A novel pulsatile blood pump design for cardiothoracic surgery - proof-of-concept in a mock circulation

Short title: Pulsatile blood pump for cardiac surgery

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Author contributions

Markus Hoenicka, Andreas Liebold and Albert Chong designed the study. Elena Weber collected the data. Markus Hoenicka analyzed the data and calculated statistics. Elena Weber and Markus Hoenicka interpreted the analyzed data. Markus Hoenicka wrote the initial draft of the manuscript. All authors critically revised the manuscript and approved it in its final form.

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Abstract

Background: Pulsatile perfusion during extracorporeal circulation is a promising concept to improve perfusion of critical organs. Clinical benefits are limited by the amount of pulsatile energy provided by standard pumps. The present study investigated the properties of a novel positive displacement blood pump in a mock circulation.

Methods: The pump was attached to an aortic model with a human-like geometry and compliance as a pseudo patient. Hemodynamic data were recorded while the pump settings were adjusted systematically.

Results: Using a regular oxygenator, maximum flow was 2.6 L/min at a pressure of 27 mmHg and a frequency (F) of 90 bpm. Pulse pressure (PP; 28.9 mmHg) and surplus hemodynamic energy (SHE; 26.1% of mean arterial pressure) were highest at F=40 bpm. Flow and pressure profiles appeared sinusoid. Using a low-resistance membrane ventilator to assess the impact of back pressure, maximum flow was 4.0 L/min at a pressure of 58.6 mmHg and F=40 bpm. At F=40 bpm, PP was 58.7 mmHg with an SHE of 33.4%. SHE decreased with increasing flow, heart rate, and systolic percentage but surpassed 10% with reasonable settings.

Conclusions: The present prototype achieved sufficient flow and pressure ranges only in the presence of a low-resistance membrane ventilator. It delivered supraphysiologic levels of pulse pressure and SHE. Further modifications are planned to establish this concept for adult pulsatile perfusion.

Key words: extracorporeal circulation, blood pump, pulsatile perfusion, surplus hemodynamic energy

Abbreviations: CPB, cardiopulmonary bypass; ECC, extracorporeal circulation; F, frequency; MiECC, minimal invasive extracorporeal circulation; PI, pulsatility index; rSHE, surplus hemodynamic energy normalized to mean arterial pressure; SHE, surplus hemodynamic energy; SAP, systolic acceleration percentage; SP, systolic percentage; SV, stroke volume.

Introduction

Cardiopulmonary bypass is a prerequisite of many types of cardiothoracic surgery. Extracorporeal circulation (ECC) provides blood flow and oxygenation during cardiac arrest by means of a heart-lung machine. Conventional roller pumps still drive the majority of ECC although minimal invasive extracorporeal circulation (MiECC) gains popularity[1]. Owing to the closed circulation without a reservoir, non-occlusive diagonal pumps are employed to permit pressure relief and volume compensation.

There has been a long-standing debate about the utility of pulsatile flow during cardiopulmonary bypass. Pulsatile and non-pulsatile flow in ECC have first been compared in an animal model withoug clear evidence of clinical differences[2]. An early non-systematic review suggested benefits of pulsatile perfusion[3], whereas later systematic reviews[4,5] were inconclusive. Meta-analyses pointed out the variability of what was termed "pulsatile" but found a protective effect of pulsatile perfusion on postoperative renal[6,7] and pulmonary[8] function. Current guidelines state that pulsatile flow "should be considered" with a medium level of evidence[9].

After finding no substantial effects of pulsation other than reduced blood losses in a prospective randomized trial with MiECC[10], we hypothesized that the transfer of pulsatile energy into the patient may be inefficient in adult cardiac surgery. In our experiments using a mock circulation and a diagonal pump[11,12], careful selection of components and optimized pump settings boosted surplus hemodynamic energy (SHE)[13,14] as a measure of pulsatile effectiveness only at low flow speeds. Alternative pump designs may help to overcome these limitations. We have previously demonstrated the utility of a novel pump design to optimize physiologic flow profiles for benchtop experiments[15]. The present study investigated the properties of a novel pulsatile blood pump with a positive displacement design in a mock circulation with a focus on SHE generation.

Materials and Methods

Mock circulation

The experiments used a mock circulation with an aortic model made of silicone with human-like geometry and compliance as a pseudo-patient. The model was perfused with a 12% (w/v) aequous solution of Dextran (average molecular weight 40 kDa, Roth, Karlsruhe, Germany) which provided a viscosity comparable to human blood. Pump outflow was routed through an oxygenator which was connected to a port on the arch of the aortic model via 9.5 mm (3/8") PVC tubing. Flow and pressure probes allowed to monitor the oxygenator, the aorta, the aortic arch branches, and the femoral arteries. Technical details of the circulation and of the aortic model have been reported previously[11,16]. Peripheral resistance of the pseudo-patient was adjusted iteratively with Hoffman pinch cocks at all exits of the aortic model until flow and pressure in all monitored vessels were within 5% of the target values[16]. One such combination of pinch cock settings was considered to represent one "patient", equivalent to one biological replicate, which was used to generate a full dataset with one of the extracorporeal circulation setups as explained below. This adjustment of peripheral resistances was repeated independentlyto generate data of n=6 slightly different "patients" per extracorporeal circulation setup. This number of "patients" was considered sufficient based on previous experiences with this model[11,16].

Triphasic Trilab pump

The pump was a prototype manufactured by Triphasic Cardiac Pump Pty Ltd, Nedlands, WA, Australia. The core of the pulsatile pump consisted of a 25.6 mm (1") silicone tubing with a spring-loaded disc check valve (JUPITER model 130, Valbrass, Italy; opening pressure 0.02 bar ≙ 15 mmHg) at the inlet, and a reciprocating presser plate operated by a stepper motor (Fig. 1). The size of the presser plate and the diameter of the silicone tubing determined the maximum volume displacement per cycle. The stepper motor was controlled via a Raspberry Pi single-board computer with an attached 7-inch color touch screen. The software used in this study offered four controls: frequency (F), stroke volume (SV), systolic percentage (SP), and systolic acceleration percentage (SAP). The purposes of these controls are explained in Fig. 1. The SP control affects the duration of the systole (Fig. 1 B), whereas the SAP setting controls how fast the presser plate reaches its endpoint (Fig. 1 C). A lower systolic acceleration percentage translates to a higher rotational speed of the drive shaft. The pump inlet was connected to a custom-made reservoir via a 25.6 mm silicone tubing. The diastolic filling of the pump was driven by the elastic forces that returned the silicone tubing into its uncompressed shape. This was assisted by a hydrostatic pressure of 26 mmHg between the reservoir and the pump inlet. The outlet was connected to the oxygenator via 9.5 mm (3/8") PVC tubing. As explained in the results section, a second check valve of the swing-disc type (Non return PVC-U valve, Van de Lande, Raamsdonksveer, Netherlands; disc and hinge made from rubber without any detectable opening pressure) was retrofitted between pump outlet and oxygenator.

Experimental protocols

Two major setups of the extracorporeal circulation were tested. In the first set of experiments a Quadrox-i oxygenator for adult ECC (Maquet, Rastatt, Germany) was used. The circuit was heated to 37° C by means of a heater-cooler unit (T3, Stöckert, Munich, Germany). In the second set a low-resistance iLA membrane ventilator targeted at lung support (Xenios, Heilbronn, Germany) was used. The circuit operated at room temperature (23° C) owing to the lack of a heat exchanger. In order to characterize the influence of the pump controls on flow, pressure, and SHE, the following matrix of settings were tested sequentially in each "patient" as two-factor experiments:

- vary SV and F with SP=50% and SAP=50%
- vary SV and SP with F=60 bpm and SAP=50%

- vary SV and SAP with F=60 bpm and SP=50%

F was increased in increments of 10 bpm, increments of SP and SAP were 10%. SV was increased from 10% in increments of 20% up to 90% with the iLA membrane ventilator. The latter was limited to 80% with the Quadrox-i oxygenator to avoid excessive pump noises.

Data analysis

Data were recorded by a custom LabVIEW (National Instruments, Munich, Germany)-based software through a NI-DAQ data acquisition system at a rate of approx. 25 readings per second. At least 10 consecutive pump cycles were analyzed of each reading. Owing to the sinusoid pressure profiles, mean arterial pressure (MAP) was calculated as arithmetic mean of the aortic pressure data. Energy equivalent pressure and relative SHE (rSHE, expressed as % of MAP) were computed from aortic flow and pressure data by numeric integration as described previously[16]. The pulsatility index PI was computed as $(V_{max} - V_{min})/V_{mean}$, with V_{max} and V_{min} indicating the highest and lowest measured flow rates, respectively, and V_{mean} indicating the arithmetic mean of the flow velocity within the evaluated time interval. The latter was considered an appropriate measure of the average flow owing to the sinusoid flow pattern.

Data were analyzed by the software R[17]. Values are reported as median (1st quartile to 3rd quartile). Data of two-factor experiments were analyzed with mixed models (nlme package), using the pump settings as fixed factors and the "patients" as source of random errors. Differences between several levels of a factor were analyzed with Tukey post-hoc tests, considering that the data were assumed to be normally distributed with an equal number of "patients" per condition, and that a conservative test was appropriate to minimize false-positive (=significant) results. The influence of factors was considered significant if the error probability p was less than 0.05. For the sake of clarity, statistical differences between settings are presented in detail only for the highest level of SV as this was considered most relevant for adult ECC. These data were compared with the Conover test, assuming significant differences if p was less than 0.05.

Results

Initial pump operation experiences

Pilot experiments indicated a short duration of negative pressures and retrograde flow during diastole at low flow (data not shown). This indicated a partially retrograde filling of the pump tubing which was rectified by retrofitting a check valve between pump outlet and oxygenator. This second check valve was present in all experiments shown below.

Flow and pressure readings at the low flow rates provided by SV=10% displayed huge dispersions of the computed rSHE values owing to next-to-zero pressures and flows during diastole (data not shown). As these excessive rSHE values were of no practical relevance, rSHE was evaluated only at SV settings of 30% and higher.

Operation with a regular oxygenator

The increase of flow and MAP with stroke volume in the presence of the Quadrox-i oxygenator was monotonic, whereas rSHE decreased in the same fashion (Figs. 2 through 4). Pulse pressure increased with stroke volume until it reached a plateau at SV=50% and higher.

Influence of heart rate

Stroke volume and heart rate significantly affected flow, MAP, pulse amplitude, and rSHE ($p<0.0001$ for both factors; Fig. 2).

With SP and SAP constant and SV=80%, flow and MAP increased with the heart rate ($p<0.0001$; supplemental table 1). Maximum flow was 2.59 L/min (2.41 L/min to 2.79 L/min) at F=90 bpm. MAP peaked at 27.0 mmHg (23.9 mmHg to 30.0 mmHg), also at F=90 bpm. Pulse pressure decreased with the heart rate from 28.9 mmHg (24.3 mmHg to 33.9 mmHg) at F=40 bpm to 15.6 mmHg (13.6 mmHg to 17.7 mmHg) at F=90 bpm ($p<0.0001$). rSHE also decreased with the heart rate, dropping from 26.1% (23.5% to 28.1%) at F=40 bpm to 7.0% (6.5% to 7.6%) at F=90 bpm ($p<0.0001$). Hemodynamic data with the highest rSHE are summarized in Table 1.

Influence of systolic percentage

Stroke volume and systolic percentage significantly affected flow, MAP, pulse pressure, and rSHE ($p<0.0001$ for both factors; Fig. 3).

With F and SAP constant and SV=80%, flow and MAP increased with the systolic percentage ($p<0.0001$; supplemental table 1). The highest flow was 2.62 L/min (2.43 L/min to 2.83 L/min), and the highest MAP was 27.3 mmHg (24.0 mmHg to 30.5 mmHg) at SP=80%. Pulse pressure was not affected significantly by SP ($p=0.14$). rSHE decreased from 22.4% (20.3% to 24.5%) to 8.4% (7.9% to 9.2%) with increasing SP ($p<0.0001$). Table 1 presents hemodynamic data with the highest rSHE.

Influence of systolic acceleration percentage

Stroke volume and systolic acceleration percentage significantly affected flow, MAP, pulse pressure, and rSHE ($p<0.0001$ for both factors; Fig. 4).

With F and SP constant and SV=80%, flow and MAP tended to decrease with increasing SAP although this was not considered significant ($p=0.08$ and $p=0.13$, respectively; supplemental table 1). Pulse pressure was not significantly affected by SAP ($p=0.12$). rSHE increased significantly with increasing SAP ($p=0.02$) from 11.6% (10.4% to 13.0%) to 14.9% (13.6% to 15.9%). Hemodynamic data with the highest rSHE are shown in table 1.

Flow and pressure profiles

Both flow and pressure profiles appeared to be sinusoid (Fig. 5 A,B). However, at systole flow tended to build up quick and fall more slowly, whereas the reverse was true for the pressure curve. With parameters set to SV=80%, F=70 bpm, SP=50%, and SAP=50%, maximum flow during systole exceeded 4.3 L/min and dropped below 0.75 L/min during diastole. Aortic pressure ranged between 17.5 mmHg and 41 mmHg.

Operation with a low-resistance oxygenator

The general responses of the system to increasing stroke volume resembled the results shown above for the Quadrox-i oxygenator (Figs. 6 through 8). However, in the presence of the low-resistance iLA membrane ventilator pulse pressure increased with stroke volume until it reached a plateau or a peak at SV=50% (SV=60% for F=40 bpm).

Influence of heart rate

Stroke volume and heart rate significantly affected flow, MAP, pulse amplitude, and rSHE ($p<0.0001$ for both factors; Fig. 6).

With SP and SAP constant and SV=90%, flow and MAP increased with the heart rate ($p<0.0001$; supplemental table 2). Maximum flow reached 4.00 L/min (3.96 L/min to 4.03 L/min) at F=90 bpm which created a mean arterial pressure of 58.6 mmHg (57.9 mmHg to 59.0 mmHg). Pulse pressure was highest at a heart rate of F=40 bpm, reaching 58.7 mmHg (58.5 mmHg to 59.1 mmHg), and dropped to 31.2 mmHg (30.8 mmHg to 31.2 mmHg) at F=90 bpm ($p<0.0001$). rSHE also declined with increasing heart rate, ranging from 33.4% (33.2% to 33.9%) at F=40 bpm to 7.7% (7.7% to 7.9%) at F= 90 bpm ($p<0.0001$). Hemodynamic data with the highest rSHE level are shown in table 2.

Influence of systolic percentage

Stroke volume and systolic percentage significantly affected flow, MAP, pulse pressure, and rSHE ($p<0.0001$ for both factors; Fig. 7).

With constant default settings of F and SAP and SV=90%, flow and MAP increased with the systolic percentage ($p<0.0001$; supplemental table 2). Maximum observed flow was 3.95 L/min (3.92 L/min to 3.98 L/min), which caused a maximum MAP of 58.6 mmHg (58.0 mmHg to 59.2 mmHg) at SP=80%. Pulse pressure decreased significantly with increasing SP (p<0.0001), ranging from 27.7 mmHg (27.6 mmHg to 28.0 mmHg) to 9.5 mmHg (0.2 mmHg to 9.8 mmHg). rSHE decreased from 27.7% (27.6% to 28.0%) to 9.5% (9.2% to 9.8%) with increasing SP (p<0.0001). Hemodynamic data with peak rSHE levels are summarized in table 2.

Influence of systolic acceleration percentage

Stroke volume and systolic acceleration percentage significantly affected flow, MAP, pulse pressure, and rSHE (p≤0.0001 for both factors; Fig. 8).

With F and SP constant and SV=90%, flow and MAP decrease significantly with increasing SAP (p<0.0001; supplemental table 2). The highest flow equaled 3.91 L/min (3.90 L/min to 3.94 L/min) at a MAP of 57.2 mmHg (56.9 mmHg to 57.5 mmHg). Pulse pressure was significantly reduced by increased SAP (p<0.0001) and ranged from 43.0 mmHg (42.8 mmHg to 43.5 mmHg) to 41.6 mmHg (41.4 mmHg to 41.6 mmHg). rSHE increased significantly with increasing SAP (p<0.0001), ranging from 13.4% (13.3% to 13.5%) to 15.4% (15.4% to 15.6%). Table 2 shows hemodynamic data with the highest rSHE levels.

Flow and pressure profiles

The pressure profile was close to sinusoid, although pressure appeared to build up slower than it dropped at systole (Fig. 5 C,D). The flow curve showed an asymmetric systole, with a sinusoid increase followed by a rapid but small decrease of flow after the peak, and a subsequent slower decrease of flow until diastole. With parameters set to SV=90%, F=70 bpm, SP=50%, and SAP=50%, maximum flow during systole exceeded 6.9 L/min and dropped below 0.7 L/min during diastole. Aortic pressure ranged between 43 mmHg and 73 mmHg.

The mode of action of the systolic acceleration percentage setting was investigated in a setup with SV=90%, F=60 bpm, and SP=50% (Fig. 5 E,F). With the presser plate closing slowly (SAP=80%), the flow and pressure profiles appeared fairly sinusoid. With a rapid setting (SAP=20%), there was an apparent gain of flow until systole reached its maximum. This was paralleled with an elevated pressure over the entire cycle, which was most prominent at the start of systole.

Discussion

The present study evaluated the potential of a novel blood pump for pulsatile extracorporeal circulation in an aortic perfusion model. Flow and pressure profiles indicated supraphysiologic amplitudes of both parameters and a dependence on flow resistance in the perfusion model. Pulse amplitude was reasonable, and SHE was higher compared to diagonal pumps and roller pumps, allowing the perfusion with a physiologic pulsatile energy even in adults.

Pulsatile perfusion has been performed with good results in pediatric cardiac surgery, showing benefits for cerebral and renal blood flow in a piglet model[18] as well as better maintenance of fibrinolytic balance in pediatric patients[19]. The results in adult cardiac surgery, which requires up to three times higher flow rates to maintain adequate tissue perfusion, have been mixed. Sunagawa et al.[20] concluded in their review of available trials that the benefits of pulsatile ECC may have been underestimated in the past as a result of the mediocre pulsatile energy provided both by roller pumps and centrifugal pumps. This is in line with the conclusions that we drew from our own pulsatility trial[10]. Considering the bell-shaped flow dependency of SHE[11], currently available centrifugal pumps are indeed more suitable for pulsatile ECC in pediatric patients.

The Triphasic pump provided flow and pressure patterns which did not resemble physiologic waveforms in the presence of a flow resistance typical for adult CPB. Both flow and pressure showed sinusoid patterns. A study conducted in a pig model compared a pulse duplicator creating near-physiologic pulse waveforms with a conventional roller pump operating in pulsatile and non-pulsatile modes[21]. Neither organ perfusion nor inflammatory response showed significant benefits of physiologic pulsatile flow. Recently a novel and advanced pulsatile pump has been introduced and tested in an animal model of pediatric ECC[22], but there are no clinical data available to date. Therefore, a benefit of physiologic flow and pressure patterns still awaits to be proven.

The pump was optimized to provide SHE equaling or exceeding that of the adult human heart which creates approx. 10% of MAP. Mean flow did not exceed 2.5 L/min with a regular oxygenator. A flow of 2.2 to 2.8 L/min per m^2 of body surface area is considered appropriate[9], which amounts to at least 4.4 L/min for an average adult patient. MAP did not exceed 30 mmHg with a regular oxygenator, although the pulse pressure was adjustable in a physiologic range. Current guidelines recommend to maintain a MAP between 50 mmHg and 80 mmHg[9]. However, the pressure generated by the pump is but one factor in the resulting MAP of a patient. The mock circulation was not designed to mimic the application of vasopressors or the effects of volume therapy. In terms of flow and pressure the present implementation of the pump design does not yet satisfy the requirements for adult ECC. According to its design goals, SHE was exceptionally high, exceeding 50% of MAP in some conditions with a regular oxygenator.

We investigated the influence of the oxygenator's flow resistance on pump performance. In the presence of a low-resistance iLA membrane ventilator, flow rates of up to 4 L/min were possible, and the mean pressure approached 60 mmHg. Both values are reasonably close to the requirements of an average adult patient but would clearly not cover all cases. Pulse pressure was strongly dependent on the heart rate. A slow heart rate of 40 bpm allowed the MAP to drop to levels that resulted in pulse pressures approaching 60 mmHg at high flow, whereas heart rates of 60 bpm to 70 bpm resulted in pulse pressures of approx. 40 mmHg. SHE depended strongly on heart rate, being highest at low heart rates, and on the systolic percentage, again being highest at lower systolic fractions. SHE exceeded 10% of MAP in all conditions, leaving room for further optimizations of the remaining parameters. These results indicate that further improvements of the pump need to focus on improving the power to better cope with the flow resistance present in adult CPB.

The effect of the stroke volume setting was straightforward, with higher settings increasing flow and MAP as expected. The geometry of the pump tubing and the presser plate may require adjustments to achieve higher flow rates and pressures. Increased heart rates helped to achieve maximum flow and pressure levels. On the other hand, both pulse pressure and SHE decreased with increasing heart rates. This indicates an incomplete pump filling during diastole at high frequencies. The compliance and rigidity of the pump tubing may benefit from fine-tuning. Alternatively, retrofitting the equivalent of an atrium may improve pump filling as well. Increasing systolic percentage was beneficial for flow and MAP, but decreased pulse pressure and SHE. The parameter systolic acceleration percentage also showed significant effects although the effect sizes were smaller compared to the other parameters. Reducing systolic acceleration percentages, i.e. more rapid presser plate rotation, caused increases in flow, MAP, and pulse pressure, whereas SHE values were lower. Flow and pressure patterns reveal the mechanism of this setting in further detail (Fig. 5 E,F). A low systolic acceleration percentage increased the slope of flow at the start of systole. The maximum flow was higher for a short period of time compared to a high SAP setting. Otherwise the two profiles were superimposable. The slope of the pressure profile was affected far less, but the pressure was slightly elevated throughout the entire cycle and even more so at the start of systole. This seemingly different responses of flow and pressure may arise from the different positions of flow meter and pressure probe. Their mounting positions in compliant and non-compliant parts of the mock circulation, respectively, as well as fluid inertia between their positions may affect the readings in the described manner. As the SHE remained above physiologic values in all conditions, this setting can be used to further boost flow and MAP.

The present study was limited by several shortcomings. The effects of pump parameters was analyzed sequentially, therefore two out of four parameters were at reasonable defaults while the remaining parameters were varied. Systematic testing of all conceivable combinations was not possible within a reasonable timeframe. However, the effects of the parameters can be extrapolated reasonably well. Also, we did not attempt to modify the flow and pressure patterns which would have required modified software with an additional set of controls. With the exception of a few minor modifications like the second check valve, mechanical improvements of the pump were not possible within the present study and will have to be assessed later.

The findings of this study will be used to improve the present implementation of the pump design. Aside from mechanical alterations, e.g. adjustments of the pump tubing diameter and the size of the presser plate, the pump design lends itself well to simple and rapid changes of the pump control system. The software used in this study was designed to test the influences of parameters that resemble the controls of a diagonal pump. Alternative controls, e.g. parameters which influence the flow and pressure patterns, are straightforward to implement and will allow future improvements of the concept.

In summary, the Triphasic pump was able to deliver supraphysiologic levels of SHE in most conditions, although flow and pressure in the presence of a regular oxygenator need to be improved to allow perfusion of adult patients. In general there is a trade-off between achieving high flow rates and high MAP and generating high SHE. Irrespective of this limitation, rSHE reached a maximum of 26.1% of MAP in the presence of a regular oxygenator, and 33.4% with a low-resistance membrane oxygenator, at the highest flow rate setting and suitable settings of SP and SAP.

Conflicts of Interest

Albert Chong is CEO of Triphasic Cardiac Pump Pty Ltd, has applied for two patents related to pulsatile blood pumps, and has made a prototype of the Triphasic Trilab pump with a customized graphical interface available for the purposes of this study. The study was investigator-initiated and was not paid for nor influenced by the pump manufacturer. The authors declare that they have no other conflicts of interest.

Data availability

The data of the present study have been published in an open access repository[23].

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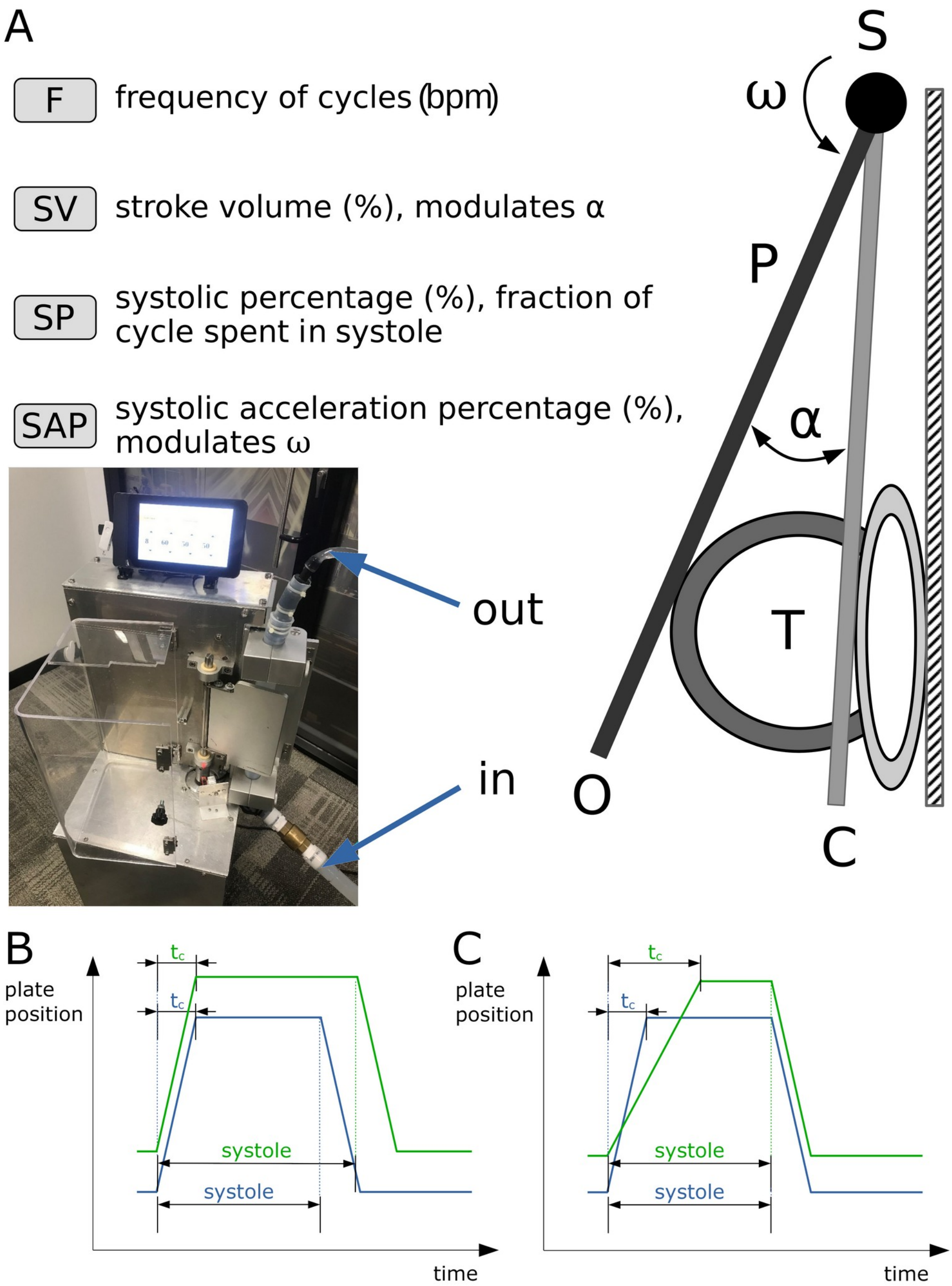
Figures

Fig. 1:



Functional principle and controls of the Triphasic pump. (A) Pump tubing (T), presser plate (P), and drive shaft (S) seen from above in the open (O, dark grey) and closed (C, light gray) positions; α, angle of presser plate movement; ω, rotational speed. Insert: overview image of the pump. (B) Effect of the SP control explained as a schematic waveform of the presser plate position. Increasing the SP setting from the lower blue line to the upper green line extends the fraction of the cycle spent in systole without affecting the time t_c required to reach the presser plate endpoint. The curves are offset along the y axis arbitrarily to reduce clutter. (C) Effect of the SAP control. Increasing the SAP setting from the lower blue line to the upper green line extends the fraction of the systole spent in reaching the endpoint by decreasing the speed of the closing presser plate without affecting the duration of the systole.

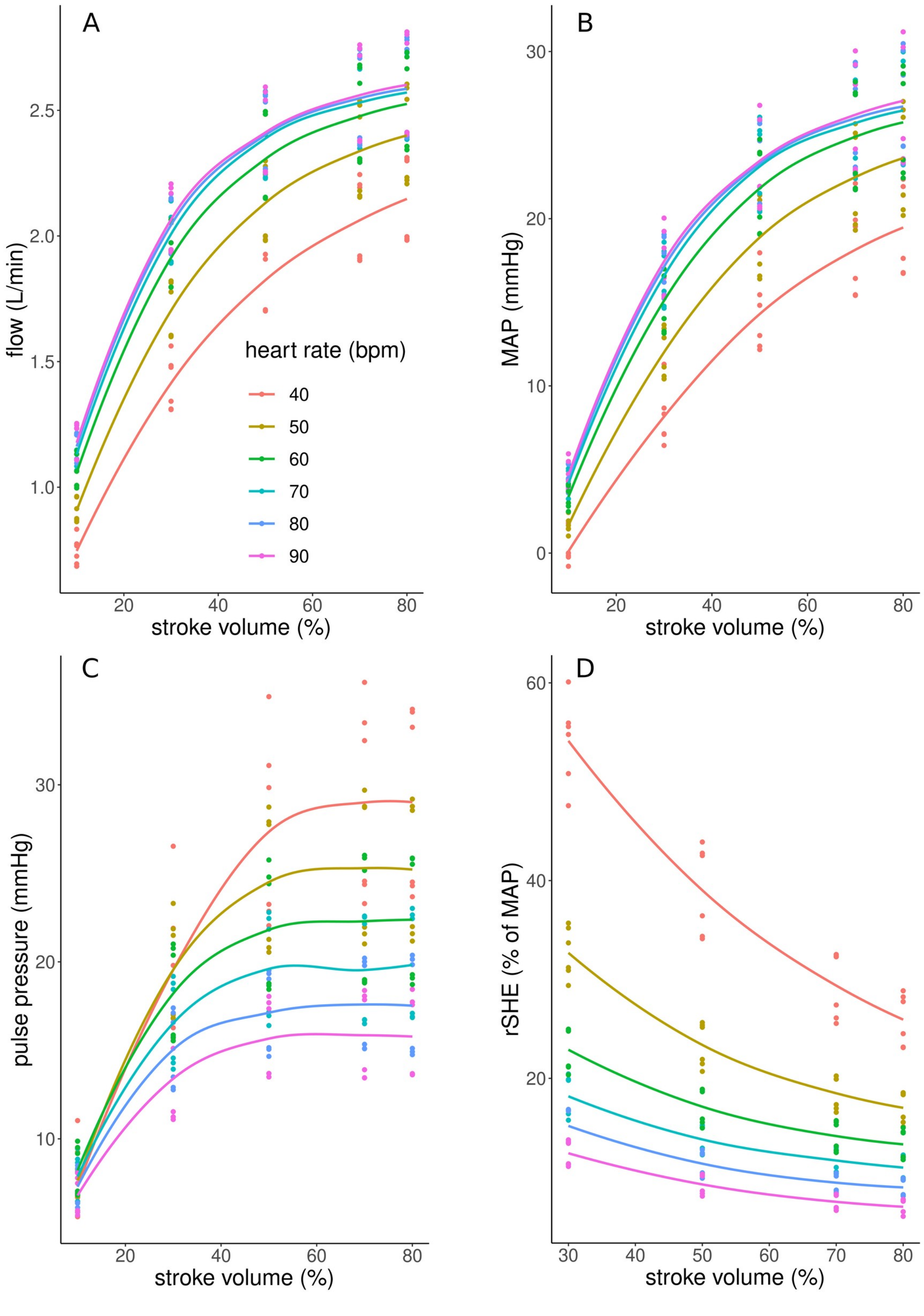


Fig. 2: Triphasic pump with Quadrox-i oxygenator. Effect of stroke volume and heart rate with systolic percentage=50% and systolic acceleration percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure. n=6.

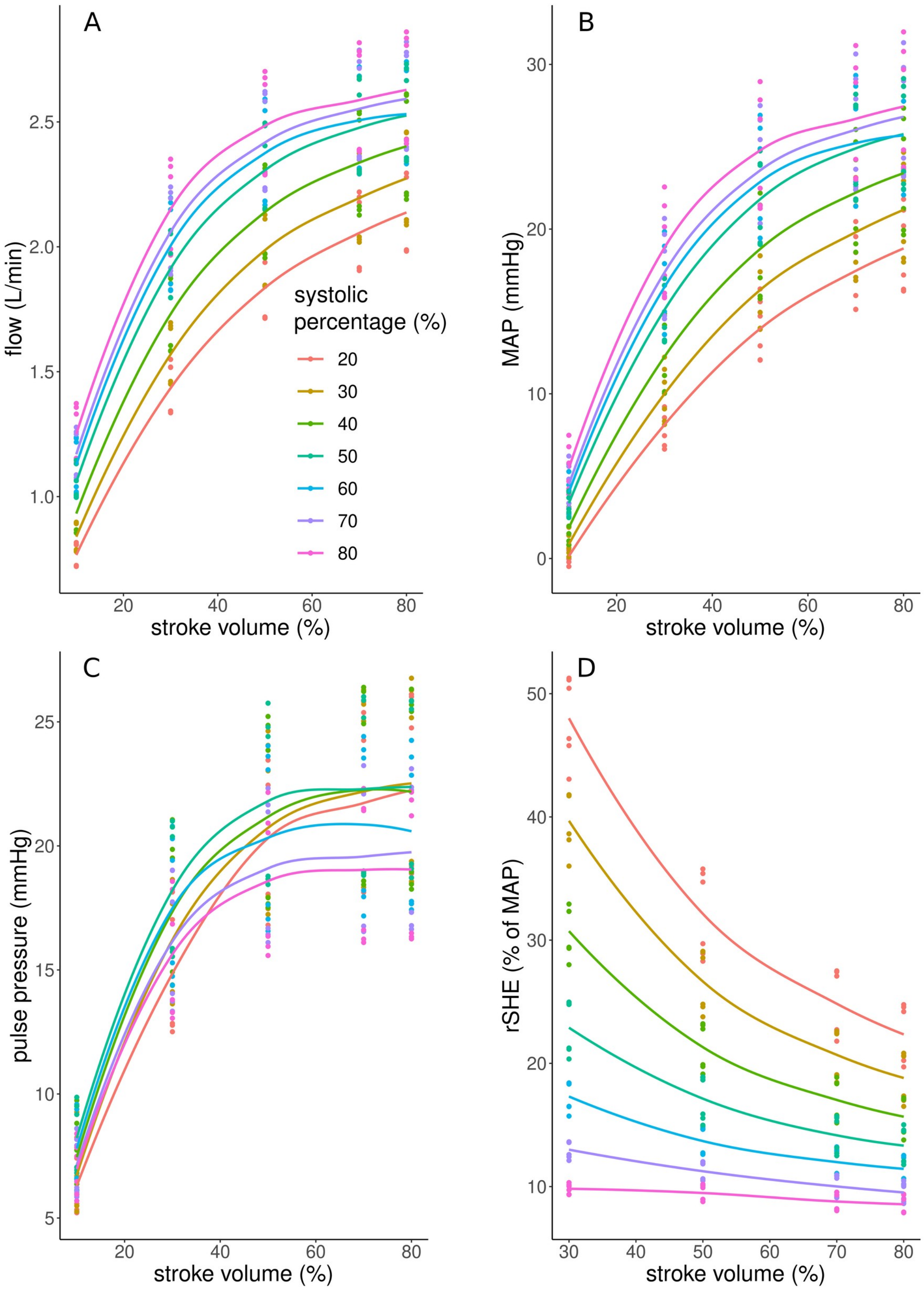


Fig. 3: Triphasic pump with Quadrox-i oxygenator. Effect of stroke volume and systolic percentage with heart rate=60 bpm and systolic acceleration percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure.n=6.

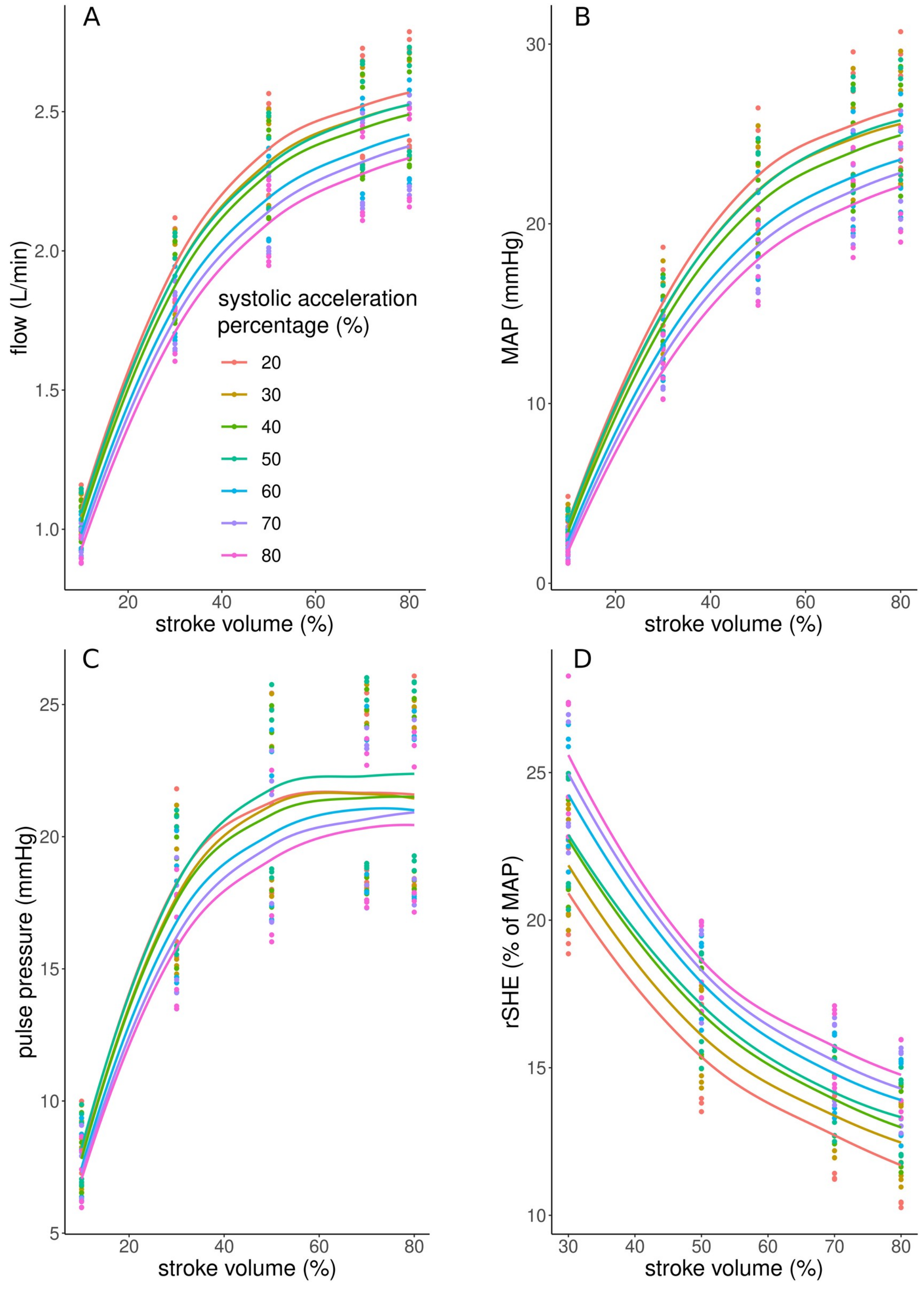


Fig. 4: Triphasic pump with Quadrox-i oxygenator. Effect of stroke volume and systolic acceleration percentage with heart rate=60 bpm and systolic percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure. n=6.

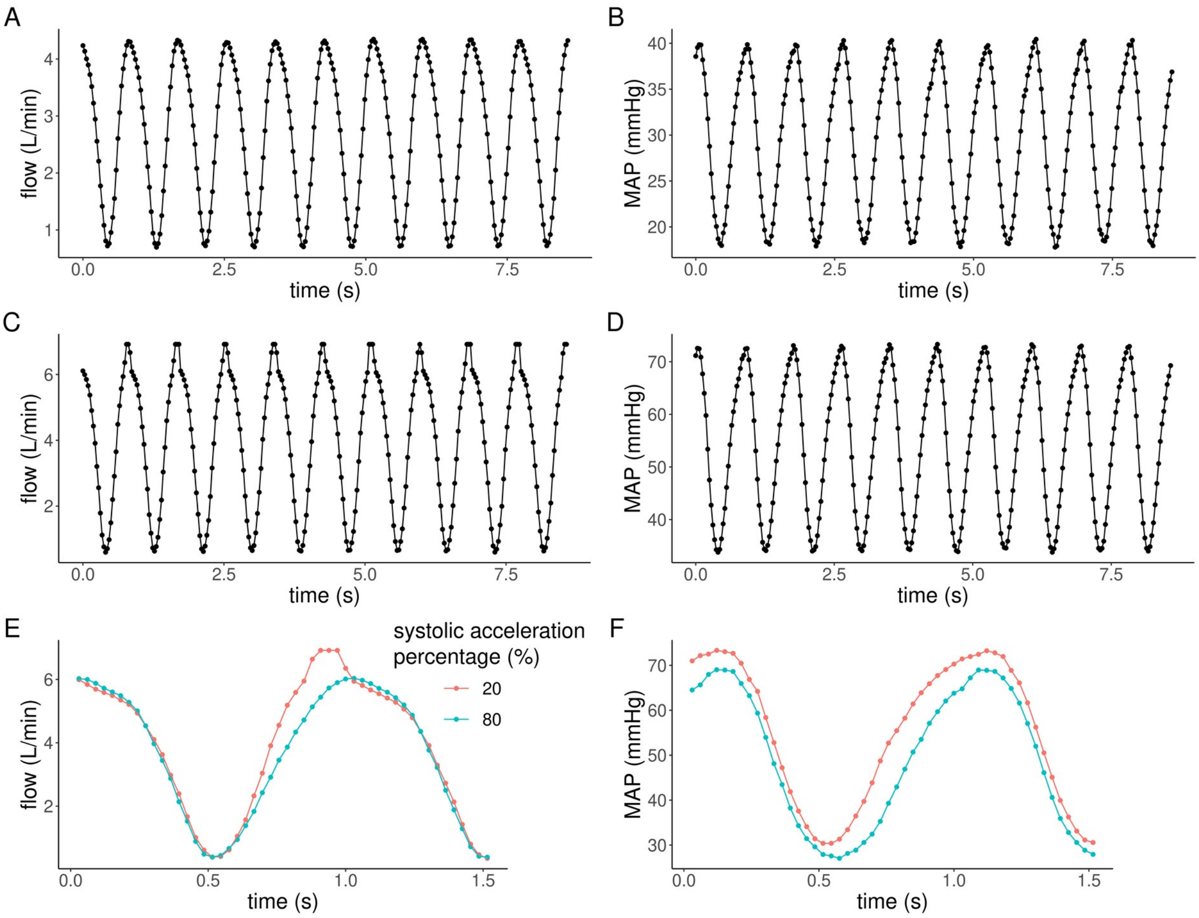


Fig. 5: Aortic flow and pressure profiles of the Triphasic pump. (A,B) Quadrox-i oxygenator, stroke volume=80%, heart rate=70 bpm, systolic percentage=50%, systolic acceleration percentage 50%. (C,D) iLA membrane ventilator, stroke volume=90%, heart rate=70 bpm, systolic percentage=50%, systolic acceleration percentage 50%. (E,F) iLA membrane ventilator, effect of systolic acceleration percentage. Stroke volume=90%, heart rate=60 bpm, systolic percentage=50%. MAP, mean arterial pressure; rSHE, relative surplus hemodynamic energy computed from aortic flow and pressure data. All profiles are representative for n=6 independent determinations.

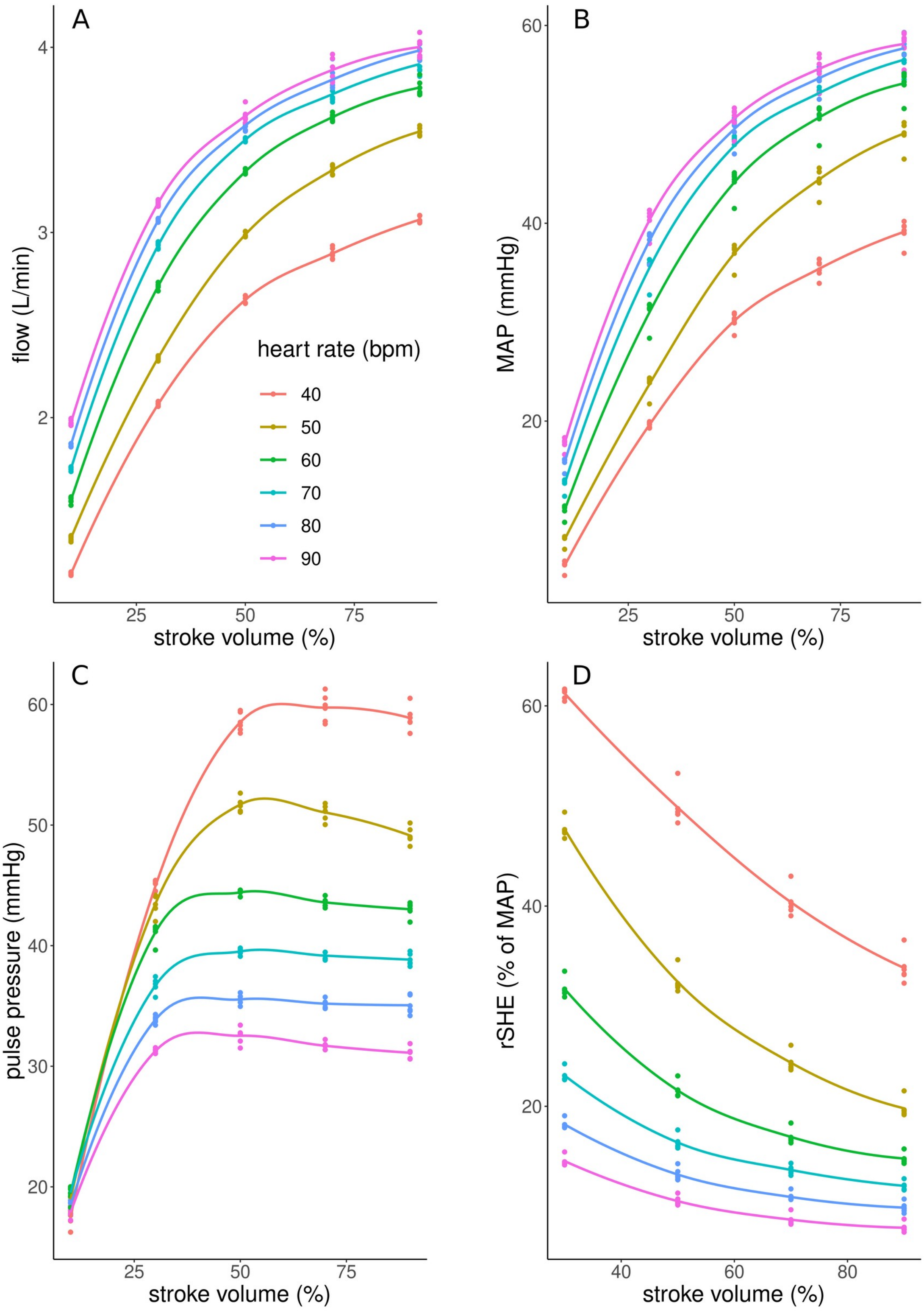


Fig. 6: Triphasic pump with iLA membrane ventilator. Effect of stroke volume and heart rate with systolic percentage=50% and systolic acceleration percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure. n=6.

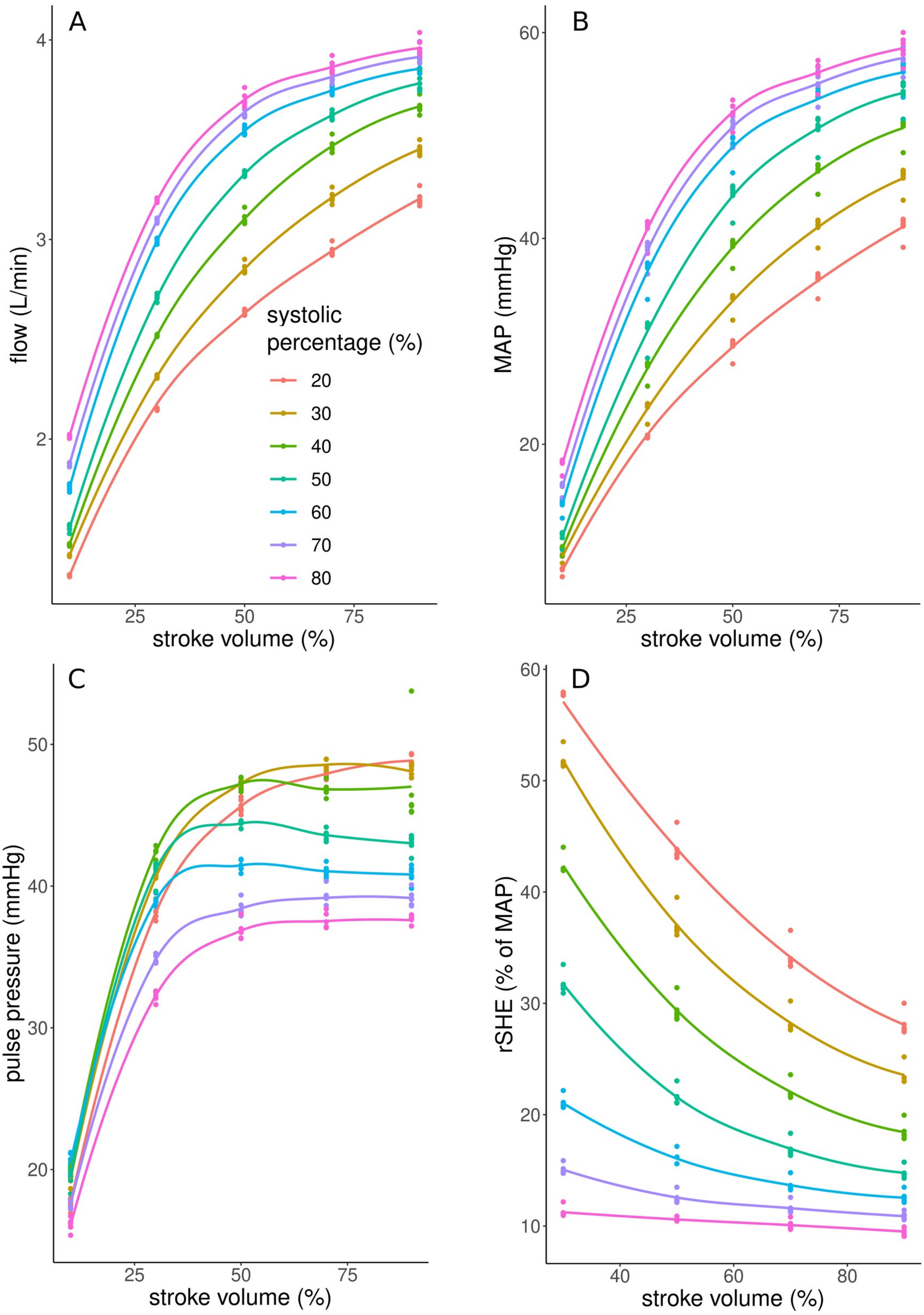


Fig. 7: Triphasic pump with iLA membrane ventilator. Effect of stroke volume and systolic percentage with heart rate=60 bpm and systolic acceleration percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure. n=6.

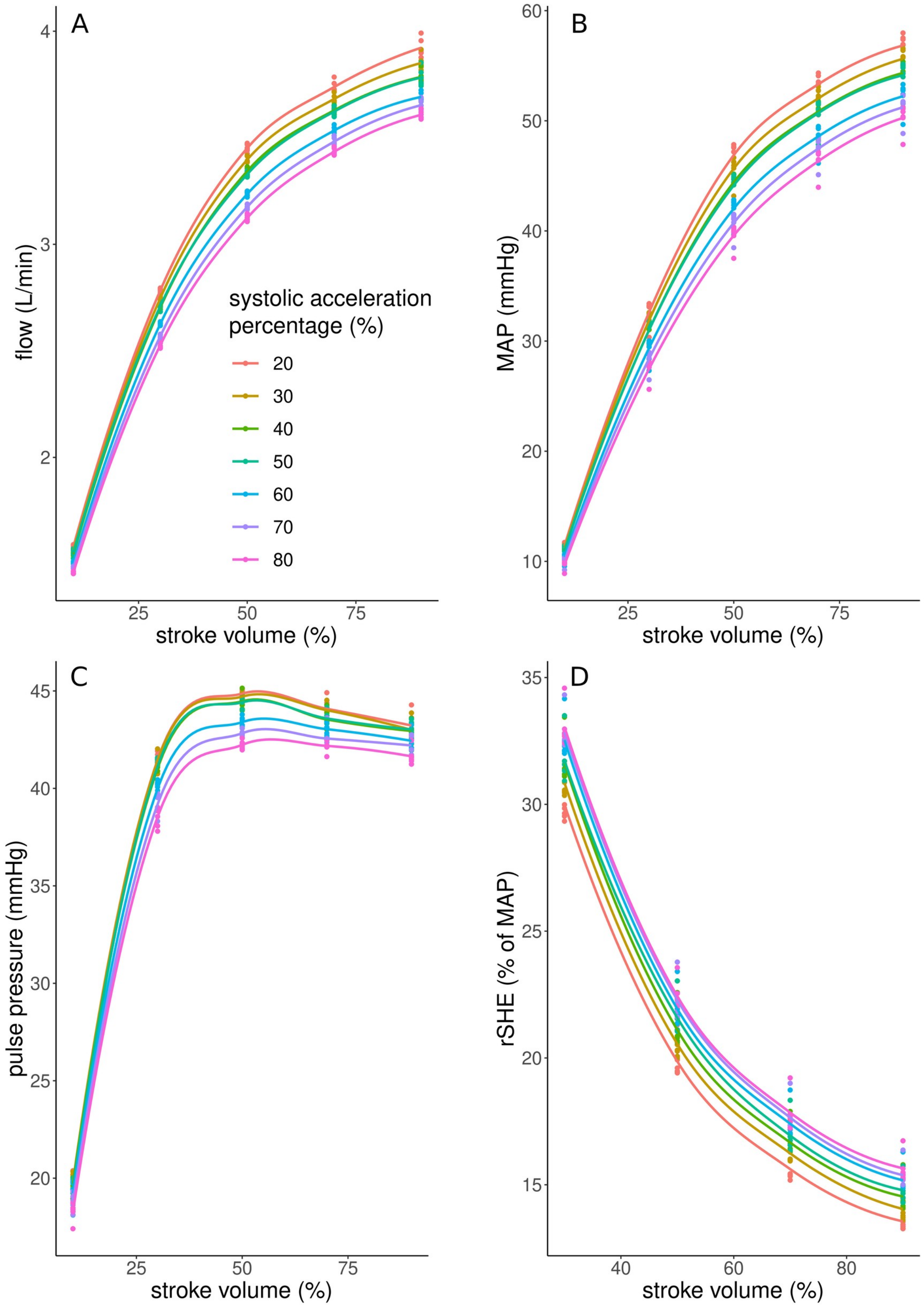


Fig. 8: Triphasic pump with iLA membrane ventilator. Effect of stroke volume and systolic acceleration percentage with heart rate=60 bpm and systolic percentage=50% on aortic flow (A), mean arterial pressure (MAP; B), aortic pulse pressure (C), and relative surplus hemodynamic energy (rSHE; D) computed from aortic flow and pressure. n=6.

Table 1: Maximum relative surplus hemodynamic energy (rSHE) values at the highest stroke volume setting in the presence of the Quadrox-i oxygenator (n=6). SV, stroke volume; F, frequency; SP, systolic percentage; SAP, systolic acceleration percentage; MAP, mean arterial pressure.

condition	optimized parameter	rSHE (% of MAP)	flow (L/min)	MAP (mmHg)	pulse pressure (mmHg)	pulsatility index
SV=80%, SP=50%, SAP=50%	F=40 bpm	26.1 (23.5 to 28.1)	2.15 (1.99 to 2.30)	19.5 (17.0 to 21.8)	28.9 (24.3 to 33.9)	1.61 (1.56 to 1.65)
SV=80%, F=60 bpm, SAP=50%	SP=20%	22.4 (20.3 to 24.5)	2.13 (1.99 to 2.29)	18.7 (16.6 to 20.9)	22.0 (19.0 to 25.7)	1.73 (1.68 to 1.77)
SV=80%, F=60 bpm, SP=50%	SAP=80%	14.9 (13.6 to 15.9)	2.33 (2.18 to 2.49)	22.1 (19.8 to 24.3)	20.3 (17.6 to 23.2)	1.39 (1.34 to 1.43)

Table 2: Maximum relative surplus hemodynamic energy (rSHE) values at the highest stroke volume setting in the presence of the iLA membrane ventilator (n=6). SV, stroke volume; F, frequency; SP, systolic percentage; SAP, systolic acceleration percentage; MAP, mean arterial pressure.

condition	optimized parameter	rSHE (% of MAP)	flow (L/min)	MAP (mmHg)	pulse pressure (mmHg)	pulsatility index
SV=90%, SP=50%, SAP=50%	F=40 bpm	33.4 (33.2 to 33.9)	3.06 (3.06 to 3.08)	39.5 (39.1 to 39.7)	58.7 (58.5 to 59.1)	1.94 (1.93 to 1.95)
SV=90%, F=60 bpm, SAP=50%	SP=20%	27.7 (27.6 to 28.0)	3.19 (3.18 to 3.21)	41.4 (41.2 to 41.7)	48.7 (48.6 to 49.1)	2.16 (2.12 to 2.17)
SV=90%, F=60 bpm, SP=50%	SAP=80%	15.4 (15.4 to 15.6)	3.60 (3.59 to 3.62)	50.6 (50.3 to 51.0)	41.6 (41.4 to 41.6)	1.57 (1.56 to 1.57)