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Hemodynamic energy during pulsatile extracorporeal circulation using flexible and rigid arterial tubing: a reassessment

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Abstract

Introduction: Pulsatile extracorporeal circulation may improve organ perfusion during cardiac surgery. Some minimally invasive extracorporeal circulation (MiECC) systems allow pulsatile perfusion. The present study investigated the influence of arterial tubing compliance on hemodynamic energy transfer into the patient.

Methods: Aortic models with adult human geometry were perfused in a mock circulation. A MiECC system was connected using either high-compliance silicone tubing or standard kit tubing. Energy equivalent pressure (EEP) and surplus hemodynamic energy (SHE) were computed from flow and pressure data. Aortic models with physiological and sub-physiological compliance were tested to assess the influence of the pseudo-patient.

Results: Non-pulsatile flow did not generate SHE. SHE during pulsatile flow in the compliant aortic model was significantly higher with kit tubing compared to silicone tubing. Maximum SHE was achieved at 1.6 L/min with kit tubing (7.7% of mean arterial pressure) and with silicone tubing (4.9%). Using the low-compliance aortic model, SHE with kit tubing reached a higher maximum of 14.2% at 1.8 L/min compared to silicone tubing (11.8% at 1.5 L/min).

Conclusions: Flexible arterial tubing did not preserve more hemodynamic energy from a pulsatile pump compared to standard kit tubing in a model of adult extracorporeal circulation. The pseudo-patient's compliance significantly affected the properties of the mock circulation.

Keywords

perfusion model; MiECC; hemodynamic energy; pulsatile perfusion; tubing

Introduction

Conventional extracorporeal circulation (ECC) using a heart-lung machine is pulsatile by the design of the roller pumps, albeit with a very low pulse amplitude compared to a healthy human heart. Minimally invasive extracorporeal circulation (MiECC) systems use centrifugal or diagonal pumps instead of occlusive roller pumps which are not compatible with their closed-loop design. By default, these pump types are operated at a constant rotational speed and are, thus, inherently non-pulsatile. Putative benefits of pulsatile ECC have been discussed controversially since open heart surgery has been established; the physiology of pulsatile ECC has been investigated as early as four decades ago when reliable pulsatile pumps became available,[1] presuming that physiological pulsation improves organ perfusion.

The Deltastream DP3 diagonal pump can optionally be operated in a pulsatile mode. Pulsation is achieved by modulating the rotational speed periodically. The additional effect in terms of energy transfer of pulsatile over non-pulsatile perfusion with otherwise identical conditions can be quantified by determining the energy equivalent pressure (EEP) and the surplus hemodynamic energy (SHE).[2,3] The latter is positive only during pulsatile flow. The magnitude of SHE available to the patient is determined by its magnitude at the pump exit and by any attenuating effects of ECC components between the pump and the patient's own circulation.

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Whereas oxygenators and arterial filters come into mind as potential attenuators of SHE, first Wang, Kunselman and Undar reported an attenuation of SHE by the standard rigid tubing shipped with commercial tubing sets compared to flexible latex tubing in a mock circulation sized for neonatal and pediatric patients.[4] As this result is somewhat counterintuitive, a re-evaluation was warranted to gain further insight. Previously, our lab has investigated extracorporeal membrane oxygenation cannulation sites using an elaborate mock circulation including the DP3 diagonal pump.[5] The goal of the present study was to reassess the impact of tubing compliance on energy transfer to the patient during pulsatile operation of a MiECC in this model of adult ECC.

Materials and methods

Mock circulation

A mock circulation was set up to perfuse an aortic model resembling a human aorta in terms of geometry and elastic properties. An in-depth description of the system and its components has been published previously.[5] In brief, a ventricular assist device (VAD, Medos, Heilbronn, Germany) perfused the aortic model with a 12% aqueous solution of dextran (average molecular weight 40 kDa, Roth, Karlsruhe, Germany) which had a viscosity similar to blood. The outflow at the main branches of the aortic arch and at the bifurcation was collected in a reservoir which, again, fed the pump ventricle. Flow rates and pressures were measured pre-oxygenator and in the aortic model. Peripheral resistance was simulated by Hoffman pinchcocks on the outflow tubing.

Aortic models

Fabrication and properties of the two aortic models used in this project have been described elsewhere.[5] In brief, wax casts of a human aorta were covered with suitable polymerizing materials. Type of polymer and the required thickness to achieve suitable elastic properties were arrived at empirically. Silicone model 1 was an early attempt that resulted in too low a relative compliance of 0.0012/mmHg. This model served as a low-compliance control in the present study. Silicone model 2 was made from the same material (Abformsilikon Typ 12 mittelhart Sh 30; Troll Factory, Riede, Germany), but had a wall thickness of only 1-2 mm, resulting in physiologically relative compliance of 0.0049/mmHg in the relevant range of 80-120 mmHg. This model was used as a pseudo-patient with physiological compliance.

Minimized extracorporeal circulation

A simplified minimized extracorporeal circulation was attached to the mock circulation in a configuration that resembles the clinical situation. A DP3 diagonal pump operated by a Deltastream console (Medos) was fed from the above-mentioned reservoir, corresponding to the location of the venous cannula. The medium was pumped through an oxygenator (QUADROX-i adult, Maquet, Rastatt, Germany) into the aortic arch. To this end, the aortic models were equipped with an artificial side branch in a position that resembled the placement of the aortic cannula in vivo. A hypothermia unit (T3, Stöckert, Munich, Germany) maintained a temperature of 37°C in the circulation.

By default, a commercial tubing set (rheoparin-coated adult support set, Medos) was used to set up the extracorporeal circulation. The set contained polyvinyl chloride (PVC) tubing (ECC noDOP, Raumedic, Helmbrechts, Germany) with an inner diameter of 3/8 inch (9.5 mm) and a wall thickness of 3/32 inch (2.4 mm). For the experiments with flexible tubing, all tubing between the DP3 pump and the aortic model was replaced by platinum-cured silicone tubing (HelixMark, Freudenberg Medical, Kaiserslautern, Germany) with the same inner diameter and a wall thickness of 1/16 in (1.6 mm).

The MiECC was operated both in pulsatile and in non-pulsatile mode as described previously.[5]

Mock loop and extracorporeal circulation operation

Each experiment started with the VAD circulating the medium with open pinchcocks while the MiECC was resting. All pinchcocks were closed step-wise until flow and pressure values were close to the expected physiological values.[5] Then, the VAD was shut down and the MiECC flow was increased from 0 to 3.5 L/min in 0.5 L/min increments. After each change of flow rate, the system was allowed to settle for at least one minute before readings were taken. All experiments were repeated independently, resulting in $n = 6$ datasets ("patients") per combination of tubing type and aortic model (total $n = 24$).

Data collection and analysis

EEP and relative SHE, given in % of the arterial pressure, were calculated from aortic pressure and flow data as outlined previously.[5] EEP and SHE as functions of flow rate were modelled with cubic least square fits and the resulting coefficients were used to compute the maxima of the curves. Data were analyzed by mixed

Table 1. EEP (mmHg) as a function of non-pulsatile flow rate, type of aortic model and type of tubing. Data are presented as median (1st quartile to 3rd quartile). P-values refer to the comparison of tubing. n = 6 per condition.

Flow (L/min)	Compliant aortic model			Low-compliance aortic model		
	Kit tubing	Silicone tubing	p	Kit tubing	Silicone tubing	p
0.5	29.3 (29.3–29.3)	28.9 (28.5–29.3)	0.238	32.3 (32.3–32.3)	30.8 (30.7–31.9)	0.028
1.0	34.2 (33.8–34.5)	33.8 (33.0–34.5)	0.395	37.5 (37.5–37.5)	36.0 (35.4–37.7)	0.139
1.5	40.1 (39.8–41.1)	39.8 (39.0–41.1)	0.738	44.3 (44.3–44.3)	43.5 (42.4–44.6)	0.252
2.0	47.6 (46.7–48.6)	47.9 (46.5–49.5)	0.879	52.5 (52.5–52.5)	51.4 (49.9–52.3)	0.068
2.5	56.3 (55.5–57.5)	55.6 (54.8–57.2)	0.620	62.2 (61.7–62.3)	61.1 (58.5–61.5)	0.046
3.0	66.6 (65.4–67.5)	66.0 (65.4–66.6)	0.778	71.8 (71.4–72.0)	71.6 (69.0–72.6)	0.381
3.5	76.5 (75.3–77.8)	76.2 (75.8–77.1)	0.648	82.3 (82.0–82.5)	83.3 (80.8–84.0)	0.942

model analysis with pulse, MiECC flow rate, aortic model and tubing type as independent factors and "patients" as a source of random effects. Statistics were computed with R and its nlme package.[6] Differences between flow rates were further analyzed by Tukey post hoc tests. Effects of factors and their interactions as well as differences in post hoc tests were considered significant if their error probability p was less than 0.05.

Results

Non-pulsatile flow

Non-pulsatile flow did not generate any SHE, regardless of flow rate, tubing type and aortic model. Arterial pressures and, thus, EEP during non-pulsatile flow depended on flow rate ($p<0.0001$), tubing type ($p<0.0075$) and aortic model ($p<0.0001$). Subgroup analysis showed no influence of tubing type on EEP if the compliant aortic model was used ($p = 0.315$) whereas there was a significantly higher EEP in kit tubing compared to silicone tubing ($p = 0.014$) if the non-compliant aortic model was tested (Table 1).

Influence of tubing type on pulsatile flow

Mean aortic pressure did not depend on pulsation in the compliant aortic model ($p>0.15$) whereas use of the low-compliance aortic model resulted in slightly, but significantly higher aortic pressures during pulsatile flow at 1.5 L/min (45.15 mmHg [44.57-45.70] vs. 44.25 mmHg [43.50-44.45]; $p = 0.025$) and at 2.0 L/min (53.39 mmHg [52.82-53.74] vs. 52.47 mmHg [51.57-52.50]; $p = 0.012$). Pulsatile flow led to a positive SHE of 3.38% (1.98-5.09%) for all conditions combined. EEP and SHE as functions of pump flow using the compliant aortic model are depicted in Figure 1A and B, respectively. While EEP increased in an almost linear fashion with pump flow, SHE showed a maximum in the lower range of tested flow rates. Both flow rate and tubing type significantly affected EEP and SHE ($p<0.0001$). Aggregated EEPs and results of post hoc tests are reported in Table 2. EEP was higher with kit tubing compared to silicone tubing although this reached significance only at three out of seven flow rates. In contrast, SHE was significantly higher with kit tubing at all flow rates (Table 3). Maximum SHE computed from the regression curves was 7.7% with kit tubing and 4.9% with silicone tubing; both were reached at 1.6 L/min.

Influence of aortic model on pulsatile flow

Perfusion of the low-compliance aortic model brought about an almost linear increase of EEP with flow and the value depended significantly on tubing type and on pump flow ($p<0.0001$, Figure 1C). Aggregated values and results of post hoc tests are given in Table 2. These indicate higher EEP with kit tubing compared to silicone tubing, which was significant at three out of seven flow rates. In contrast, there was no overall significant influence of flow rate ($p = 0.443$) and of tubing type ($p = 0.329$) on SHE (Figure 1D). Post hoc tests (Table 3) indicate that the lack of overall influence of flow rate can be attributed to SHE being similar at flow rates up to 1.0 L/min, while SHE was higher with kit tubing at flow rates of 1.5 L/min and above.

The low compliance aortic model caused the EEP values to be significantly higher by at least 1.12-fold compared to the compliant aortic model, independent of the type of kit tubing ($p<0.0001$). SHE measured with the low-compliance aorta was also higher with both kit tubing and silicone tubing (>1.85-fold; $p<0.0001$). Maximum SHE was 14.2% with kit tubing at 1.8 L/min and 11.8% with silicone tubing at 1.5 L/min.

Discussion

Conventional ECC has been suspected to induce systemic inflammatory reactions[7] and to increase the risk of developing acute kidney injury[8] and cognitive dysfunction[9] postoperatively. MiECC was developed to

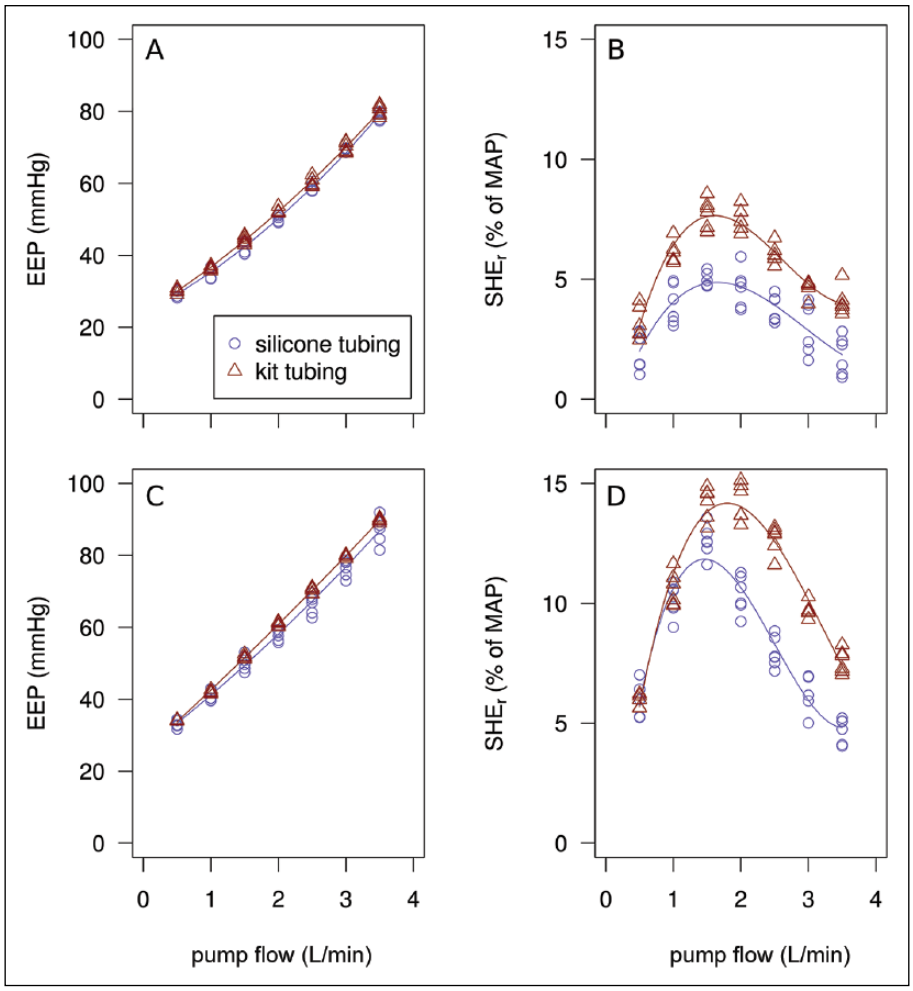

Figure 1. Energy equivalent pressure (EEP, left panels) and SHE normalized to aortic pressure (SHE$_r$, right panels) as a function of pulsatile flow. Kit tubing (triangles) compared to silicone tubing with higher compliance (circles). Using a compliant human aortic model (A, B), tubing type significantly affected EEP and SHE$_r$. Using the low compliance human aortic model (C, D), tubing type significantly affected EEP, but not SHE$_r$.

Table 2. Energy equivalent pressure (EEP; mmHg) as a function of pulsatile flow rate, type of aortic model and type of tubing. Data are presented as median (1st quartile to 3rd quartile). P-values refer to the comparison of tubing. n = 6 per condition.

Flow (L/min)	Compliant aortic model			Low-compliance aortic model		
	Kit tubing	Silicone tubing	p	Kit tubing	Silicone tubing	p
0.5	30.1 (29.9–30.6)	29.4 (28.6–30.2)	0.151	34.0 (34.0–34.2)	32.8 (32.6–33.8)	0.053
1.0	36.1 (36.0–36.5)	35.1 (33.6–36.7)	0.180	41.8 (41.7–42.1)	40.3 (39.8–42.2)	0.153
1.5	44.2 (43.5–45.0)	42.0 (40.5–43.6)	0.047	51.6 (51.3–51.8)	50.3 (48.9–51.7)	0.148
2.0	52.1 (51.9–53.3)	50.0 (49.4–50.8)	0.006	61.1 (60.6–61.4)	58.2 (56.7–59.2)	0.014
2.5	60.3 (59.4–61.0)	58.7 (58.0–59.4)	0.076	70.5 (69.7–70.8)	67.3 (64.7–68.3)	0.016
3.0	69.7 (68.8–71.1)	69.0 (68.6–69.5)	0.206	80.1 (79.8–80.1)	77.3 (75.1–78.2)	0.017
3.5	80.0 (79.0–81.2)	78.4 (77.7–79.6)	0.035	89.6 (89.5–89.9)	87.9 (85.3–89.1)	0.138

alleviate these unwanted effects. Non-essential components were eliminated, lines were kept as short as possible and surfaces were coated with heparin or other biosurfaces.[10–12] As an added benefit, some MiECC systems allow pulsatile perfusion as an alternative to the default non-pulsatile flow. The increased hemodynamic energy is expected to improve critical organ perfusion. However, not all studies were able to demonstrate salutary effects[13] and large randomized trials have yet to be conducted.

Table 3. Relative surplus hemodynamic energy (SHE; % of mean arterial pressure) as a function of pulsatile flow rate, type of aortic model and type of tubing. Data are presented as median (1st quartile to 3rd quartile). P-values refer to the comparison of tubing. n = 6 per condition.

Flow (L/min)	Compliant aortic model			Low-compliance aortic model		
	Kit tubing	Silicone tubing	p	Kit tubing	Silicone tubing	p
0.5	2.91 (2.72–3.65)	2.00 (1.43–2.74)	0.0436	5.99 (5.73–6.11)	6.02 (5.45–6.33)	0.848
1.0	5.97 (5.79–6.23)	3.81 (3.29–4.69)	0.0015	10.48 (10.02–11.02)	10.20 (9.82–10.58)	0.0734
1.5	7.89 (7.33–8.06)	4.86 (4.74–5.16)	<0.0001	14.42 (13.77–14.60)	12.56 (12.35–12.83)	0.0041
2.0	7.42 (7.20–7.77)	4.76 (4.04–4.91)	0.0007	14.18 (13.68–14.85)	10.33 (9.95–11.00)	0.0004
2.5	6.00 (5.90–6.15)	3.76 (3.34–4.18)	0.0004	12.92 (12.53–13.04)	7.77 (7.59–8.37)	<0.0001
3.0	4.78 (4.67–4.82)	3.07 (2.15–3.88)	0.0159	9.64 (9.62–9.70)	6.55 (5.99–6.95)	0.0001
3.5	3.90 (3.76–4.08)	1.84 (1.14–2.38)	0.0004	7.56 (7.20–7.89)	4.90 (4.27–5.08)	<0.0001

Advantages of "flexible" (i.e. high compliance) tubing in pulsatile ECC circuits have previously been postulated using a model of pediatric life support.[4] From a theoretical point of view, distension of high compliance tubing during systole absorbs energy which, assuming an energy conversion efficiency less than unity, partly dissipates when the tubing returns to its previous diameter during diastole. Therefore, the highest preservation of pulsatile energy should be expected with rigid tubing. Our data are in agreement with these theoretical considerations and failed to show salutary effects of high-compliance silicone tubing over PVC tubing under any of the tested conditions.

The EEP and SHE versus pump flow diagrams of the present study indicate that the kit tubing (PVC) tends to result in a better preservation of hemodynamic energy compared to the more compliant silicone tubing. While EEP differences were significant only at a few flow rates, SHE was significantly higher at all flow rates. In order to elucidate the influence of the pseudo-patient's compliance, the experiments were repeated with an aortic model of sub-physiological compliance. Although there was a similar dependency on flow rate, SHE was no longer significantly different between tubing types at flow rates up to 1.0 L/min. That is, a low-compliance pseudo-patient diminishes the benefit of rigid tubing, especially at low flow rates. The low compliance aortic model also caused a small, but significant increase in aortic pressure compared to the standard model with physiological compliance. With standard kit tubing, the maximum SHE was 1.8 times higher and with flexible tubing it was 2.4 times higher compared to the compliant aortic model. The flow rate at which the maximum SHE was detectable increased from 1.59 L/min to 1.78 L/min with kit tubing while it decreased from 1.61 L/min to 1.45 L/min with flexible tubing. These data indicate that the compliance of the pseudo-patient affects pressure and energy data measured in models of extracorporeal circulation. The pseudo-patient should, therefore, be seen as a critical component and designed with due care. An approximation of the human geometry and of the physiological elastic properties, both with the target patient population in mind, seem to be a good starting point to obtain results which can be transferred to clinical applications.

This influence of the pseudo-patient may, in fact, help to explain the opposing results of Wang, et al.[4] Besides differences in the oxygenator and the applied flow rates (Medos Hilite up to 1.2 L/min as is common in pediatric ECC vs. Quadrox up to 3.5 L/min in the present study), the preceding study used a fluid-filled bag as a pseudo-patient, which the authors acknowledged as a potential limitation. The apparent advantage of high compliance tubing in their setup may be explained by the mechanism of the pump. The DP3 is a diagonal pump whose pulsation is generated by modulating the rotational speed of the drive. As the pump is non-occlusive, flow decreases with increasing discharge pressure. Apparently, a closed-loop perfusion system requires some degree of compliance to facilitate SHE generation by the pump in the first place, as EEP depends on flow. This might explain why the present study found no benefits of flexible tubing in the presence of the compliant pseudo-patient, whereas Wang, et al. may have found better results after their non-compliant model was retrofitted with flexible arterial tubing that provided a sufficient system compliance.

The interpretation of the present study data is mainly limited by the medium and by the pseudo-patient. Although the non-Newtonian properties of blood are more important in capillary flow compared to the large-diameter aorta, hemodynamic energy readings may have been affected by our choice of a viscous, but cell-free medium. The pseudo-patient used in this study was designed to simulate geometric and elastic properties of native aortas, thus, covering especially the Windkessel effect, but there was no attempt to model the elastic properties of the remaining flow beds. This may have limited the mechanical properties of the pseudo-patient.

In conclusion, the results of the present study suggest that flexible arterial tubing does not show advantages over standard kit tubing in adult MiECC in terms of preservation of hemodynamic energy from a pulsatile

diagonal pump. The results obtained in the perfusion model depended significantly on the properties of the pseudo-patient. It seems advisable to model geometric and elastic properties after the expected patient population of any clinical application to arrive at valid conclusions from such models.

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