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Determination of Vascular Waterfall Phenomenon by Bedside Measurement of Mean Systemic Filling Pressure and Critical Closing Pressure in the Intensive Care Unit

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Abstract

Background—Mean systemic filling pressure (Pmsf) can be determined at the bedside by measuring central venous pressure (Pcv) and cardiac output (CO) during inspiratory hold maneuvers. Critical closing pressure (Pcc) can be determined using the same method measuring arterial pressure (Pa) and CO. If $P_{cc} > P_{msf}$ there is then a vascular waterfall. In this study we assessed the existence of a waterfall and its implications for the calculation of vascular resistances by determining Pmsf and Pcc at the bedside.

Methods—In 10 mechanically ventilated postcardiac surgery patients inspiratory hold maneuvers were performed, transiently increasing Pcv and decreasing Pa and CO to four different steady-state levels. For each patient values of Pcv and CO were plotted in a venous return curve to determine Pmsf. Similarly, Pcc was determined with a ventricular output curve plotted for Pa and CO. Measurements were performed in each patient before and after volume expansion with 0.5 l colloid and vascular resistances were calculated.

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Results—For every patient the relationship between the four measurements of Pcv and CO and of Pa and CO was linear. Baseline Pmsf was 18.7 ± 4.0 (mean $\pm$ SD) mmHg and differed significantly from Pcc 45.5 ± 11.1 mmHg; ($p < 0.0001$). The difference of Pcc and Pmsf was 26.8 ± 10.7 mmHg, indicating the presence of a systemic vascular waterfall. Volume expansion increased Pmsf (26.3 ± 3.2 mmHg), Pcc (51.5 ± 9.0 mmHg) and CO (5.5 ± 1.8 to 6.8 ± 1.8 l·min⁻¹). Arterial (upstream of Pcc) and venous (down-stream of Pmsf) vascular resistance were 8.27 ± 4.45 and 2.75 ± 1.23 mmHg·min·l⁻¹; the sum of both (11.01 mmHg·min·l⁻¹) was significantly different from total systemic vascular resistance (16.56 ± 8.57 mmHg·min·l⁻¹, $p = 0.005$). Arterial resistance was related to total resistance.

Conclusions—Vascular pressure gradients in cardiac surgery patients suggest the presence of a vascular waterfall phenomenon, which is not affected by CO. Thus measures of total systemic vascular resistance may become irrelevant in assessing systemic vasomotor tone.

Introduction

In the classical view cardiac output (CO) is determined by cardiac function (contractility, heart rate), preload and afterload, despite Guyton's studies on venous return.¹ For short time periods venous return and CO can differ, but averaged over time venous return must be equal to CO. When the heart is stopped and a large arteriovenous fistula opened, arterial and venous pressures rapidly equilibrate to one pressure, which is called mean systemic filling pressure (Pmsf).² Pmsf reflects the mean weighted up-stream pressure for venous return to the heart. The difference between Pmsf and right atrial pressure or central venous pressure (Pcv) during steady-state flow represents the pressure gradient for venous return, and if CO is known, one can calculate the resistance to venous return as the ratio of driving pressure to flow. Recently we demonstrated that it was possible to determine Pmsf at the bedside in mechanically ventilated postcardiac surgery patients with an intact circulation.³ Applying inspiratory holds of increasing airway pressure levels Pcv increases and CO decreases to a steady-state level (Figure 1). From the values of Pcv and CO at different airway pressures, a venous return curve can be constructed (Figure 2). When CO is extrapolated to zero, Pcv will equal Pmsf. Pmsf is in turn determined by stressed blood volume and systemic vascular compliance. Thus, measuring Pmsf allows more insight into variables and mechanisms that control the peripheral circulation in critically ill patients, such as systemic venous resistance (Rv), stressed and unstressed volume and vascular compliance.^{4,5}

During ventricular fibrillation for testing an implantable cardioverter/defibrillator in humans both Pcv and arterial blood pressure (Pa) were measured and a gap between Pa and Pcv persisted.^{6–8} This gap between Pa and Pcv was also found in dogs on cardiac bypass after stopping bypass for 20 seconds.⁹ This stop-flow Pa value is called the arterial critical closing pressure (Pcc). Thus, arterial Pcc is the pressure under which the flow between the arterial and venous side of circulation is stopped despite the persistence of a pressure gradient. Beyond this critical closing locus vascular pressures decrease rapidly to Pmsf. If there is a Pcc to Pmsf pressure gradient, we refer to it as a vascular waterfall. Once blood flows over the Pcc edge of the waterfall, the height of the waterfall has no effect on flow. With our technique of inspiratory hold maneuvers to calculate Pmsf as the zero flow intercept of venous pressure we can also determine Pcc as the zero intercept of Pa. These measurements can be performed at the bedside and in patients with a beating heart and blood flow.³

The existence of a vascular waterfall has implications for the calculation of systemic vascular resistance and in our understanding of the determinants of blood flow distribution.¹⁰ Traditionally total systemic vascular resistance is defined as $R_s = [Pa - Pcv] / CO$. However, this construct taken from the electrical circuit theory of current flowing through a wire presumes a constant pressure decrease from input site to output site, such that

increasing output pressure (Pcv) decreases this pressure gradient and thus decreases CO. In the presence of a waterfall (or Starling resistor) there are 2 separate pressure gradients, one Pa gradient from the central arterial circuit (Pa) to Pcc and another venous pressure gradient from Pmsf to Pcv. Thus two separate but in series vascular resistances can be identified, one upstream of Pcc defining arterial resistance (Ra) and one downstream of Pmsf defining Rv.

The aim of our study was to determine whether there is a Pcc to Pmsf pressure gradient during steady-state flow conditions at the bedside and if so how changes in CO due to intravascular volume loading might affect it. We hypothesized that intravascular fluid administration will increase Pmsf and CO but not change Pcc.

Methods

Ten postoperative patients after aortic valve replacement, mitral valve surgery or coronary artery bypass surgery instrumented with a pulmonary artery catheter were included in the study. The study was approved by the University Medical Ethics Committee of Leiden University and the University of Pittsburgh, whereas the study was performed in Leiden University Medical Center. Patient's written informed consent was obtained. Patients with congestive heart failure (New York Heart Association class 4), postoperative valvular insufficiency, aortic aneurysm or extensive peripheral arterial vascular disease, postoperative arrhythmia or intraaortic balloon counter-pulsation were excluded.

Postoperative anesthesia was maintained with propofol and sufentanil. Patients' lungs were mechanically ventilated (Evita4 servo ventilator Draeger, Lubeck, Germany) in synchronized intermittent mandatory ventilation mode with tidal volumes of 6–8 ml·kg⁻¹ and a respiratory rate of 12–14 breaths·min⁻¹ to achieve normocapnia (arterial P_{CO2} between 40–45 mmHg). A positive end-expiratory pressure of 5 cmH₂O and a fraction of inspired oxygen (FiO₂) of 0.4 were applied. During the study period all patients were hemodynamically stable and no changes in vasoactive medication were made.

Arterial blood pressure was monitored via a 20-G, 3.8 cm long fluid-filled radial artery catheter. Pcv was measured with a central venous catheter inserted in the right internal jugular vein (MultiCath 3 venous catheter, Vigon GmbH & Co, Aachen, Germany). Both were connected to pressure transducers (PX600F, Edwards Lifesciences) and referenced to the intersection of the anterior axillary line and the fifth intercostal space. Airway pressure was measured at the entrance of the endotracheal tube and balanced at zero level against ambient air. CO was obtained beat-to-beat by modelflow pulse contour analysis as previously described and validated.^{11–13}

Within 1 hour after arrival at the intensive care unit, the protocol started and mechanical ventilation was switched from synchronized intermittent mandatory ventilation to airway pressure release ventilation to allow external control of the ventilator to perform inspiratory hold maneuvers. Respiratory rate, FiO₂, positive end-expiratory pressure, and tidal volumes were kept unchanged. No spontaneous breathing efforts were observed during the study. Pa and Pcv were recorded at a sample frequency of 100 Hz and 0.2 mmHg resolution on computer disk for offline data analysis. We calibrated the pulse contour CO measurements with 3 thermodilution CO measurements equally spread over the ventilatory cycle. During the observation period no changes were made in ventilatory settings, sedation and vasoactive medication.

Steady-state Pa, Pcv and CO were measured over the last 3 seconds of 12-second inspiratory hold maneuvers at plateau pressures of 5, 15, 25 and 35 cmH₂O, as we previously described by us.³ With increasing airway pressure, Pcv increases and CO and Pa decrease to a steady-state between 7 and 12 seconds after start of the inspiratory hold (Figure 1). The resulting

values of Pcv were plotted against CO in a venous return curve for the four inspiratory hold procedures and a linear regression line was fitted through these data points (Figure 2). Similarly, in a ventricular output curve Pa was plotted against CO for the same inspiratory hold maneuvers (Figure 2). Measurements were done during baseline conditions and after administration of 500 ml hydroxyethyl starch (130/0.4) over 15 minutes to assess changes in CO, Pcc and Pmsf after intravascular volume expansion for each patient.

Pmsf was defined as the zero flow intercept of the venous return curve as previously described.³ Pcc was the extrapolation of Pa to zero flow in the ventricular output curve (Figure 2). For each patient linear regressions for the four pairs of Pcv and CO, and of Pa and CO were fitted using a least-squares method. Lilliefors' method was used to test for normality. The pairwise differences for Pcc at baseline and after intravascular fluid administration, and for the pairwise differences for Rs and the sum of Rv and Ra, were inconsistent with normal distribution. The other pairwise data were not inconsistent with normal distribution ($p > 0.05$). The differences between Pmsf and Pcc were tested by a paired Student's t-test. A significant difference between Pmsf and Pcc was considered consistent with a vascular waterfall. Systemic arterial vascular resistance was defined as $Ra = [Pa - Pcc] / CO$, and systemic venous vascular resistance as $Rv = [Pmsf - Pcv] / CO$. Total systemic vascular resistance was calculated as $Rs = [Pa - Pcv] / CO$. The difference between Rs and the sum of Ra and Rv, reflecting the hydrostatic energy loss across the vascular waterfall, was tested with a Wilcoxon signed ranks test. Linear regression between Ra and Rs include 95% confidence interval (95%CI) for bias and slope, together with the Pearson correlation. The changes in CO, Pmsf, Pcc, the gap between Pcc and Pmsf, Ra, Rv and the slopes of both the venous return and the ventricular output curves induced by intravascular volume expansion were tested by paired Student's t-tests or Wilcoxon signed ranks test as indicated by the Lilliefors' test for normality. Data are presented as mean $\pm$ SD. Differences with a $p < 0.05$ were considered significant.

Results

Ten patients were included in the study. Patient characteristics are shown in Table 1. The venous return and ventricular output curves data for all individuals before and after 500 ml intravascular fluid administration shown in Table 2. The goodness of fit of these curves through the data obtained from the inspiratory hold maneuvers, given by R^2 , is remarkably high. The slopes of the venous return and ventricular output curves as well as the values for Pmsf and Pcc ranged over 2:1 ratios indicating significant different hemodynamic conditions for individual patients.

Baseline measurements. In all patients a linear relationship between CO and Pcv and between CO and Pa was found, with an averaged slope of -0.438 ± 0.164 ($l \cdot \min^{-1} \cdot \text{mmHg}^{-1}$) and of 0.140 ± 0.064 ($l \cdot \min^{-1} \cdot \text{mmHg}^{-1}$), respectively. In Table 3 the hemodynamic values before and after intravascular volume administration are shown. Baseline mean Pmsf was 18.7 ± 4.0 mmHg and mean Pcc was 45.5 ± 11.1 mmHg. In every patient a pressure gap between Pcc and Pmsf was observed (range 16–46 mmHg). The values of Pmsf and Pcc were significantly different ($p < 0.0001$) with a mean difference at baseline of 26.8 ± 10.7 mmHg, indicating the presence of a vascular waterfall. Ignoring the presence of a waterfall, Rs would have been calculated as 16.56 ± 8.57 mmHg·min·l⁻¹. However, considering a waterfall, Ra was 8.27 ± 4.45 mmHg·min·l⁻¹, Rv was 2.75 ± 1.23 mmHg·min·l⁻¹ and the sum of Ra and Rv was 11.01 ± 5.52 mmHg·min·l⁻¹, which is significantly different from Rs ($p = 0.005$) and reflects at least a 30% hydrodynamic energy loss across the vascular waterfall.

Volume loading. Pmsf, Pcv, Pcc and CO increased with intravascular volume administration as did the pressure gradient for venous return (Pmsf-Pcv) (Table 3). The pressure gradient Pcc-Pmsf did not change significantly with intravascular volume administration. The slope of the ventricular output curve declined ($p=0.046$) reflecting the decrease in Ra, while the slope of the venous return curve and its calculated Rv did not change significantly.

We investigated a possible relation between Rs and Ra, because Rs and Ra significantly changed whereas Rv did not change with intravascular fluid administration. The results of individual data are indicated in Figure 3. The relation between Ra and Rs ($Ra=0.52$ (95%CI 0.44–0.62) · $Rs-0.55$ (95%CI -2.11 +1.02), Pearson correlation 0.945) appeared highly significant.

Discussion

This study shows that both Pmsf and Pcc can be determined at the bedside in intensive care patients with intact dynamic circulation. The pressure gap of 26.8 ± 10.7 mmHg between Pcc and Pmsf indicates that a waterfall phenomenon is likely to be present. These data are consistent with the findings of several animal studies^{14,15} as well as those reported in humans.^{6–8} However, the human studies were performed in patients during ventricular fibrillation and total circulatory arrest. The duration of circulatory arrest in humans ranged from 7.5 seconds⁷ to 30 seconds.⁸ Schipke et al.⁶ reported a mean Pcc of 24.2 ± 5.3 mmHg during cardiac arrest after 13 ± 2 seconds. Kottenberg-Aschenmacher et al.⁸ found values of Pcc of 26.6 and 23.9 mmHg after 15 and 30 seconds of cardiac arrest. However, using a predictive model of heart beating data, i.e., on the aortic pressure decay, these authors found a significantly higher value (53 ± 15.6 mmHg). The Pcc value of 45.5 ± 11.1 mmHg in our study is in the range Kottenberg-Aschenmacher et al.⁸ found on heart beating data, but is substantially higher than values found during cardiac arrest. The discrepancy between heart beating and cardiac arrest values can be explained by a leak in the waterfall. As long as the volume supply exceeds the volume loss, the height of the waterfall will be intact. This is the case in the intact circulation, which was preserved in our study. However, when supply becomes less than the volume loss, as is the case during a cardiac arrest, the drain of arterial blood through those vascular waterfalls with lower local Pcc values will result in a reduction of measured Pcc.

Despite the difference of absolute values of Pcc for the intact circulation versus circulatory arrest, the observed pressure gap of 26.8 mmHg between Pcc and Pmsf in our patients is remarkably similar to the values Jellinek, Schipke and Kottenberg-Aschenmacher et al. report.^{6–8} In animal stop-flow studies the pressure gap between arterial and venous pressure was already well known and was the reason for using a pump or large arteriovenous fistula to move blood from the arterial compartment to the venous compartment in order to achieve equilibrium pressure during the stop-flow period.² The implications of a Pcc significantly greater than Pmsf are that our interpretation of vasomotor tone and vascular resistance must change.

Classically Rs is calculated as the ratio of the pressure difference between mean Pa and mean Pcv, and CO. Kottenberg-Aschenmacher et al.⁸ already pointed out that Rs has to be partitioned into an Ra and a Rv, or rather the resistance before and after the waterfall. Our study extends their findings. We were able to calculate arterial resistance as $Ra = [Pa - Pcc] / CO$ and venous resistance as $Rv = [Pmsf - Pcv] / CO$. Based on our findings we conclude that Rs is an entity that does not exist in vascular physiology and calculated Rs overestimates the sum of Ra and Rv. In Figure 4 a dotted line is plotted directly after the waterfall, because it is not known whether or not the waterfall ends directly in vascular lacunae (where Pmsf is located). Furthermore, we have no information about the presence of parallel bloodstreams

to the waterfall. However, if the clinician at the bedside wants to know whether arterial tone is increased, decreased, or normal, and how it changes in response to time and treatment, then he or she needs to measure CO, Pa, and Pcc. Ra can be calculated directly from CO, Pa, and Pcc (Figure 3). Measurement of Pcc and Pmsf and calculation of Ra and Rv allows us to understand physiology and the point of action of vasoactive medication and in the future could guide the clinician in the hemodynamic treatment of critically ill patients.

The response to intravascular volume administration is an increase in Pmsf, while a stable value of Pcc is expected. With the analogy of a lake filled by a waterfall, adding volume will increase the filling pressure below the waterfall, but the pressure at the edge of the waterfall would not be changed. Surprisingly, Pcc did increase after intravascular volume expansion, although less than Pmsf did. We do not have an explanation for this finding. Importantly there was an increase in both Pmsf and the pressure gradient for venous return with intravascular volume expansion, resulting in an increase in CO. Resistance to venous return did not change with fluid expansion in our study. Although we do not have a solid explanation for the decrease in Ra with intravascular volume administration, vascular stress-relaxation associated with increased flow and baroreceptors-induced decreased sympathetic tone are potential mechanisms for this phenomenon. We saw only a minor decrease in heart rate after intravascular volume administration whereas pulse pressure (systolic blood pressure, diastolic blood pressure) increased less (24%) than stroke volume increased (30%). These findings are also consistent with baroreceptors-induced arterial vasodilation.

For the inspiratory hold method to define vascular state, several assumptions are made. First a steady-state in which venous return equals CO must be created. Figure 1 demonstrates that during an inspiratory hold a plateau in Pcv, Pa and CO is reached during the last seconds of the inspiratory pause. Second, measurements must be done before autonomic reflexes occur. We did not observe any change in heart rate, Pcv or Pa during the last seconds of the inspiratory hold. This might have been caused by the use of propofol and sufentanil, which can depress baroreceptor reflexes.^{16–18} Third, a linear relationship between CO and Pcv and between CO and Pa is needed to be able to extrapolate to the point of zero flow. The presence of such linear relations was, indeed, shown by Guyton¹, in several animal studies^{19–22} and in our study in humans.³

Before concluding that there is a waterfall phenomenon, other possible explanations for the pressure gap between Pcc and Pmsf need to be addressed. An underestimation of Pmsf by our method is unlikely. On the contrary, the positive intrathoracic pressure in theory can increase effective circulatory volume by squeezing blood from the liver and the pulmonary vessels.²³ An overestimation or underestimation of Pcc could be possible, because of the extrapolation of the CO-Pa curve beyond the data range (Figure 2). However for the inspiratory holds of 35 cmH₂O in some patients CO reached very low values during a few seconds, almost abolishing the need for extrapolation. However, none of these potential arguments explain the large pressure gap between Pcc and Pmsf of 26.8 mmHg.

Where are waterfalls located and what is their function? The exact location of the vascular waterfall is not known, but generally an arteriolar or precapillary locus is assumed.^{10,24} In all animal studies critical closing pressures higher than venous pressures were found.^{25,26} From stop-flow experiments in animals, such local Pcc to venous pressure gaps were reported for brain,^{27,28} kidneys²⁹ and coronaries.⁸ Importantly, the organ-specific Pcc values are often different reflecting organ-specific vascular flow control.

Why are there waterfalls, and what is their purpose? First, since different organs may have different Pcc values, with the heart and the brain probably having lower Pcc values than muscle, kidney and gut, they allow for vital organ perfusion at lower Pa values.

Furthermore vital organ perfusion is maintained transiently during stop-flow conditions. After cardiac arrest arterial blood pressure will be reduced to Pcc. Because Pcv slowly increases to the level of Pmsf, a pressure gradient (between Pcc and Pmsf) will be preserved for some time. Thus at least temporarily some flow and perfusion pressure is maintained to the brain and heart. Indeed during ventricular fibrillation in pigs, flow in the left carotid artery was preserved at a low level for minutes.³⁰ Second, and perhaps more importantly, short-lasting changes in Pcv induced by intrathoracic pressure changes (by inspiration, coughing or Valsalva maneuvers) will only affect the downstream portion of the waterfall, thereby maintaining the stability of circulatory flow from the arteries into the organs. Only after some time, will an increase in Pcv decrease venous return and thus CO.²⁴

Although the size of the study group was small, the gap between Pmsf and Pcc was large in every patient during baseline conditions and after intravascular volume expansion. Because only cardiac surgery patients with relative intact ventricular function were included, these conclusions may not carry the same magnitude of interrelation in patients with impaired ventricular function. The small size of the study population did not allow conclusion on subgroups as responders and nonresponders to the intravascular fluid administration as all our subjects increased CO in response to intravascular volume administration.

Conclusions

With our bedside measurement of Pcc and Pmsf we showed that there is a systemic vascular waterfall in cardiac surgery patients and the practitioner is now able to estimate Ra and Rv separately. The vascular waterfall is not affected by intravascular fluid administration. Furthermore, because of this vascular waterfall in excess of 25 mmHg estimations of vasomotor tone using calculations of systemic vascular resistance will both overestimate actual vasomotor tone and may not accurately represent changes in vasomotor tone.

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Figure 1.

Effects of an inspiratory hold maneuver on arterial pressure (Prad), central venous pressure (Pcv), airway pressure (Pvent) and beat to beat cardiac output (COMf). Preceding the hold maneuver the effects of a normal ventilatory cycle are plotted. Note the rapid restoration to baseline (within 4 seconds).

Figure 2.

Relationship between cardiac output (CO) and central venous pressure (Pcv) in a venous return curve and between CO and arterial blood pressure (Pa) in a ventricular output curve for an individual patient. Extrapolation to the zero-flow intercept leads to mean systemic filling pressure (Pmsf) for the venous return curve and to critical closing pressure (Pcc) for the ventricular output curve.

Figure 3.

Relationship between arterial vascular resistance (R_a) and total systemic vascular resistance (R_s). R_a is calculated as (mean arterial blood pressure - critical closing pressure)/cardiac output. R_s is calculated as (mean arterial blood pressure - central venous pressure)/cardiac output. The filled squares represent measurements at baseline, the open squares represent measurements after intravascular volume administration.

Figure 4.

Schematic graph of the pressure trend from arterial blood pressure (P_a) to critical closing pressure (P_{cc}), mean systemic filling pressure (P_{msf}) to venous pressure (P_v). The pressure decrease between P_{cc} and P_{msf} (the vascular waterfall) shows that total systemic vascular resistance (R_s) does not exist. Instead vascular resistance can be divided in a resistance upstream of the waterfall (arterial resistance R_a) and downstream (venous resistance R_v). The dotted line between the waterfall and P_{msf} indicates that it is unknown how close to the waterfall P_{msf} is located.

Table 1

Patient characteristics

No	Sex	Age (yrs)	Weight (kg)	Length (cm)	Surgery	Inotropics ($\mu\text{g kg}^{-1} \cdot \text{min}^{-1}$)	Propofol (mg h^{-1})	Sufentanil ($\mu\text{g h}^{-1}$)
1	M	60	80	172	CABG		300	15
2	M	57	78	169	CABG	Dobu 2	300	15
3	M	79	78	174	AVR	Dobu 5	200	10
4	M	50	90	190	AVR	NPN 0.25	300	15
5	M	80	90	172	CABG	Nor 0.01	200	10
6	F	64	83	167	CABG	Nor 0.04, Dobu 3	200	10
7	M	50	112	183	CABG	Nor 0.06	500	15
8	M	71	73	179	CABG	Nor 0.09, Dobu 5	120	5
9	M	75	95	173	CABG		300	10
10	M	56	69	175	MVP+TVP	Nor 0.06	170	10
mean		64	85	175			259	12
SD		11	12	7			107	3

CABG, coronary artery bypass grafting; AVR, aortic valve replacement; MVP+TVP, mitral valve and tricuspid valve repair; Dobu, dobutamine; NPN, nitroprusside sodium; Nor, norepinephrine; SD, standard deviation.

Table 2
Venous return and ventricular output curves for all individuals before and after 500 ml intravascular fluid administration

No	Baseline slope				After 500 mL intravascular fluid administration			
	Pmsf	R ²	Pmsf	Pec	Pmsf	R ²	Pec	Pec
	L·min ⁻¹ ·mmHg ⁻¹		L·min ⁻¹ ·mmHg ⁻¹	mmHg	L·min ⁻¹ ·mmHg ⁻¹		mmHg	mmHg
1	-0.548	0.996	15.5	0.145	0.949	0.983	28.7	60.6
2	-0.440	0.995	21.2	0.195	0.894	0.999	24.4	42.5
3	-0.663	0.989	16.0	0.132	0.997	0.987	27.4	45.5
4	-0.198	0.997	19.6	0.054	0.990	0.999	29.0	61.8
5	-0.454	0.994	19.2	0.170	0.996	0.988	19.6	43.3
6	-0.587	0.937	15.3	0.166	0.997	0.972	24.3	62.5
7	-0.565	0.995	14.1	0.130	0.996	0.769	27.8	46.4
8	-0.459	0.971	28.0	0.262	0.978	0.985	30.5	59.0
9	-0.257	0.997	19.2	0.091	0.956	0.956	24.2	53.9
10	-0.211	0.911	18.6	0.055	0.992	0.997	27.0	39.5
Mean	-0.438	0.978	18.7	0.140	0.974	0.964	26.3	51.5
SD	0.164	0.030	4.0	0.064	0.033	0.070	3.2	9.0

Pmsf, mean systemic filling pressure; Pec, critical closing pressure; SD, standard deviation.

Table 3
Hemodynamic data of patients at baseline condition and after intravascular volume expansion

	Baseline		Volume expansion		p
	mean	SD	mean	SD	
Pa (mmHg)	85.5	15.4	91.4	13.5	0.059
Pev (mmHg)	4.8	1.8	7.1	2.6	0.011
CO (l·min ⁻¹)	5.5	1.8	6.8	1.8	0.010
HR (min ⁻¹)	91	13	88	10	0.149
SV (ml)	61.5	20.2	78.5	18.7	0.012
PP (mmHg)	61.0	15.0	75.4	15.9	0.001
Pec (mmHg)	45.5	11.1	51.5	9.0	0.013 ^a
Pmsf (mmHg)	18.7	4.0	26.3	3.2	<0.001
Slope VO (l·min ⁻¹ ·mmHg ⁻¹)	0.140	0.064	0.205	0.135	0.046
Slope VR (l·min ⁻¹ ·mmHg ⁻¹)	-0.438	0.164	-0.408	0.125	0.450
Pcc-Pmsf (mmHg)	26.8	10.7	25.2	8.2	0.454
Pmsf-Pev (mmHg)	13.8	4.0	19.2	3.1	<0.0001
Rs (mmHg·min·l ⁻¹)	16.56	8.57	13.49	5.77	0.028
Ra (mmHg·min·l ⁻¹)	8.27	4.45	6.54	3.67	0.008
Rv (mmHg·min·l ⁻¹)	2.75	1.23	3.00	1.01	0.350

Values are means ± SD; n=10 patients. Pa, mean arterial blood pressure; Pev, central venous pressure; Pmsf, mean systemic filling pressure; Pcc, critical closing pressure; Pmsf-Pev, venous return curve; VR, venous return curve; RS, total systemic vascular resistance; Ra, arterial vascular resistance; Rv, venous vascular resistance. Statistical comparison, p, paired t-test between baseline and volume expansion;

^aWilcoxon signed ranks test.