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Cardiac mechanoenergetic cost of elevated plasma viscosity after moderate hemodilution

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Abstract

The purpose of this study was to investigate how plasma viscosity affects cardiac and vascular function during moderate hemodilution. Twelve anesthetized hamsters were hemodiluted by 40% of blood volume with two different viscosity plasma expanders. Experimental groups were based on the plasma expander viscosity, namely: high viscosity plasma expander (HVPE, 6.3 mPa s) and low viscosity plasma expander (LVPE, 2.2 mPa s). Left ventricular (LV) function was intracardiacally measured with a high temporal resolution miniaturized conductance catheter, and concurrent pressure-volume results were used to calculate different LV indices. Independently of the plasma expander, hemodilution decreased hematocrit to 28% in both groups. LVPE hemodilution reduced whole blood viscosity by 40% without changing plasma viscosity, while HVPE hemodilution reduced whole blood viscosity by 23%, and almost doubled plasma viscosity relative to baseline. High viscosity plasma expander hemodilution significantly increased cardiac output, stroke volume and stroke work compared to baseline, whereas LVPE hemodilution did not. Furthermore, an increase in plasma viscosity during moderate hemodilution produced a higher energy transfer per unit volume of ejected blood. Systemic vascular resistance decreased after hemodilution in both groups. Counter-intuitively, HVPE hemodilution showed lower vascular resistance and vascular hindrance than LVPE hemodilution. This result suggests that geometrical changes in the circulatory system are induced by the increase in plasma viscosity. In conclusion, an increase in plasma viscosity after moderate hemodilution directly influenced cardiac and vascular function by maintaining hydraulic power and reducing systemic vascular resistance through vasodilation.

Keywords

Cardiac function; anemia; volume expansion; plasma viscosity; conductance catheter

1. Introduction

The lowering of hematocrit (Hct) via hemodilution with plasma expanders (PE) decreases oxygen carrying capacity and changes blood rheological properties. In response to the

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decrease in Hct, cardiac output (CO) increases due to reduction in vascular resistance and to maintain oxygenation [9, 11, 14, 19]. Changes in blood viscosity directly affect vascular wall shear stress, and the synthesis of vascular endothelial shear dependent mediators, such as nitric oxide (NO) [17, 21, 22, 34, 37]. Mechanistically, an acute decrease in Hct paired with an increase in plasma viscosity can partially preserve whole blood viscosity. However, as anemic blood flows through blood vessels, the erythrocytes migrate away from the vessel wall, forming a cell-rich core region and a cell-depleted layer near the wall. Based on this model, an increase in plasma viscosity with high viscosity PE (HVPE) should maintain vascular endothelial shear stress to the magnitude attained with non diluted blood, without fully restoring blood viscosity.

Studies in the microcirculation, using an acute extreme hemodilution (11% Hct) in the hamster chamber model, have shown that HVPE significantly improved microvascular function, organ blood flow and induced higher perivascular nitric oxide (NO) concentration compared to low viscosity PE (LVPE) [4–6, 34]. Microvascular effects induced by hemodilution can directly influence cardiac function by affecting cardiac microvascular perfusion, or indirectly by affecting the cardiovascular system. Techniques such as biplane fluorography, thermodilution, flow probes, micromanometers, conductance catheters and echocardiography are used to assess cardiac function in normal and pathological stages [2, 13, 15, 16, 35, 39]. However, analysis of small animal cardiac function *in vivo* is complex and challenging. The recent development of a miniaturized conductance catheter, that allows continuous real-time measurement for left ventricular (LV) pressure and volume, provides insight to the cardiac function of small animals [12, 15, 25, 26].

The objective of this study was to investigate the effects of increased plasma viscosity on left ventricular during moderate hemodilution. Acute anemic conditions were induced by isovolemic hemodilution of 40% of the blood volume. The two plasma expanders evaluated, were formulated using dextran 2000 kDa at matching colloidal osmotic pressure (COP), to achieve different viscosities (at 6%, 6.3 mPa.s and 2%, 2.2 mPa.s). Left ventricular function was assessed by an intracardiac pressure-volume measurement with a conductance catheter.

2. Methods

2.1 Animal preparation

Investigation was performed in anesthetized 60 – 70g male Golden Syrian 18 hamsters (Charles River Laboratories, Boston, MA). Animal handling and care followed the NIH Guide for Care and Use of Laboratory Animals and Position of the American Heart Association on Research Animal Use. The experimental protocol was approved by the local animal care committee. All animals were selected from a similar population and within a narrow window of age and weight, and all underwent identical preparation. Anesthesia was induced by i.p. injection of sodium pentobarbital (50 mg/kg) and core body temperature was maintained using a heating pad. Animal preparation included: i) left jugular vein, right common carotid artery, and left femoral artery catheterization, and ii) tracheotomy (polyethylene-90 tube to facilitate spontaneous breathing). The toe pinching test was performed at least every 3–5 min, and animals who responded were given a small dose of sodium pentobarbital (10–15mg/kg, i.p.), to prevent animal discomfort.

2.2. Inclusion criteria

Animals were suitable for the experiments if: mean blood arterial pressure (MAP) > 80 mmHg, heart rate (HR) > 320 beat/minute and systemic hematocrit (Hct) > 45%.

2.3 Systemic parameters

MAP and HR were monitored continuously (MP150, Biopac System Inc.; Santa Barbara, CA), except when: i) blood was sampled or ii) during blood exchange. The Hct was determined from centrifuged arterial blood samples taken in heparinized capillary tubes. Hemoglobin (Hb) content was measured spectrophotometrically (Hemocue, Stockholm, Sweden).

2.4. Cardiac function measurements

A closed chest method was performed in this study. The right common carotid artery was exposed to a 1.4F pressure-volume conductance catheter (PV catheter; SPR-839, Millar Instruments; Houston, TX) insertion and the PV catheter was advanced, passing it through the aortic valve into the left ventricle (LV) [26]. At baseline and at the end of an experiment, a bolus of 15% hypertonic saline (10 μ l) was intravenously injected to determine the conductance measured by the catheter of the surrounding myocardial tissue, frequently called parallel volume (V_p) [3]. The pressure and volume signals were continuously acquired (MPVS300, Millar Instruments; Houston, TX) and digitalized (PowerLab 8/30, ADInstruments; Colorado Springs, CO). Left ventricular volume was measured continuously in conductance units (relative volume unit, RVU) and converted to actual blood volume (μ l) at the end of the experiment using a known-volume cuvette calibration [26].

2.5. Cardiac pressure-volume indices

Cardiac function data were analyzed with PVAN software (version 3.6, Millar Instruments, TX). All cardiac function parameters were averaged from 8 – 12 cardiac cycles at each time point. End systolic pressure (P_{es}) and end diastolic volume (V_{ed}) were directly measured. Maximum and minimum rates of pressure change (dp/dt_{max} and dp/dt_{min}), relaxation time constant (τ), cardiac output (CO), stroke work (SW) and stroke volume (SV) and end-systolic volume (V_{es}) were calculated. Systemic vascular resistance (SVR) was calculated as driving pressure divided by flow, $SVR = MAP/CO$. Systemic vascular hindrance (SVH) reflects the contribution of vascular geometry to SVR, and was calculated as SVR divided by the blood viscosity.

2.6. Estimated wall shear stress ratio between groups

The estimated wall shear rate (WSR) and wall shear stress (WSS) ratios between groups were calculated assuming blood as a Newtonian fluid and the Poiseuille's law for the circulatory system. This model simplifies the whole circulatory system in front of the heart with a single tube that follows Poiseuille's law. Therefore based on these assumptions, WSR can be calculated with the expression $4Q/\pi r^3$, where Q is volumetric flow rate or cardiac output and r is half of the vessel diameter. Additionally, the measured vascular resistance following Poiseuille's law is directly proportional to the length (L) of the vessel and the

viscosity (η) of the blood, and inversely proportional to the radius to the fourth power (r^4). Therefore, the measured vascular hindrance is a function of the length (L) divided by the radius to the fourth power (r^4). Using these assumptions, the ratio between measured systemic vascular hindrance for LVPE and HVPE is proportional to L/r^4 , and L is assumed constant in both conditions.

The ratio of WSR between HVPE and LVPE was expressed by:

$$\frac{WSR_{HVPE}}{WSR_{LVPE}} = \frac{CO_{HVPE}}{CO_{LVPE}} \times \left[\frac{SVH_{HVPE}}{SVH_{LVPE}} \right]^{3/4}$$

2.7. Test solutions

The plasma expanders were formulated using dextran 2000 kDa (Pharma-Cosmos, Holbaek, Denmark) at 6% for the *high viscosity plasma expander* (HVPE) and 2% for the *low viscosity plasma expander* (LVPE) in 0.9% sodium chloride. COP was adjusted for both solutions using human serum albumin diluted in 0.9% sodium chloride. Table 1 shows viscosity and COP of the test solutions.

2.8. Moderate isovolemic hemodilution protocol

Animals were exchanged 40% of blood volume (BV) with the test solution, lowering systemic Hct by ~45%. Total BV was estimated as 7% of body weight. Test solutions were infused into the jugular vein catheter at a rate of 100 μ l/min, and blood simultaneously withdrawn at the same rate from the left femoral artery using a dual syringe pump (33 syringe pump, Harvard Apparatus, Holliston, MA). After hemodilution, the animals were followed over 1 hour. MAP, HR and LV pressure-volume were continuously recorded and blood was collected at the end of each experiment for measurements of viscosity, plasma COP and conductance catheter calibration. Figure 1 illustrates the experimental protocols.

2.9. Experimental groups

Prior to baseline assessment, animals were randomly divided into two experimental groups [1], each of 6 animals, according to the test solution used for the moderate hemodilution; the high (1. HVPE) and low (2. LVPE)) viscosity plasma expanders.

2.10. Blood and plasma expander biophysical properties

Viscosity was measured at a shear rate of 160 s^{-1} using a cone-plate viscometer (Brookfield Engineering Laboratories; Middleboro, MA). Colloid osmotic pressure was determined using a membrane colloid osmometer (model 4420, Wescor; Logan, UT).

2.11. Statistical analysis

Results are presented as mean $\pm$ standard deviation. The values are shown as the actual values or values relative to the baseline. The Grubbs' method was used to assess the closeness of all measured parameters at baseline. This method quantifies how far each parameter value is from the other values obtained from the population. Data between interested time points in a same group were analyzed using analysis of variance for repeated

measurement (ANOVA) and followed by post hoc analyses with the Dunnett's multiple comparison tests. A two-way ANOVA nonparametric repeated measurement was performed to compare significance between groups, and, when appropriate, post hoc analyses were performed using Bonferroni tests. All statistics were calculated using GraphPad Prism 4.01 (GraphPad Software, San Diego, CA). Results were considered statistically significant if $p < 0.05$.

3. Results

All 12 animals entered the study and tolerated the experimental protocol; their mean weights were 67.8 ± 4.2 g and 65.2 ± 2.3 g in the HVPE and LVPE groups, respectively. All animals included in the study passed the Grubbs' test ensuring that all the measured parameter values at baseline were within a similar population ($p < 0.05$).

3.1. Systemic parameters

The changes in MAP are presented in Fig. 2. At 60 min after hemodilution MAP was drastically reduced in both groups compared to baseline ($p < 0.05$), by 16% and 27% of baseline in the HVPE and LVPE groups, respectively. The HVPE group had significantly higher MAP than the LVPE group ($p < 0.05$). The values of the heart rate, Hct and hemoglobin content (Hb) are given in Table 2. Heart rate decreased significantly in both groups ($p < 0.05$). Hematocrit and Hb decreased by 48% in both groups ($p < 0.05$).

3.2. Viscosity of blood and plasma

Blood and plasma viscosities are given in Table 3 and show that LVPE hemodilution reduced blood viscosity to 60% of that in non-diluted blood, while plasma viscosity was maintained at the value of the non-diluted plasma. HVPE reduced blood viscosity to 77% of that in non-diluted blood, but increased plasma viscosity by 90% from that in non-diluted plasma ($p < 0.05$). Non-diluted blood and plasma viscosity, and COP were obtained from a different groups of animals.

3.3. Cardiac function

Cardiac pressure-volume indices are presented in Table 4. Indices related to LV pressure, $dP/dt_{\max}$, $dP/dt_{\min}$ and P_{es} , decreased compared to baseline in both groups. In contrast, indices related to LV volume, CO, SW and SV increased for HVPE compared to baseline ($p < 0.05$), while they remained no different from baseline for LVPE. However, no significant difference between groups was found in these cardiac function indices, except in the case of P_{es} at HD30. The end-systolic elastance (E_{es}) determined from the slope of the linear relationship between P_{es} and V_{es} was significantly higher in the group hemodiluted with LVPE than in the group hemodiluted with HVPE (Fig. 3). In the early phase (first 30 mins) post hemodilution, the cardiac function indices did not differ between the HVPE and LVPE groups. However, 60 min after hemodilution, $dP/dt_{\max}$, CO, SW and SV were significantly higher in the HVPE group ($p < 0.05$).

3.4. Vascular resistance and hindrance

Figures 4A illustrates the effect of hemodilution on SVR and Fig. 4B the effect on SVH. Systemic vascular resistance decreased in both groups, but SVH was significantly different in the HVPE group compared to LVPE; thus, SVH significantly decreased from baseline in HVPE, but significantly increased from baseline in LVPE.

3.5. Cardiac mechanoenergetics

Changes in LV work per unit volume, SW normalized by SV (SW/SV), are presented in Fig. 4C. Over time, after hemodilution (HD) the energy necessary to pump an identical volume of blood for HVPE was not different from baseline, whereas for LVPE it was significantly lower than baseline and lower than for HVPE as time progressed from 0 – 60 min, ($p < 0.05$).

3.6. Estimated wall shear rate and wall shear stress ratios

The estimated WSR and WSS ratios between HVPE/LVPE after hemodilution are presented in Fig.5. In the first 30 min, WSR for HVPE was lower than that for LVPE, but over the last 30 min it was similar to that for LVPE. In contrast, WSS calculated from blood and plasma viscosity was much greater for HVPE than for LVPE.

4. Discussion

The principal finding of the study is that isovolemic hemodilution to 28% Hct with high viscosity plasma expander (HVPE, 6% dextran 2000 kDa, 6.3 cp, COP 43.0 mmHg) maintained blood pressure, end systolic pressure and volume, reduced systemic vascular hindrance and increased stroke work per stroke volume compared to low viscosity plasma expander (LVPE, 2% dextran 2000 kDa, 2.2 cp, COP 43.3 mmHg). End-systolic volume (V_{es}) changes, over time after hemodilution between groups, are mostly attributed to the progressive increase in left ventricular stroke volume in the HVPE group, whereas stroke volume in the LVPE group was maintained after hemodilution. Stroke volume is ultimately determined by the interaction between its preload, the contractile state of the myocardium and the after-load that the ventricle faces. Preload is often reflected by V_{ed} , which refers to the length of the sarcomeres in cardiac muscle prior to contraction. Although not statistically significant, HVPE increased V_{ed} after hemodilution, thus increased the preload on the heart and, through the Starling mechanism, increased the amount of blood ejected. Furthermore, the cardiac after-load can be defined as all forces opposing the heart during systole, which are reflected by the SVR. In summary, after hemodilution with LVPE, blood viscosity decreased, peripheral vascular resistance increased, and left ventricular ejection impedance increased, therefore V_{es} decreased. Contrarily, after hemodilution with HVPE, left ventricular ejection impedance decreased, and V_{es} was maintained; consequently adequate cardiac emptying and systolic function was maintained. Additionally, HVPE improved load-dependent cardiac function indices, in combination with higher stroke work compared to baseline and LVPE. Counter-intuitively, hemodilution with HVPE decreased systemic vascular resistance and hindrance compared to baseline and LVPE, respectively.

Both hemodilution groups, HVPE and LVPE, presented hypotension, decreased HR, and lowered left ventricular pressure and SVR compared to baseline. These results are in agreement with the work reported by Estafanous *et al.* and Shinoda *et al.* in their control group, but differ from that Murray *et al.*, who found that hemodilution slightly increases MAP and HR [10, 23, 29]. The marked decrease in SVR and SVH after HVPE hemodilution implies geometrical change in the vasculature to explain the reduced resistance, compared to LVPE. According to Poiseuille's law, the resistance to flow depends directly on the magnitude of the fluid viscosity and varies inversely as the fourth power of the tube radius. Studies of acute hemodilution using the hamsters fitted with a window chamber have enabled the use of intravital microscopy to analyze local hemodynamics in microvessels. These have shown that HVPE hemodilution produces microvascular vasodilation, lowers microvascular resistance and increases capillary pressure compared to LVPE [4, 5]. Our findings indicate that the microvascular changes in peripheral tissues correlate with the observed systemic effects measured using the miniaturized conductance catheter.

Hemodilution decreases blood intrinsic oxygen carrying capacity and blood viscosity, which leads to increased CO and sustains oxygen delivery to tissues [9, 29]. In our experimental model, oxygen carrying capacities for both PE were identical due to similar Hct, and oxygen delivery to tissues improved as CO increased. End-systolic pressure was initially not different between PE, although as time passed, the end systolic pressure in animals hemodiluted with LVPE decreased compared to HVPE, reflecting differences on load, on the cardiac systolic behavior. Maximum rate of pressure change ($dP/dt_{\max}$) was not different post hemodilution between PE, and only 60 min after the exchange $dP/dt_{\max}$ was higher for HVPE compared to LVPE. Peak dP/dt has been used as an index of ventricular performance; however, it is known to be load dependent, which in part, explains the later differences between PE. On the other hand, the minimum rate of pressure change ($dP/dt_{\min}$) is a load independent parameter, and it decreased in both groups after hemodilution, suggesting distortion of the normal myocardial performance. Previous studies demonstrated that increased plasma viscosity during acute hemodilution improved skeletal muscle microvascular blood flow and functional capillary density [4, 21, 28]. Such improvements in microvascular function after HVPE hemodilution could be present in cardiac tissues and play in concert with the lower vascular resistance, explaining the enhanced cardiac function with HVPE compared to LVPE.

Both plasma expanders used in this study had a similar volume expansion due to the similar Hct and plasma COP after hemodilution. The differences in viscosity, and therefore shear stress on the vascular endothelium, are responsible for the difference in load-dependent indices such as SV, CO and SW. The mechanistic explanation for the cardiovascular changes and plasma viscosity and shear stress involves the vascular endothelium, which behaves as a receptor-effector structure, sensing different physical or chemical stimuli that occur inside the vessel. The endothelium therefore modifies the vessel shape or releases the necessary products to counteract the effect of the stimulus, and maintain homeostasis. The endothelium is capable of producing a large variety of different molecules, agonists and antagonists (NO, prostaglandins, endothelin, to name a few), balancing the effects in both directions. Isolated heart studies have demonstrated that higher viscosity, with the perfusion

solution, induced the NO production [17]. Several studies have reported that an increase in endothelial NO synthase levels augments venous return or preload [9, 20, 27], and an enhancement of shear stress by increasing fluid viscosity at a given shear rate increases eNOS expression in endothelial cell culture and *in vivo* [34, 36–38]. Our results after hemodilution demonstrated that an equivalent wall shear stress is higher in an HVPE group than that in a LVPE group, leading to increased venous return (V_{ed}) and reduced systemic vascular resistance. Therefore, HVPE causes shear stress stimuli on vascular endothelial cells more than does LVPE.

Hemodilution with HVPE presented a higher SW, LV pressure-volume loop area, compared to LVPE hemodilution. In addition, normalized work, (SW/SV), done per unit volume representing a load-independent index, was similar in both groups in the early phase (first 30 min) after hemodilution. Interestingly, 60 min after hemodilution, HVPE hemodilution sustained 95% of baseline SW/SV ratio, whereas this ratio dropped to 87% of baseline in the LVPE hemodilution group. An increase of SW/SV implies that more energy per unit of volume was used and more oxygen was consumed [24, 31, 32]. Therefore, this result suggests that the heart consumes more oxygen after HVPE compared to LVPE hemodilution. The balance between oxygen delivery to and oxygen consumption of the cardiac muscle defines the mechano-energetic limit for cardiac pumping performance, indicating a superior and sustained perfusion after HVPE hemodilution relative to LVPE hemodilution. A study using anesthetized dogs with isovolemic exchange to 24% Hct, further showed that increasing plasma viscosity with high molecular weight dextran, enhances myocardial blood flow [8].

Studies using a similar technique to address cardiac function had found considerable differences in cardiac function with different anesthetic agents [26]. Various animal models may be more sensitive to the cardio-depressive effects of injectable anesthetic agents and each animal species seem to respond differently [7, 18]. Previous investigations in hamsters have shown that pentobarbital anesthesia produces stable cardiac, lung, and airways mechanics, which allows for long-term studies [30, 33]. In our study, the initial dose of sodium pentobarbital for surgical preparation was five times higher than the dose given post hemodilution, if the animals responded to a toe pinching. The cardio-depressive effects of pentobarbital, if any, were similar in both groups, and the differences in cardiac function were mostly caused by the different biophysical properties of the plasma expanders used to induce the hemodilution. The results of our study suggest that autonomic integrity remains in both groups after hemodilution until the end of the observation time, as HR was only decreased to 94 and 93% of baseline for HVPE and LVPE, respectively.

The hydraulic power, or work per unit time transmitted by the heart to the blood, can be defined as the product associated with blood pressure and cardiac output (Fig. 6). The cardiovascular system is regulated through adaptive control systems, which inherently possess the capacity to modify its own parameters, based on the state of the system, in order to optimize system performance. The cardiac response depends on the maintenance of cardiac filling and adequate myocardial oxygenation, which itself is almost exclusively dependent on coronary blood flow. Adequate oxygenation of the myocardium after hemodilution is beyond the scope of this study, but further research to particularly identify

the sensitivity of the myocardium to blood oxygen content (hemodilution) is needed, because no extra myocardial work was needed to maintain higher CO when HVPE was used. Moreover, the stability achieved with HVPE after hemodilution over 60 min compared to LVPE suggests that partially maintaining blood viscosity post hemodilution produces a superior impedance matching between the left ventricle and the systemic circulation. This result supports the main hypothesis that at reduced oxygen carrying capacity blood rheological properties, plasma viscosity specifically, determines cardiac function. Our hypothesis indicate that cardiac function is affected by the energy required to eject diluted blood, and the central and peripheral circulation resistance to diluted blood, which together determine how the heart perfuses itself. For the heart to provide energy to flowing blood in the peripheral vascular system, it must convert chemical energy into mechanical energy. This supports the notion that higher SW with HVPE results, in part, from sufficient oxygen supply to the heart to eject the blood into the systemic circulation. These results also support the notion that HVPE has beneficial effects compared to LVPE, by sustaining heart hydraulic power conditions after hemodilution. However, HVPE attenuates the load-independent contractile performance of the heart, as shown by a lower end-systolic elastance (E_{es}) compared to LVPE. This indicates that cardiac inotropy may be affected by changing blood viscosity. Despite the HVPE lowered E_{es} of the heart, the cardiovascular system compensated this attenuation with vasodilation, reducing systemic vascular resistance and maintaining hydraulic power.

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Fig. 1.

Hemodilution protocol. Baseline characterization was performed before hemodilution. 40% blood volume was exchanged with test solutions (HVPE; viscosity = 6.3 mPa s or LVPE; viscosity = 2.2 mPa s). Observation period was 1 hour after exchange. Hct, hematocrit; BL, baseline; HD, hemodilution.

Fig. 2. Mean arterial pressure (MAP) measured at baseline (BL), at 0, 15, 30 and 60 minutes after hemodilution (HD0, HD15, HD30, HD60). †, $p < 0.05$ compared to baseline. ‡, $p < 0.05$ between groups at specific time points.

Fig. 3.

Relation between end-systolic pressure (P_{es}) and end-systolic volume (V_{es}) during hemodilution. The insert presents the end-systolic elastance (E_{es}) determined from the slope of the linear relationship between P_{es} and V_{es} . Solid lines are the linear regression for each experimental group (LVPE: $P_{es} = 2.77 (V_{es}) + 74.04$, $r = 0.97$; HVPE: $P_{es} = 1.67 (V_{es}) + 96.08$, $r = 0.77$).

Fig. 4.

(A) Systemic vascular resistance (SVR) at each time point after hemodilution; (B) Systemic vascular hindrance (SVH) at last time point; and (C) The work done by the heart per stroke volume (SW/SV ratio) at each time point after hemodilution. The baseline mean and standard deviation for i) systemic vascular resistance is $9 \pm 2 \text{ mmHg} \cdot \text{min} \cdot \text{ml}^{-1}$, and ii) stroke work per stroke volume is $108 \pm 5 \text{ mmHg}$. Broken lines represent the values at baseline. †, $p < 0.05$ compared to baseline within a same group. ‡, $p < 0.05$ between groups at a specific time point.

Fig. 5. Equivalent wall shear rate (WSR) and wall shear stress (WSS) in an HVPE group relative to an LVPE group. The WSS ratios are based on apparent blood viscosity (WSS_{Blood}) and plasma 3 viscosity (WSS_{Plasma}).

Fig. 6.

Hydraulic power ($\text{MAP} \times \text{CO}$) against normalized stroke work per stroke volume (SW/SV). The second factor contributing to the determination of systemic hydraulic power is the left ventricular afterload.

TABLE 1

Physical properties of the solutions.

Solution	Viscosity * (cp)	COP (mmHg)	Composition
LVPE	2.23	43.0	2% dextran 2000 kDa + 10% HAS
HVPE	6.34	43.3	6% dextran 2000 kDa + 10% HAS

* Shear rate of 160 s^{-1} at 37°C . Values are means.

TABLE 2

Heart rate and laboratory parameters.

Parameters	Baseline (BL)		60 min Hemodilution (HD60)	
	HVPE	LVPE	HVPE	LVPE
Hct, %	53±2	54±4	27±2 [†]	28±1 [†]
Hb, g/dl	15.8±0.7	15.5±0.9	8.2±0.7 [†]	8.5±0.5 [†]
HR, bpm	486±39	480±24	456±34 [†]	447±33 [†]

Values are means ± SD. Hct, hematocrit; Hb, hemoglobin; HR, heart rate.

[†] $P < 0.05$ compared with baseline within a same group.

TABLE 3

Rheological properties of non-diluted hamster blood (obtained from a different group of animals) and after hemodilution (samples obtained at the end of the experiment).

60 min after Hemodilution	Hct (%)	Blood viscosity * (cP)	Plasma viscosity * (cP)	Plasma COP (mmHg)
Non-diluted Blood	52 ± 1	4.7 ± 0.6	1.1 ± 0.1	16 ± 2
HVPE	27±2 [†]	3.6 ± 0.2 [†] [‡]	2.1 ± 0.1 [†] [‡]	18 ± 2
LVPE	28 ± 1 [†]	2.8 ± 0.3 [†]	1.2 ± 0.1	15 ± 2

* Shear rate of 160 s⁻¹ at 37°C. Values are means ± SD.

[†] $P < 0.05$ compared to baseline within a same group;

[‡] $P < 0.05$ compared between groups.

TABLE 4

Cardiac function indices derived by pressure-volume conductance catheter.

		BL	HD0	HD15	HD30	HD60
P_{es} (mmHg)	LVPE	118±2	114±4	109±7	95±13 [‡]	96±9 [‡]
	HVPE	118±6	112±8	111±7 [‡]	109±10 ^{‡,‡}	105±10 [‡]
dp/dt_{max} (×10 ³ mmHg/s)	LVPE	15.1±1.3	14.8±1.2	14.4±2.1	13.0±2.0	11.0±1.9 [‡]
	HVPE	12.8±1.2	12.2±1.6	11.7±1.8	11.8±2.4	12.0±1.5
dp/dt_{min} (×10 ³ mmHg/s)	LVPE	-12.1±1.6	-13.5±1.2	-11.6±1.0	-10.1±0.7 [‡]	-9.1±1.3 [‡]
	HVPE	-14.0±1.5	-12.9±2.1	-11.8±1.5 [‡]	-11.3±1.7 [‡]	-9.4±1.8 [‡]
SV (μl)	LVPE	24.5±4.4	24.8±5.7	25.5±5.9	25.5±4.3	25.4±3.3
	HVPE	20.6±3.8	24.2±5.7	24.8±6.7 [‡]	26.0±7.6 [‡]	27.7±8.3 [‡]
HR (bpm)	LVPE	480±24	472±26	468±27	458±25	447±33 [‡]
	HVPE	486±39	488±34	472±31	469±30	456±34 [‡]
CO (ml/min)	LVPE	11.8±2.2	12.1±2.6	12.1±2.6	11.9±1.5	11.3±1.1
	HVPE	10.0±2.0	11.3±2.7 [‡]	11.6±3.0 [‡]	11.8±3.0 [‡]	12.5±3.5 [‡]
SW (×10 ³ mmHg-μl)	LVPE	2.5±0.6	2.6±0.7	2.7±0.8	2.6±0.6	2.4±0.4
	HVPE	2.2±0.5	2.6±0.6	2.6±0.7 [‡]	2.7±0.8 [‡]	2.8±0.9 [‡]
V_{ed} (μl)	LVPE	32.6±5.7	35.2±9.7	34.1±10.6	32.1±12.1	32.8±12.0
	HVPE	35.6±10.5	38.4±12.8	41.7±14.0	41.9±14.6	41.5±13.2
Tau (s ⁻¹)	LVPE	6.1±0.6	6.0±0.4	6.4±0.3	6.7±0.5 [‡]	7.0±0.6 [‡]
	HVPE	6.2±1.0	6.3±0.9	6.6±1.0	6.8±1.2 [‡]	7.3±1.3 [‡]

Values are means ± SD.,

[‡] P<0.05 compared to baseline within a same group;^{‡‡} P<0.05 compared between groups.