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MAIN TEXT

Improving adult pulsatile minimal invasive extracorporeal circulation in a mock circulation

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Abstract

Background: Pulsatile extracorporeal circulation (ECC) may improve perfusion of critical organs during cardiac surgery. This study analyzed the influence of the components of a minimal invasive ECC (MiECC) on the transfer of pulsatile energy into the pseudo-patient of a mock circulation.

Methods: An aortic model with human-like geometry and compliance was perfused by a diagonal pump. Surplus hemodynamic energy (SHE) was determined from flow and pressure data. Five adult-size oxygenator models and three sizes of cannulas were compared. Pulsatile pump settings were optimized, and parallel dual-pump configurations were evaluated.

Results: Oxygenator models showed up to twofold differences in pressure gradients and influenced SHE at flow rates up to 2.0 L min^{-1}. Adjustments of frequency, systole duration, and rotational speed gain significantly improved SHE compared with empirical settings, with SHE above 21% of mean arterial pressure at flow rates of 1.0 L min^{-1} to 1.5 L min^{-1} and SHE above 5% at 3.5 L min^{-1}. Small diameter cannula (15 Fr) limited SHE compared with larger cannula (21 Fr and 23 Fr). Two diagonal pumps did not provide higher SHE than a single pump, but permitted additional control over pulse pressure and SHE by varying the total fraction of pulsatile flow and the fraction of flow bypassing the oxygenator.

Conclusions: Proper selection of components and optimizations of pump settings significantly improved pulse pressure and SHE of pulsatile MiECC. Surplus hemodynamic energy depended on flow rate with a maximum at 1.0 L min^{-1}–1.5 L min^{-1}. Pulsatile MiECC may specifically assist organ perfusion during phases of low flow.

KEYWORDS

cannula, diagonal pump, minimal invasive extracorporeal circulation, oxygenator, pulsatile perfusion, surplus hemodynamic energy

Anke Dürr and Elena Weber contributed equally.

1 | INTRODUCTION

Extracorporeal circulation (ECC) maintains blood flow and gas exchange during cardiac arrest in cardiothoracic surgery. Pulsatile flow is known to affect the body at the subcellular level,[1] the cellular level,[2] and the organ level.[3] However, it is still a matter of debate whether pulsatile flow during ECC benefits the patients, especially in terms of postoperative renal function,[4] pulmonary function,[5] and cognitive function.[6,7] Randomized controlled trials found a reduction of mortality by pulsatile ECC[8] and a reduction of postoperative blood losses.[9] To date, there are no large randomized controlled trials comparing pulsatile and continuous flow in MiECC.

Although it is tempting to use the readily available pulse pressure as a measure of pulsatility, the concept of energy equivalent pressure (EEP)[10,11] provides a more rational approach. Surplus hemodynamic energy (SHE) is the difference between EEP and mean arterial pressure (MAP) and describes the energy gained by pulsation compared with an equivalent continuous flow. Differences in SHE may explain the diverse results about the benefits of pulsatile flow. We have previously demonstrated the importance of low-compliance minimal invasive ECC (MiECC) tubing for the transfer of pulsatile energy into the patient in a mock circulation.[12] The purpose of the present study was to assess the importance of the remaining downstream components of a pulsatile MiECC system and to look into alternative drive configurations that may improve SHE generation.

2 | MATERIALS AND METHODS

2.1 | Mock circulation

The layout of the mock circulation is documented in Figure 1. All components were connected with 9.5 mm (3/8 inch) polyvinyl chloride (PVC) tubing with a wall thickness of 2.4 mm (3/32 inch), except for the roller pump which used 12.7 mm (1/2 inch)/2.4 mm (3/32 inch) PVC tubing. An absolute pressure probe (Wagner, Offenbach/Main, Germany) monitored the aortic pressure with an accuracy of 0.25%. Differences between

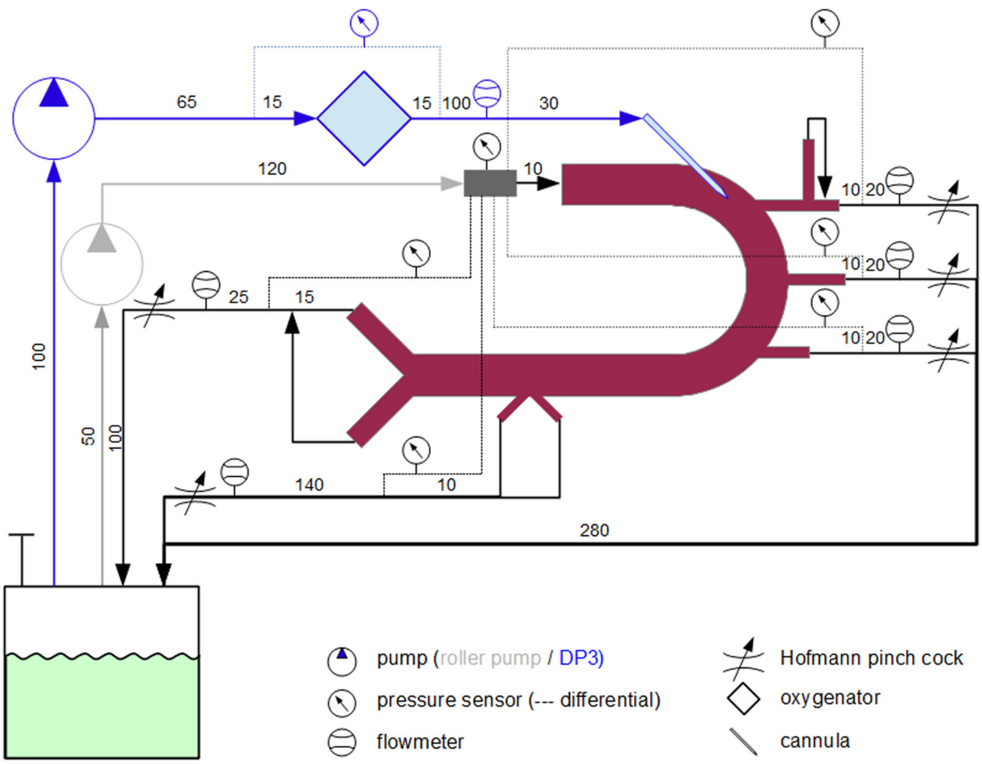

FIGURE 1 Schematic diagram of the mock circulation. The aortic model (red) had a human-like geometry and contained all relevant side branches (in flow direction: brachiocephalic, left common carotid, left subclavian, paired renal, and paired femoral arteries). The roller pump and associated light gray tubing were used to initialize peripheral flow resistances only. The extracorporeal circulation, consisting of a DP3 pump, an oxygenator, and a cannula, is shown in blue. Arrows represent tubing and flow direction. Dotted lines depict the static connections of differential pressure probes with the source and with a manifold which also housed an absolute pressure probe to monitor the aortic pressure. Numbers indicate approximate tubing segment lengths in centimeters (not drawn to scale).

aortic and peripheral pressure, and pressure drop across oxygenators, were measured with differential pressure probes (EL-PRESS, Bronkhorst, Ruurlo, Netherlands; 0.5% accuracy). Ultrasonic flowmeters (Flowmax 400i, MIB, Ihringen-Wasenweiler, Germany; 1.0% accuracy) were used to monitor medium flow. Analog data signals were acquired with an NI-DAQ data acquisition system (National Instruments, Munich, Germany) and recorded with a custom LabVIEW (National Instruments)-based software at a rate of approximately 25 data points per second. Silicone aortic models were prepared as described previously.[13] Aortic model 2 (aorta 2) was based on the same geometry as the existing[13] model (aorta 1). It supported interchangeable cannulas and was used as pseudo-patient for the comparison of cannula diameters. All other measurements used aorta 1. The specific compliances were 4.90 E-3 mm Hg^{-1} and 4.26 E-3 mm Hg^{-1} for aorta 1 and aorta 2, respectively. Both were within the range of human aortas.[14] The mock circulation was perfused with a 12% aqueous solution of dextran (average molecular weight 40 kDa, Roth, Karlsruhe, Germany) with a viscosity close to that of human blood. A roller pump (Multiflow, Stöckert Instruments, Munich) was used to initialize the pseudo-patient independently before each experiment as described previously,[13] resulting in data of $n = 6$ slightly different "patients" per series. In brief, peripheral resistances were adjusted iteratively until flow and pressure in the aorta and its branches were close to literature data.

2.2 | Minimized extracorporeal circulation

The default ECC consisted of a DP3 pump controlled by a delta stream console (Medos, Heilbronn, Germany) and an oxygenator. An arterial cannula was used in aorta 2 to determine the influence of cannula sizes, otherwise, aorta 1 was used that possessed a tubing connector with an inner diameter of 9.2 mm (equivalent to approximately 26 Fr) at the cannula position. The components were connected with a commercial PVC tubing set (rheoparin-coated adult support set, Medos). The pulsatile flow was generated by adding the rotational speed gain to the baseline speed within each cycle.[13] Initial settings had been established empirically during routine surgeries: frequency 50 bpm, systolic duration 50%, rotational speed gain 2300 min^{-1}. Surplus hemodynamic energy optimized settings were frequency 40 bpm, systolic duration 35%, rotational speed gain 2500 min^{-1}. Rotational speed was adjusted until the measured flow matched the expected values. The circulation was heated to 37°C by means of a T3 heater-cooler unit (Stöckert, Munich, Germany).

To investigate the interaction of two pulsatile pumps, a second DP3 pump/delta stream console unit was added to the system (Figure 2). The pumps shared the reservoir via a Y connector. Another Y connector reunited the flows of both pumps. To assess the importance of flow resistance to the resulting pulsation, the flow of the second pump was either passed through the oxygenator or bypassed the oxygenator. Synchronous operation of the pumps was achieved manually by means of the pressure and flow displays of the consoles and of the data acquisition system. Flow data indicate the combined flow by both pumps.

2.3 | Oxygenators and cannulas

Oxygenator models that were routinely used by our perfusionists were included in this study. The following models had a built-in arterial filter: Quadrox-i Adult (Maquet, Rastatt, Germany), Hilite AF 7000 (Medos), Affinity Fusion (Medtronic, Meerbusch, Germany), and Inspire 8F M (LivaNova, Munich, Germany). To assess the influence of the arterial filter, the Hilite 7000 LT (Medos) was also included. This model was identical to the Hilite 7000 AF except that it did not contain an arterial filter. To investigate the impact of cannula diameter, arterial cannulas (HLS, Maquet) were compared in sizes of 15 Fr (5.0 mm outer diameter/3.9 mm orifice inner diameter), 21 Fr (7.0 mm/6.0 mm), and 23 Fr (7.7 mm/6.7 mm), covering the lower and upper ends of this model's size range.

2.4 | Data collection and analysis

After changing any parameters, at least 1 min of data was skipped before 10 consecutive pulsatile cycles or an equivalent segment of continuous flow data was selected to extract the values of the hemodynamic variables. Flow and mean arterial pressure (MAP) were evaluated as standard hemodynamic data. Pulse pressure, energy equivalent pressure (EEP), and SHE normalized to the MAP were calculated from the flow and pressure data as described previously.[13]

Data were analyzed with R[15] and its nlme package for mixed model analysis. Variables were expressed as mixed models, using parameters such as frequency and systolic duration as fixed factors, and the "patients" as sources of random errors. Effects of several levels of a factor were analyzed with Tukey posttests. Factors and posttests were considered significant if the error probability p was less than 0.05. Plots show individual data points if possible. Otherwise, medians and interquartile

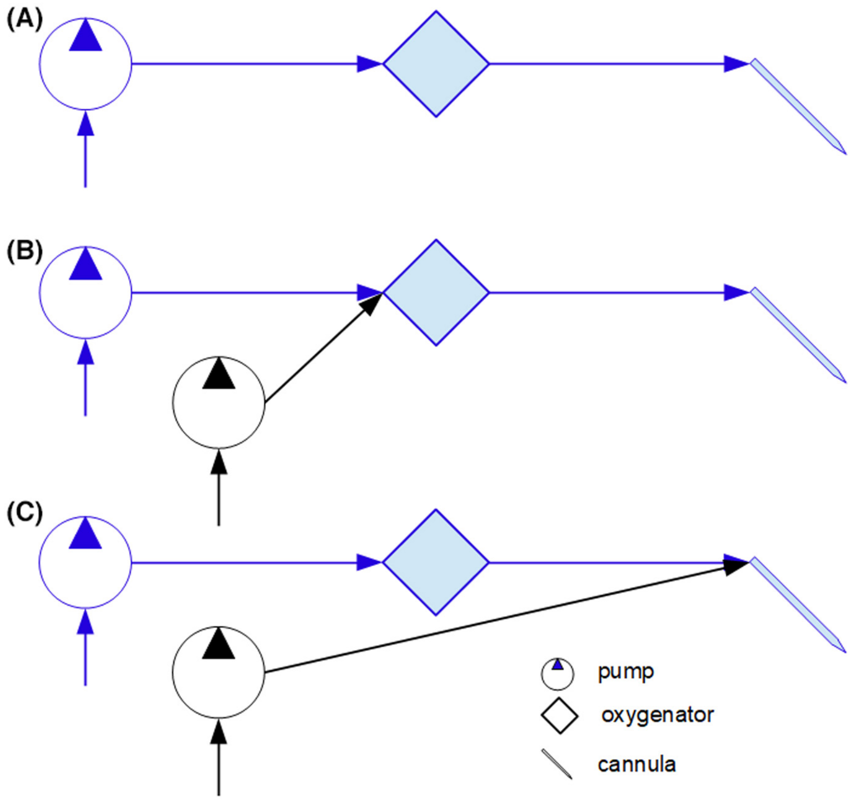

FIGURE 2 Schematic diagrams of alternative extracorporeal circulation setups. (A) Default setup using a single DP3 pump (cf. Figure 1), (B and C) setups using two parallel synchronized DP3 pumps, (B) both pumps fed the oxygenator, and (C) one pump bypassed the oxygenator.

ranges were plotted to reduce clutter. Locally estimated scatterplot smoothing (LOESS) was used to fit curves to scatter plot data.

3 | RESULTS

3.1 | Influence of oxygenators

Both flow and the type of oxygenator influenced the pressure gradients across the oxygenators ($p<0.0001$, Figure 3). The gradient increased with the flow as expected. The almost twofold difference between oxygenators with a low (Quadrox-i, Affinity Fusion) and a high-pressure gradient (Inspire 8F M) required equivalent rises in basal rotational speeds to maintain the target flow (Table 1). At the highest flow of 3.5 L min^{-1}, there was no significant difference in pressure gradients between Affinity Fusion and Quadrox-i ($p = 0.914$) and between Hilite models AF 7000 and 7000 LT ($p = 1$, all other comparisons $p<0.0001$). Flow and oxygenator type also affected MAP ($p<0.0001$). Mean arterial pressure increased with the flow, but there was no obvious dependency on the pressure gradient. At 3.5 L min^{-1}, both Hilite models and Quadrox-i were equivalent ($p>0.76$), as were Inspire 8F M and Affinity Fusion ($p = 0.97$, all other comparisons $p<0.01$). Surplus hemodynamic energy peaked at 1.5 L min^{-1}–2.0 L min^{-1} and depended both on flow and oxygenator type ($p<0.0001$). At a flow rate of 1.5 L min^{-1}, SHE with an Inspire 8F M was significantly higher ($p<0.0002$) than all other models that did not differ from each other ($p>0.32$). Oxygenators had no influence on SHE at flow rates of 2.0 L min^{-1} and higher ($p>0.5$). The Quadrox-i oxygenator was selected for all subsequent experiments.

3.2 | Optimization of single pump settings

Flow rate and pulse frequency affected SHE significantly ($p<0.0001$; Figure 3A–C). Low pulse frequencies improved SHE, most notably at intermediate flow rates of 1–2 L min^{-1}. The highest SHE of 16.0% (15.5%–16.7%) was observed at a flow of 1.5 L min^{-1} and a frequency of 40 bpm. This was significantly higher ($p<0.001$) than the SHE levels at all other flow rates. At the highest flow of 3.5 L min^{-1}, SHE ranged from 5.5% (5.3% to 5.7%) at 40 bpm to 1.7% (1.7% to 1.7%) at 90 bpm ($p<0.0001$). The influences of flow rate and systole percentage on SHE were considered significant ($p<0.0001$). At flow rates of

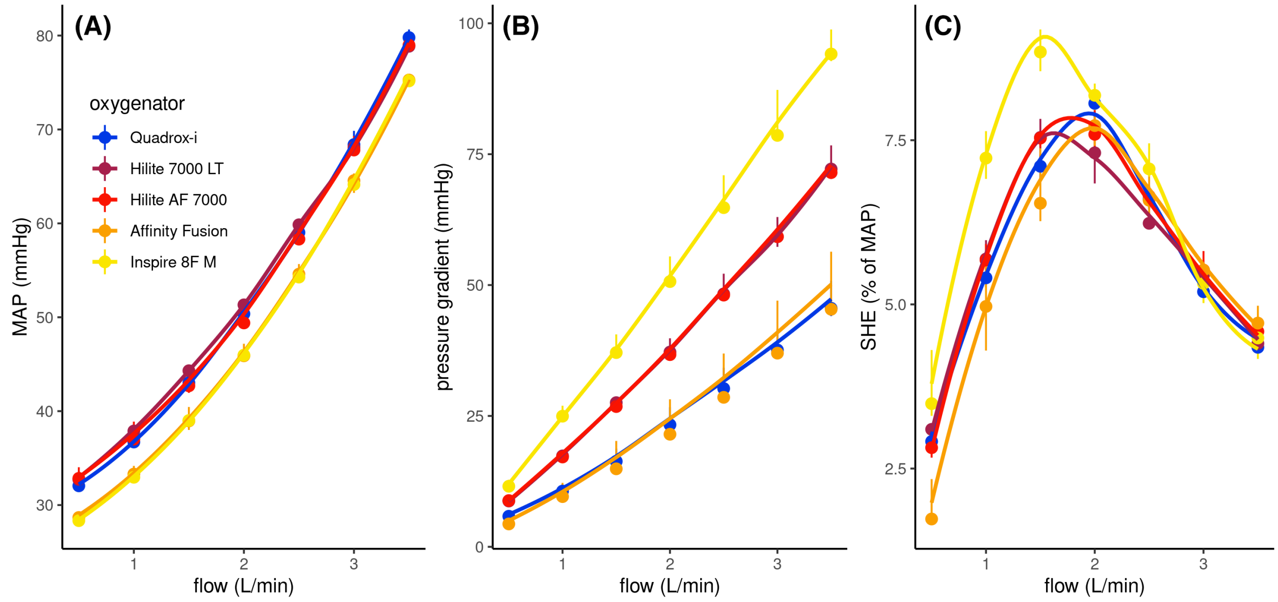

FIGURE 3 Flow dependence of mean arterial pressure (MAP, panel A), the pressure gradient across the oxygenator (B), and surplus hemodynamic energy (SHE, panel C) normalized to MAP during pulsatile flow (frequency 50 min^{-1}, systolic duration 50%, rotational speed gain 2300 min^{-1}) with a single DP3 diagonal pump. Colors indicate the type of oxygenator. n = 6.

TABLE 1 Influence of oxygenator model on basal rotational pump speeds required to provide minimum and maximum flow

	Rotational speed (rpm)	
Oxygenator	**0.5 L min^{-1}**	**3.5 L min^{-1}**
Quadrox-i	1700	6900
Hilite 7000 LT	1800	7200
Hilite AF 7000	1700	7100
Affinity Fusion	1500	6900
Inspire 8F M	2000	7700

up to 1.5 L min^{-1}, a monotonous decrease of SHE with systole duration was observed. At higher flow rates, SHE peaked at 40% systole duration. Surplus hemodynamic energy was highest at a flow of 1.5 L min^{-1} and 30% systole duration ($p<0.001$ vs. all other flow rates) and reached 14.2% (13.9% to 14.7%). At the highest flow rate, SHE at 40% systole duration amounted to 4.0% (4.0% to 4.3%) which was significantly higher than SHE at 30% and 70% ($p<0.001$). Rotational speed gain caused an almost linear increase of SHE at intermediate flow rates. At flow rates of up to 1.0 L min^{-1}, SHE approached a plateau above 1500 rpm. Both flow rate and rotational speed gain had a significant influence on SHE ($p<0.0001$). Maximum SHE of 10.2% (10.1%–10.4%) was observed at a rotational speed gain of 2500 rpm and a flow of 2.0 L min^{-1} although this was not significantly different from SHE at flow rates of 1.5 L min^{-1} (p = 0.82) and 2.5 L min^{-1} (p = 0.08, all other comparisons $p<0.001$). At 3.5 L min^{-1}, a rotational speed gain of 2500 rpm resulted in a SHE of 5.2% (5.1%–5.3%) which exceeded the SHE of all other rotational speed gains at this flow rate ($p<0.0001$).

Optimized pulsatile settings were compared to the previously used empirical settings (Figure 4D,E). Effects of the factors flow and pump settings were considered significant ($p<0.0001$). The surplus hemodynamic energy of the optimized settings peaked at 1.0 L min^{-1} (p = 0.74 vs. 1.5 L min^{-1} and $p<0.001$ vs. all other flow rates) and reached 22.5% (21.3%–23.2%), whereas the empirical settings allowed a maximum SHE of 8.1% (7.7% to 8.1%) at 2.0 L min^{-1} ($p<0.001$ vs. all other flow rates). The corresponding values at the highest flow rate were 5.2% (5.0% to 5.2%) and 3.8% (3.8% to 4.2%), respectively. The surplus hemodynamic energy of optimized settings surpassed that of empirical settings at each flow rate ($p<0.0001$). Flow and pump settings influenced pulse pressure significantly ($p<0.0001$). Pulse pressure peaked at 2.0 L min^{-1} ($p<0.006$) and reached 45.7 mm Hg (44.8 mm Hg to 46.2 mm Hg), whereas there was a plateau starting at 2.5 L min^{-1} ($p<0.0001$ vs. lower and p = 1.0 vs. higher flow speeds) with a maximum of 31.5 mm Hg (31.5 mm Hg to 31.5 mm Hg) with the empirical settings. The corresponding pulse pressures at the highest flow rate were 39.5 mm Hg (39.3–40.0 mm Hg) and 31.1 mm Hg (30.8–31.5 mm Hg), respectively. Optimized settings resulted in a significantly higher pulse pressure than empirical settings at all flow rates ($p<0.0001$).

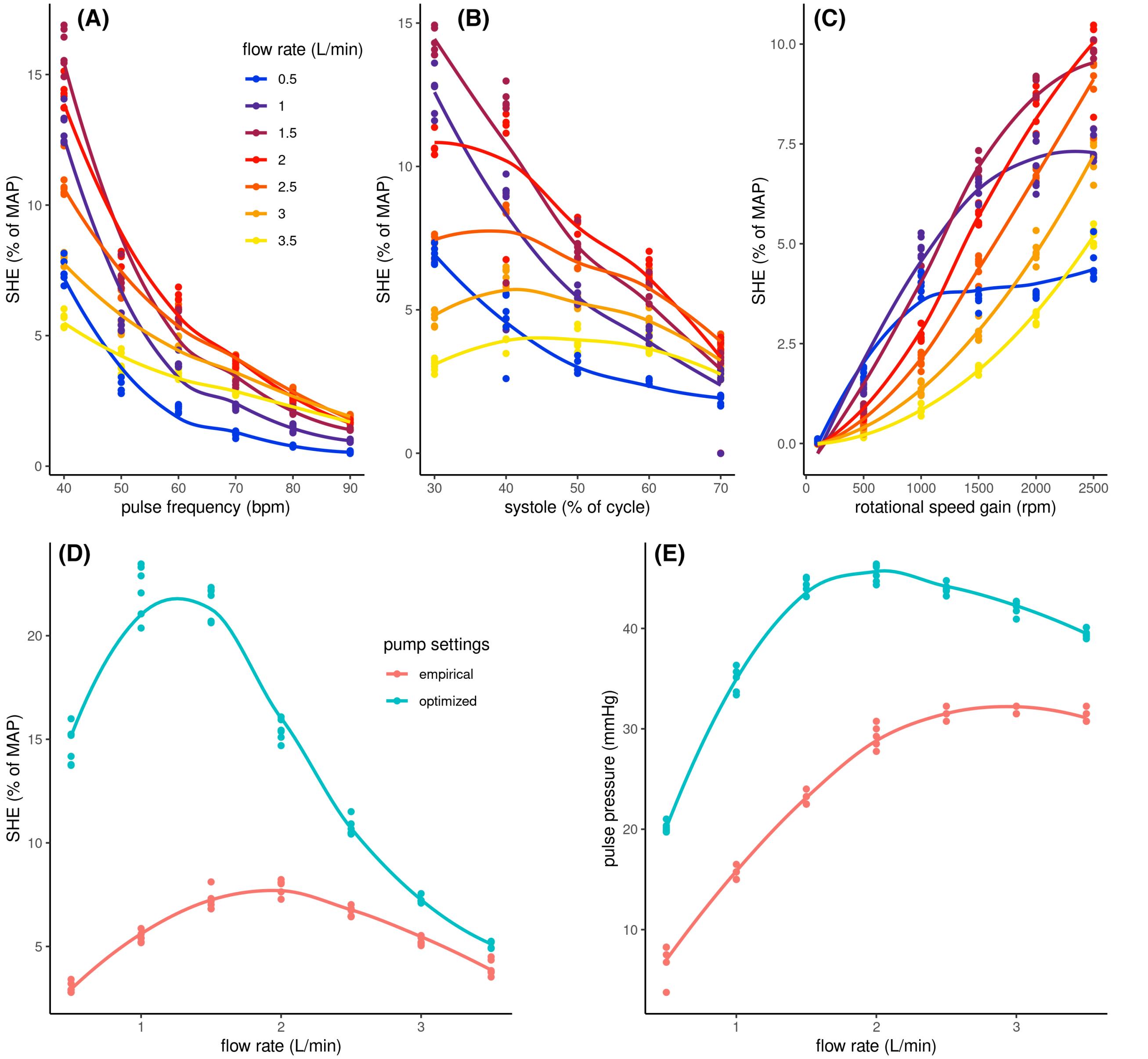

FIGURE 4 (A–C) Influence of DP3 console settings on surplus hemodynamic energy (SHE). Colors indicate the pump flow rate. (A) Influence of pulse frequency; (B) influence of systolic duration; (C) influence of rotational speed gain, that is, increase of rotational speed per cycle to create pulsatile flow; (D) SHE; and (E) pulse amplitude as a function of flow rate using the empirical settings (frequency 50 min^{-1}, systole percentage 50%, rotational speed gain 2300 min^{-1}; red lines) and the optimized settings (40 min^{-1}, 35%, 2500 min^{-1}; blue lines). $n = 6$.

3.3 | Influence of cannula diameter

The diameter of the tested cannulas significantly affected MAP and SHE ($p < 0.0001$, Figure 5). At flow rates above 1.0 L min^{-1}, MAP and SHE were significantly lower with the 15 Fr cannula ($p < 0.001$) compared with the other sizes that did not differ from each other ($p > 0.09$ and $p > 0.16$, respectively).

3.4 | Dual pump configurations: Both pumps feed the oxygenator

The outflow of both pumps was routed through the oxygenator (Figures 2B and 6A–C). The maximum flow had to be limited to 3.0 L min^{-1} in some of the pump configurations as no stable flow at 3.5 L min^{-1} could be achieved.

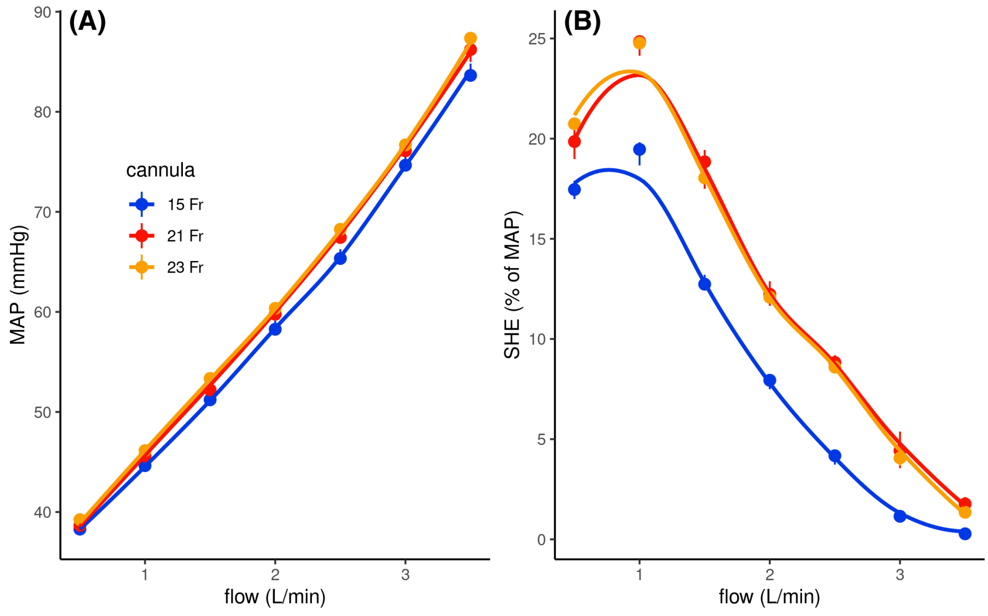

FIGURE 5 Flow dependence of mean arterial pressure (MAP, panel A) and surplus hemodynamic energy (SHE, panel B) normalized to MAP during pulsatile flow (frequency 40 min^{-1}, systolic duration 35%, rotational speed gain 2500 min^{-1}) with a single DP3 diagonal pump. Colors indicate the gauge of the cannula. $n = 6$.

3.4.1 | Mean arterial pressure and pulse pressure

Flow and pump configuration significantly affected MAP ($p<0.0001$) within ranges at each flow rate of 0.6 mm Hg or less. Pulse pressure was significantly affected by pump configurations ($p<0.0001$) and did not exceed 21 mm Hg if only one of the pumps operated in pulsatile mode. It increased monotonously to a maximum of 20.1 mm Hg (19.9 mm Hg to 20.7 mm Hg) at 3.0 L min^{-1} with 25% pulsatile flow. Curves reached a maximum of 20.7 mm Hg (20.6 mm Hg to 20.9 mm Hg) at 2.0 L min^{-1} and of 18.4 mm Hg (18.2 mm Hg to 18.5 mm Hg) at 1.5 L min^{-1} with 50% and 75% pulsatile flow, respectively. Pulse pressure was considerably higher when both pumps operated in pulsatile mode ($p<0.0001$ for all comparisons against pulsatile/continuous modes at flow rates of 1.0 L min^{-1} and higher). The highest pulse pressures were recorded when both pumps contributed equal shares of pulsatile flow ($p<0.0001$ vs. 75%/25% at flow rates of 1.5 L min^{-1} and higher). The maximum at 1.5 L min^{-1} amounted to 40.2 mm Hg (39.3 mm Hg to 40.6 mm Hg). Pulse pressure at 3.5 L min^{-1} was determined as 20.4 mm Hg (20.3 mm Hg to 20.5 mm Hg).

3.4.2 | Surplus hemodynamic energy

Surplus hemodynamic energy depended on flow and the pump configuration ($p<0.0001$), and 75% pulsatile/25% continuous flow achieved a SHE of 10.7% (10.5% to 10.9%) at 0.5 L min^{-1} but was close to the other pulsatile/continuous configurations at higher flow rates. There were peaks of 3.4% (3.2% to 3.5%) and of 1.7% (1.6% to 1.9%) SHE at 1.5 L min^{-1} using 50% and 25% pulsatile flow, respectively. Pulsatile flow from two pumps created significantly higher SHE ($p<0.0001$ for all comparisons against pulsatile/continuous configurations at all flow rates). Except for the peak at 1.0 L min^{-1} with SHE of 19.8% (19.3% to 20.4%) and 19.0% (18.7% to 19.6%) for the 50%/50% and 75%/25% pulsatile/pulsatile configurations, respectively, those modes were not significantly different from each other ($p<0.001$ for all comparisons at the remaining flow rates). The 50%/50% pulsatile/pulsatile configuration provided the highest SHE at 3.5 L min^{-1} which was 1.1% (1.0% to 1.1%).

3.5 | Dual pump configurations: One pump bypassing the oxygenator

One of the pumps bypassed the oxygenator to test whether this arrangement reduces SHE losses (Figures 5C and 6D–F).

3.5.1 | Mean arterial pressure and pulse pressure

Flow and pump configuration affected MAP significantly ($p<0.0001$). Although the curves appeared to be superimposable, there were significant differences at each flow rate up to 3.0 L min^{-1} ($p\leq 0.007$). The ranges

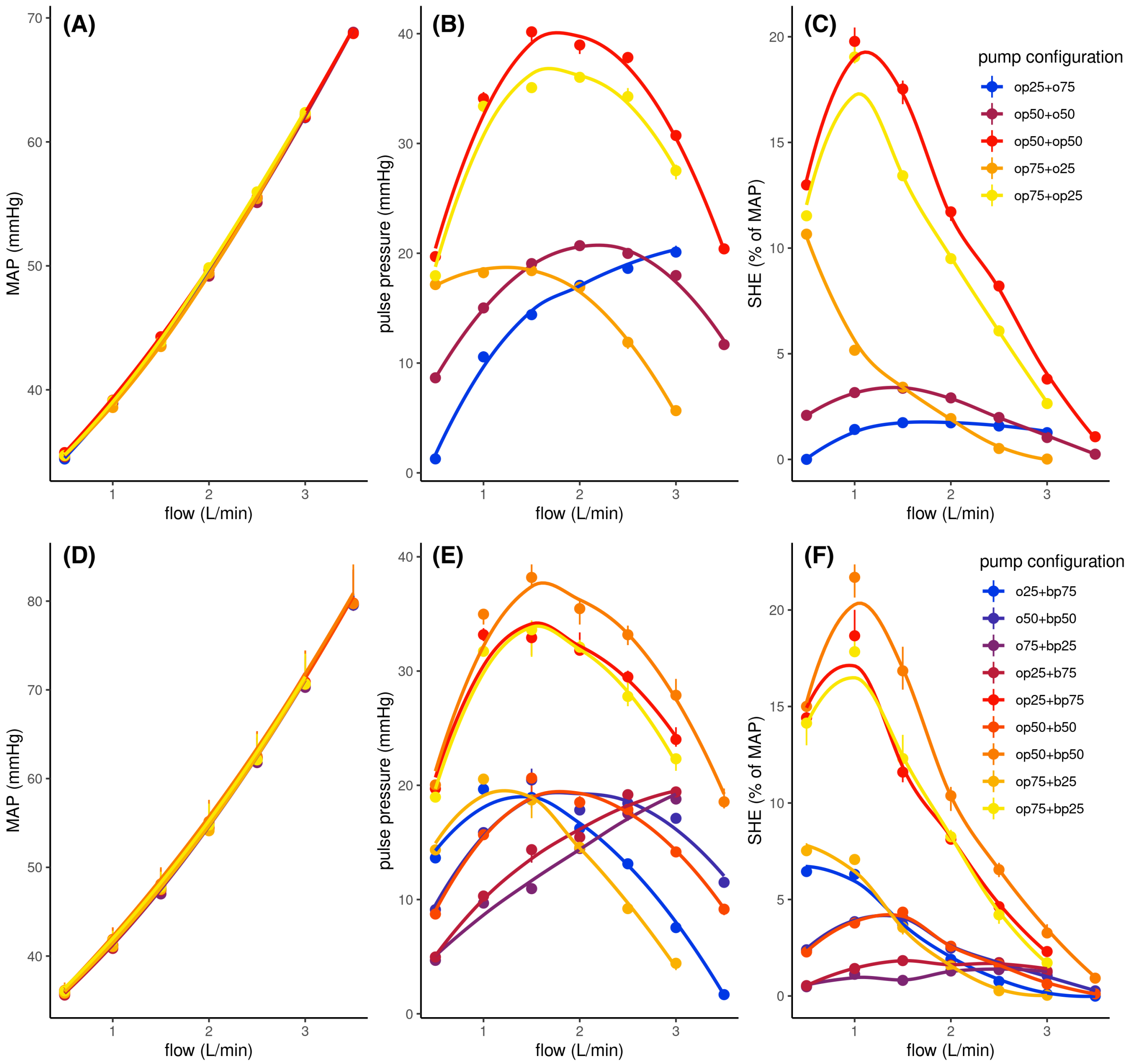

FIGURE 6 Dependency of mean arterial pressure (MAP), pulse pressure, and surplus hemodynamic energy (SHE) on flow rate in dual-pump configurations. (A–C) Both pumps with various combinations of pulsatile and nonpulsatile flow feed the oxygenator, (D–F) one pump feeds the oxygenator, and the other bypasses it. Colors indicate the pump configuration. The contribution of each pump is indicated as a percentage of total flow (25%/50%/75%) in the condition labels. "p" indicates the pulsatile operation of a pump. "o" and "b" indicate that the flow is routed through the oxygenator or that it bypasses the oxygenator, respectively. $n = 6$.

at each flow rate did not exceed 1.2 mm Hg. Pulse pressure was significantly affected by flow and pump configurations ($p < 0.0001$). The highest pulse pressure was obtained with a 50% pulsatile flow through the oxygenator/50% continuous flow through the bypass configuration and amounted to 20.6 mm Hg (18.4 mm Hg to 20.8 mm Hg). The two configurations with 25% pulsatile flow (through oxygenator or bypass)/75% continuous flow showed a monotonous increase up to the highest flow rate of 3.0 L min^{-1}, whereas all other pulsatile/continuous configurations peaked at flow rates 1.5 L min^{-1} or lower. Pulsatile/pulsatile configurations peaked at 1.5 L min^{-1} and showed significantly higher pulse pressures than all pulsatile/nonpulsatile configurations ($p < 0.001$). The two configurations with 25% and 75% pulsatile flow through oxygenator or bypass provided similar pulse pressures but differed significantly at flow rates of 1.0 and 2.5 L min^{-1} and higher ($p < 0.001$). Equal shares of pulsatile flow going through the oxygenator and bypass provided the highest pulse pressures with a peak of 38.2 mm Hg (37.4–39.3 mm Hg) at 1.5 L min^{-1}. This configuration provided significantly higher pulse pressures than all other configurations at flow rates of 1.0 L min^{-1} and higher ($p < 0.001$). Pulse pressure at 3.5 L min^{-1} amounted to 18.6 mm Hg (18.0–19.7 mm Hg).

3.5.2 | Surplus hemodynamic energy

Flow and pump configuration affected SHE significantly ($p < 0.0001$). Pump configurations using a pulsatile/continuous configuration provided generally lower SHE than pulsatile/pulsatile configurations. The highest SHE values of 7.5% (7.3% to 7.9%) were measured with 75% pulsatile flow through the oxygenator at a flow of 0.5 L min^{-1}. The highest SHE of pulsatile/continuous pump configurations at 3.0 L min^{-1} was generated with 25% pulsatile flow through the oxygenator and amounted to 1.3% (1.2% to 1.3%). With a few exceptions, equivalent configurations with opposing positions of pulsatile flow, that is, 75% continuous (oxygenator)/25% pulsatile (bypass) versus 75% pulsatile (oxygenator)/25% continuous (bypass), 50% continuous (oxygenator)/50% pulsatile (bypass) versus 50% pulsatile (oxygenator)/50% continuous (bypass), and 25% continuous (oxygenator)/75% pulsatile (bypass) versus 25% pulsatile (oxygenator)/75% continuous (bypass), differed significantly at all flow rates but no preference of either position was apparent. Pulsatile/pulsatile configurations provided significantly higher SHE than pulsatile/continuous configurations ($p < 0.001$). Configurations using 75% pulsatile flow in either position provided similar SHE within a range of 0.8 percent points at 1.0, 2.5, and 3.0 L min^{-1} ($p < 0.033$). The highest SHE ($p < 0.001$ vs. all other pump configurations at flow rates of 1.0 L min^{-1} and higher) was measured with each pump contributing equal shares of pulsatile flow. Maximum SHE was 21.7% (20.6% to 22.4%) at 1.0 L min^{-1}. Surplus hemodynamic energy at 3.5 L min^{-1} amounted to 0.9% (0.9% to 1.1%).

4 | DISCUSSION

The present study used a mock circulation to investigate the transfer of pulsatile energy into the pseudo-patient. While there were noticeable effects of oxygenator type and cannula diameter, the console settings of the diagonal pump offered the largest potential to improve pulse pressure and SHE. Dual pump configurations provided additional options to tweak the flow dependencies of these hemodynamic parameters, although there was no benefit at the highest flow rates.

The approach of the present study to improve pulsatile energy transfer into the patient addressed both the generation of pulsatile energy and the choice of MiECC components downstream of the pump. The importance of reducing the flow resistance by oxygenators, tubing, and cannula has been investigated for pediatric cardiac surgery.[16] Although this study used small-diameter tubing to minimize ECC volume, the authors reported the oxygenator to be the main resistance after the lines in the presence of a 12 Fr cannula, whereas smaller cannulas provided a larger resistance. This resembles the findings of the present study. The smallest cannula diameter of 15 Fr caused a noticeable flow resistance which caused significantly lower MAP and SHE values than larger cannulas. However, there was no difference between 21 Fr and 23 Fr, suggesting that cannula resistance did not limit SHE at cannula dimensions of 21 Fr and above.

Oxygenators differed almost twofold in terms of the pressure gradient as a measure of their flow resistance. Quadrox-i and Affinity Fusion provided the lowest flow resistance, whereas Inspire 8F M showed exceptionally high resistance. This model required an additional 800 rpm pump rotational speed to achieve the largest tested flow rate compared to the low-resistance models. This limits the utility of this oxygenator to support high flow rates in pulsatile mode, as the pump is limited to a maximum of 10 000 rpm, including the speed gain in pulsatile mode. Interestingly, the high-resistance Inspire 8F M provided the highest SHE at intermediate flow rates, whereas the somewhat lower maximum of the low-resistance models was observed at a higher flow rate. The two Hilite models showed comparable results although only the AF type had a built-in arterial filter. This suggests that the arterial filter was not critical for the overall pressure drop and postoxygenator SHE. As there were no significant differences in SHE at the highest flow rate, which was considered most representative for adult cardiac surgery, we selected the Quadrox-i for its good balance of low-pressure drop and high SHE.

The DP3 console settings were investigated systematically to move from the empirical settings toward SHE-optimized settings. Optimizations were straightforward for the reduction of the pulse frequency and the increase of the rotational speed gain, as in both cases, the relationships with SHE were monotonous. The dependency of SHE on systole percentage turned out to be more complex. At low flow rates of up to 1.5 L min^{-1}, the lowest selectable systole duration of 30% resulted in the highest SHE. Higher flow rates resulted in a SHE maximum at 40% or, in the case of the highest flow rate, a plateau between 40% and 60%. The systole duration of 35% was chosen for the optimized settings as a compromise that resulted in SHE values close to the optimum at all flow rates. A direct comparison of empirical and optimized settings showed the superiority of the latter for SHE (up to a fivefold increase) and pulse amplitude (up to a 2.5-fold increase). Unfortunately, these optimizations did not change the bell-shaped relationship between flow rate and SHE which resulted in only small but significant improvements at a flow of 3.5 L min^{-1}, resulting in a SHE of just above 5% of the MAP.

The dual-pump configurations were an attempt to improve SHE, especially at the higher flow rates which are common in adult cardiac surgery. All these attempts shared the common idea to use each pump at lower rotational speeds compared with the single-pump configuration, as these speeds coincided with a higher SHE. Several configurations were tested. (A) The maximum SHE was observed around a flow of 1.0–1.5 L min^{-1}. We were interested in SHE if this pulsatile flow was supplemented with a continuous flow by a second pump. (B) The oxygenators significantly affected SHE and pulse pressure. We figured that it might be favorable to route only a part of the total flow through the oxygenator and send the remainder directly to the cannula. (C) We wondered if two synchronized pumps added their SHE regardless of their respective contribution to the total flow.

Configurations that superimpose pulsatile flow on a continuous flow have been studied before. One study modified a centrifugal pump with a membrane that was pressurized pneumatically to generate pulsatile flow.[17] Although this pump showed good in vivo results,[18] pulse pressure was limited to approximately 20 mm Hg, and the SHE was supraphysiologic at all flow rates. Dual-pump configurations with just one of the pumps in pulsatile mode are limited by theoretical considerations. Adding a continuous flow to a pulsatile flow will increase the denominator of the EEP formula[10] without adding much to the numerator. However, the magnitude of other effects, such as a reduced efficiency of the nonocclusive diagonal pumps in a dual-pump setup, had to be determined experimentally. With both pumps feeding the oxygenator, using 75% pulsatile and 25% continuous flow provided a SHE above 10% at the lowest flow rate. At flow rates of 1.5 L min^{-1} and above, lower percentages of pulsatile flow were more effective, although SHE never exceeded 3.5%. These values reached up to 4.1% if 50% or 75% of the pulsatile flow bypassed the oxygenator. Substantially, higher SHE values were possible only with two pumps operating in pulsatile mode. Preliminary experiments (not shown) demonstrated that pump synchronization was essential to see any benefit of two pulsatile pumps. Two nonocclusive pumps pulsating in turn apparently caused a “ping-pong” style fluid shift between the pumps rather than toward the aorta. Synchronized pumps were able to generate up to 19.8% SHE with all flow through the oxygenator and 21.7% SHE with one pump bypassing the oxygenator. Neither exceeded the value obtained with an optimized single-pump setup though. Dual-pump configurations provided the highest SHE if each pump delivered 50% of the flow.

Although dual-pump configurations did not provide a higher SHE than an optimized single-pump setup, they might prove useful for other purposes. For example, Figure 6E demonstrates that by switching pump configurations, the pulse pressure can be kept close to 15 mm Hg regardless of the flow rate.

The significance of the present study was limited by a variety of factors. We focused on the influence of internal diameter on the hemodynamic effects of an ECC cannula, using arterial cannulas as a simpler substitute. This intentional simplification was necessary as aortic cannulas are manufactured with a variety of mechanisms to protect the aorta by redirecting or dispersing the flow. These often advanced tip designs influence hemodynamics of a cannula beyond the effect of its dimension.[19] A systematic comparison was beyond the scope of the present study. The dual-pump configurations may have suffered from limited inflow which could be rectified by using a custom-made reservoir with two separate connectors. We also did not test serial dual-pump configurations which may improve the filling of the pulsatile (downstream) pump as implemented in the CARL system.[20]

The results of the present study suggest that there seems to be an upper limit of SHE generated by centrifugal or diagonal pumps. The nonocclusive pump design limits back pressure but, at the same time, may not allow the generation of copious amounts of SHE at high flow rates. Several manufacturers provide occlusive pulsatile pumps to mimic physiologic blood flow in mock circulations, but the number of pulsatile pumps certified for use in humans is limited. Several studies have attempted to modulate the operation of pulsatile pumps in order to optimize their effect. Wang et al. concluded that the pulsatile control algorithms of the DP3 and i-cor pump consoles need further optimizations to provide safe and effective pulsatile flow without excessive hemolysis.[21] Drochon et al. suggested improving pulsatile flow by modulating the shapes of flow and pressure waveforms.[22] Novel pump designs may also help to overcome the current limitations of pulsatile blood pumps. Teman et al. suggested a rotary pulsatile flow pump as an enhancement of roller pumps for pediatric cardiopulmonary bypass.[23] The VentriFlo pump attempts to mimic the cardiac cycle as closely as possible and demonstrated adequate organ perfusion without hemolysis in animal studies.[24,25] We have recently tested a novel positive displacement pump design focused on exceptionally high SHE generation.[26] Surgeons may be able to select from a range of interesting and diverse concepts for pulsatile extracorporeal perfusion in the near future.

5 | CONCLUSIONS

In order to obtain the best pulsatile energy transfer into the patient, the MiECC circuit should be optimized by selecting a low-resistance oxygenator and by using the largest possible cannula diameter. The console parameters of diagonal pumps are best optimized by determining SHE rather than by judging the pulse pressure. In general, diagonal pumps provide a low SHE at flow rates most common during adult ECC. However, this seemingly unfavorable property may have only a limited negative impact if we consider that organ perfusion is rarely limited during ECC at high flow rates. Pulsatile MiECC may specifically assist organ perfusion during phases of low flow where SHE is higher than that of the human heart.

AUTHOR CONTRIBUTIONS

Markus Hoenicka, Andreas Liebold, and Günter Albrecht designed the study. Anke Dürr, Elena Weber, and Lisa Eisenmann collected, analyzed, and interpreted data. Markus Hoenicka computed the statistical analysis and wrote an initial draft of the manuscript. The manuscript was critically revised and approved by all authors.

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CONFLICT OF INTEREST

The authors declare that there were no conflicts of interest.

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