \pm 0.0^{\dagger}$	12.5 ± 0.0	$15.5 \pm 0.0^{*}$	$9.5 \pm 0.0^{\dagger}$	9.2 ± 0.0	$7.5 \pm 0.0^{*}$	38.3 ± 0.0	38.3 ± 0.0	$37.5 \pm 0.0^{*}$
		80	$9.8 \pm 0.0^{\dagger}$	11.6 ± 0.0	$14.4 \pm 0.1^{*}$	7.8 ± 0.0	7.8 ± 0.0	$6.9 \pm 0.1^{*}$	$32.8 \pm 0.0^{\dagger}$	33.4 ± 0.0	33.5 ± 0.1
	600	**40**	$12.5 \pm 0.0^{\dagger}$	15.1 ± 0.0	$18.4 \pm 0.0^{*}$	$9.5 \pm 0.0^{\dagger}$	9.9 ± 0.0	$8.7 \pm 0.0^{*}$	$55.3 \pm 0.0^{\dagger}$	53.4 ± 0.0	$52.4 \pm 0.1^{*}$
		60	$11.4 \pm 0.0^{\dagger}$	14.4 ± 0.0	$17.1 \pm 0.0^{*}$	$9.1 \pm 0.0^{\dagger}$	8.6 ± 0.0	$7.8 \pm 0.0^{*}$	$49.3 \pm 0.0^{\dagger}$	48.4 ± 0.0	$47.4 \pm 0.1^{*}$
		80	$10.6 \pm 0.0^{\dagger}$	13.5 ± 0.0	$16.3 \pm 0.0^{*}$	$7.9 \pm 0.0^{\dagger}$	7.7 ± 0.0	$6.9 \pm 0.0^{*}$	$44.4 \pm 0.0^{\dagger}$	43.5 ± 0.0	$43.0 \pm 0.1^{*}$

$^{*}P < 0.0001$ Hemocor HPH Junior versus Others.
$^{\dagger}P < 0.0001$ Hemocor HPH 400 versus Mini.
$^{\ddagger}P < 0.0001$ HL20-Roller pump versus RotaFlow Centrifugal pump.

higher resistance which decreases the flow through the hemofilter.

The pressure drop across the circuit did not depend on pseudo-patient's pressure, but it did depend on the flow rate (Fig. 3). Both pumps had similar pressure drops across the oxygenator, tubing, cannula, and circuit. For both pumps at 400 and 600 mL/min the pressure drop across the circuit was the lowest for the Hemocor HPH 400 and highest for the Hemocor HPH Junior (Fig. 3). This is the same pattern as the circuit pressure, suggesting the higher pressure drop across the circuit with the Hemocor HPH Junior is due to the increased resistance and higher circuit pressure.

The preoxygenator THE is similar for the roller pump and the centrifugal pump. The preoxygenator THE (THE generated in the circuit) was dependent on pseudo-patient's pressure and flow rate. The postarterial cannula THE was dependent on the pseudo-patient's pressure but not the flow rate, consistent with the fact that loss of THE across the circuit components was not dependent on flow rate (Fig. 4). For both pumps at 400 and 600 mL/min the THE generated was the lowest with the Hemocor HPH 400 and highest for the Hemocor HPH Junior consistent with the higher circuit pressure with the Junior due to higher resistance. For both pumps at all flow rates and pseudo-patient's pressures, the postarterial cannula THE was similar for all three hemoconcentrators (Fig. 4). This suggests that while the different hemoconcentrators may have an impact on the circuit pressure, diverted blood flow and pressure drop, there is no significant (statistically/clinically?) impact on the hemodynamic energy delivered to the patient.

Percentage of THE lost across the circuit components was dependent on pseudo-patient's pressure but not the flow rate (Table 3). For the roller pump at 400 and 600 mL/min with all pseudo-patient's pressures the THE loss across the oxygenator was similar for all three hemoconcentrators (may be statistically significant difference) (Table 3). For the centrifugal pump at all flow rates with all pseudo-patient's pressures, the THE loss across the oxygenator was the highest with the Hemocor HPH Junior and lowest with the Hemocor HPH 400, consistent with the data suggesting the Junior adds the most and the Hemocor HPH 400 adds the least resistance.

The use of a hemoconcentrator is very important in a neonatal ECMO circuit as 19–71% of neonatal ECMO patients require hemofiltration due to AKI or fluid overload which are associated with organ dysfunction and increased mortality (14). The Hemocor HPH 400 hemoconcentrator is used at Penn State Children's Hospital in-line in the NICU circuit which uses the HL-20 roller pump. Our data suggest that this hemoconcentrator in-line provides a lower circuit pressure, lower pressure drop, and moderate diverted blood flow compared to the other two hemoconcentrators (Hemocor HPH Mini and Junior). While these differences exist, there was no difference between the amount of hemodynamic energy delivered to the patient between the three hemoconcentrators due to the constant postarterial cannula pressure that was manually maintained.

Our data also suggests no differences in the performance of the NICU circuit and the PICU circuit with the roller and centrifugal pumps, respectively. While the PICU at Penn State Children's Hospital does not use an in-line hemoconcentrator in the circuit, our data demonstrate similar hemodynamic outcomes to the NICU circuit.

Limitations

While the experimental circuits are identical to clinical conditions, the in vitro pseudo-patient lacks the compliance of an in vivo patient. Because of the lack of compliance the hemodynamic performance may be different with an in vivo patient. Future animal and in vivo studies can be used to further assess the hemodynamic function of these hemoconcentrators in these circuits. Another limitation of this study includes the fact that the HL20 Roller pump shows some intrinsic pulsatility when set at a continuous flow setting, whereas the nonocclusive Rotaflow centrifugal pump allows truly nonpulsatile flow. This may influence the THE comparison between the two pumps as THE is calculated from EEP, a measure that is influenced by pulsatility. The data for the 200 mL/min flow rate was inconsistent for measures of mean circuit pressure, pressure drop, and preoxygenator THE. It is possible that this flow rate is too low to provide adequate circuit pressure. More studies should be done at this rate to assess the hemodynamic energy.

Additional experiments without a hemoconcentrator were performed but not included in the tables and figures in order to simplify the results for the readers of the *Journal*. Preoxygenator pressures were up to 5 mm Hg lower in both circuits at all experimental conditions, while diverted flow rates were approximately 15 mL/min higher without a hemoconcentrator.

CONCLUSIONS

This study compared three different hemoconcentrators (Hemocor HPH 400, Mini, and Junior) with two different neonatal ECMO circuits: The ECMO circuit used in the NICU at Penn State Children's Hospital using a roller pump, and the circuit used in the PICU at Penn State Children's Hospital using a centrifugal pump. The hemoconcentrators in these circuits were examined at three pseudo-patient pressures (40, 60, 80 mm Hg), and flow rates (200, 400, 600 mL/min) for hemodynamic parameters. Our results suggested that the roller and centrifugal pump performed similarly in terms of MP, diverted blood flow, pressure drop, and THE. Hemocor HPH Junior hemoconcentrator added the most resistance to the circuits, and Hemocor HPH 400 added the least resistance. Although this difference in resistance exists in the circuit, the THE delivered to the patient as determined by the postcannula THE calculation, showed no differences between the hemoconcentrators. This consistent THE delivery is due to the constant pseudo-patient pressure that was manually maintained at 40, 60, or 80 mm Hg. Future in vivo studies can further define the function of these three hemoconcentrators in terms of ultrafiltration ability while maintaining THE delivery to the patient.

Conflict of Interest: The authors have declared no conflicts of interest for this article.

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