Chapter 8

Determination of vascular waterfall phenomenon by bedside measurement of mean systemic filling pressure and critical closing pressure in the ICU

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Abstract

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 Pcc > Pmsf then a vascular waterfall exists. The purpose of this study was to assess the existence of a waterfall and its implications for the calculation of vascular resistances by determining mean systemic filling pressure (Pmsf) and critical closing pressure (Pcc) at the bedside. 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. 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 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 $l \cdot min^{-1}$). Arterial (upstream of Pcc) and venous (downstream of Pmsf) vascular resistance were 8.27 ± 4.45 and 2.75 ± 1.23 $mmHg \cdot min \cdot l^{-1}$; the sum of both (11.01 $mmHg \cdot min \cdot l^{-1}$) was significantly different from total systemic vascular resistance (16.56 ± 8.57 $mmHg \cdot min \cdot l^{-1}$, $p = 0.005$). Arterial resistance was related to total resistance.

In conclusion, vascular pressure gradients in cardiac surgery patients suggest the presence of a vascular waterfall phenomenon, which is not effected 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 periods, venous return and cardiac output 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 upstream 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 rises and CO declines to a steady-state level (figure 8.1). From the values of Pcv and CO at different airway pressures, a venous return curve can be constructed (figure 8.2). 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 (Rvr), 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 during 20 seconds.[9] This stop-flow Pa value is termed 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 Rsys = [Pa-Pcv]/CO. However, this construct taken from 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 two separate

pressure gradients, one arterial pressure 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 Rvr.
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 loading will increase Pmsf and CO but not change Pcc.

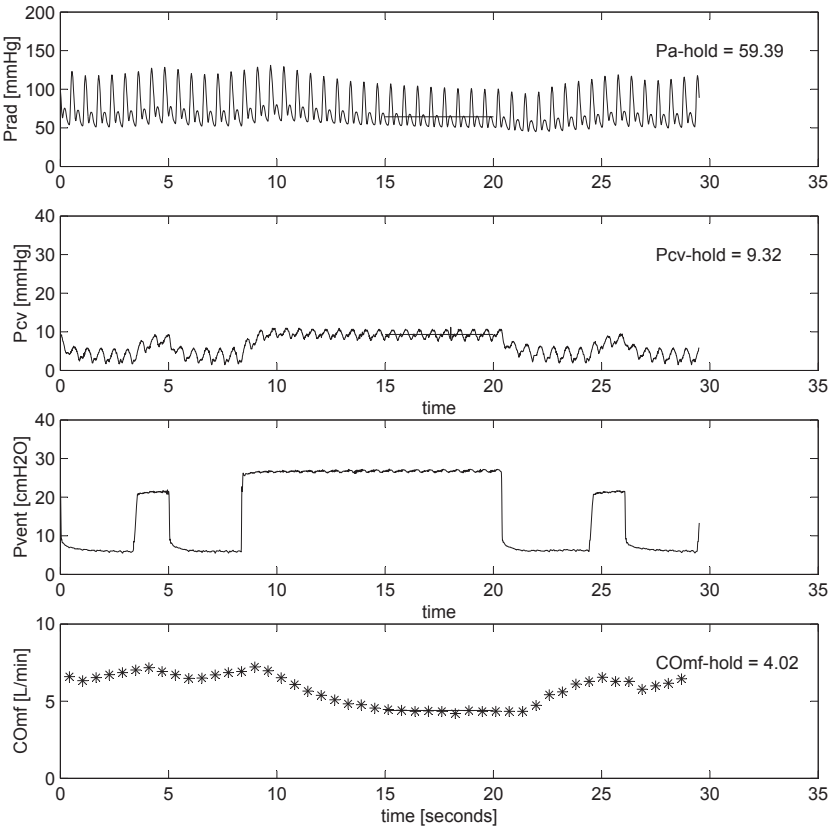

Figure 8.1 Example of an inspiratory hold maneuver
Effects of an inspiratory hold maneuver on arterial pressure (Prad), central venous pressure (Pcv), airway pressure (Pvent) and beat-to-beat cardiac output (COmf). Preceding the hold maneuver the effects of a normal ventilatory cycle are plotted. Note the rapid restoration to baseline (within 4 seconds).

Methods and materials

Patients. 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. Written informed consent was obtained from the patients. 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 intra-aortic balloon counter-pulsation were excluded.
Postoperative anesthesia was maintained with propofol and sufentanil. Patient's lungs were mechanically ventilated (Evita 4 servo ventilator; Dräger, Lübeck, Germany) in synchronized intermittent mandatory ventilation mode with tidal volumes of 6 to 8 $ml \cdot kg^{-1}$ and a respiratory rate of 12 to 14 $breaths \cdot min^{-1}$ to achieve normocapnia (arterial P_{CO2} between 40 and 45 mmHg). A positive end-expiratory pressure of 5 cmH_2O and a fraction of inspired oxygen of 0.4 were applied. During the study period, all patients were hemodynamically stable and no changes in vasoactive medication were made.

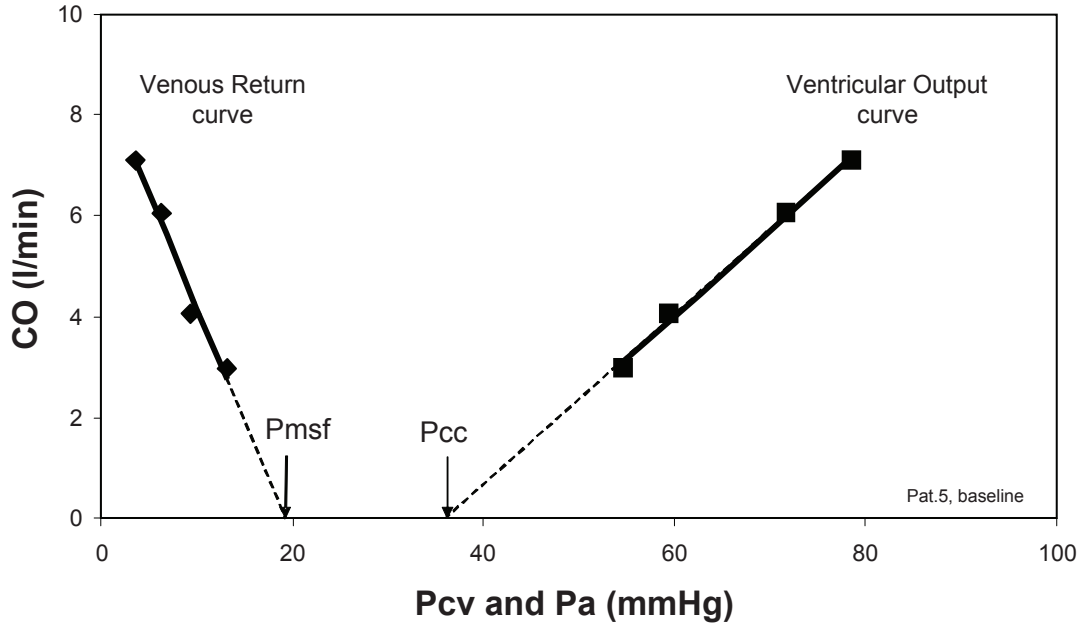

Figure 8.2 Venous return curve and cardiac function curve
Relationship between cardiac output (CO) and central venous pressure (Pcv) in a venous return curve and between CO and arterial blood pressure (Pa) in a ventricular output curve for an individual patient. Extrapolation to the zero flow intercept leads to mean systemic filling pressure (Pmsf) for the venous return curve and to critical closing pressure (Pcc) for the ventricular output curve.

Measurements. Arterial blood pressure was monitored via a 20-gauge, 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, Irvine, CA) 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]

Experimental protocol. 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, fraction of inspired oxygen, 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 cmH_2O, as we previously described.[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 8.1). 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 8.2). Similarly, in a ventricular output curve, Pa was plotted against CO for the same inspiratory hold maneuvers (figure 8.2). Measurements were done during baseline conditions and after administration of 500 ml hydroxyethylstarch (130/0.4) over 15 minutes to assess changes in CO, Pcc, and Pmsf after volume expansion for each patient.

Data analysis and statistics. 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 8.2). 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 the pairwise differences for Rsys and the sum of Rvr 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 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 Rvr = [Pmsf-Pcv]/CO. Total systemic vascular resistance was calculated as Rsys = [Pa-Pcv]/CO. The difference between Rsys and the sum of Ra and Rvr, reflecting the hydrostatic energy loss across the vascular waterfall, was tested with a Wilcoxon signed rank test. Linear regression between Ra and Rsys include 95% confidence interval (CI) for bias and slope, together with the Pearson correlation. The changes in CO, Pmsf, Pcc, the gap between Pcc and Pmsf, Ra, Rvr and the slopes of both the venous return and the ventricular output curves induced by intravascular volume expansion were tested by paired Student t-tests or Wilcoxon signed rank test as indicated by the Lilliefors test for normality. Data are presented as mean ± SD. Differences with a $p < 0.05$ were considered significant.

Results

Ten patients were included in the study. Patient characteristics are shown in table 8.1. The data of the venous return and ventricular output curves for all individuals before and after 500 ml intravascular fluid administration are shown in table 8.2. 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.

Table 8.1 Patient Characteristics

No	Gender	Age (years)	Weight (kg)	Length (cm)	Surgery	Inotropics ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	Propofol ($mg \cdot h^{-1}$)	Sufenta ($\mu g \cdot h^{-1}$)
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 4	120	5
9	M	75	95	173	CABG	Nor 0.02	200	10
10	M	56	69	175	MVP+TVP		300	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 and tricuspid valve repair; Dobu, dobutamine; NPN, nitroprusside sodium; Nor, norepinephrine; SD, standard deviation.

Table 8.2 Venous return and ventricular output curves for all individuals before and after 500 ml intravascular fluid administration

	Baseline						After 500 ml fluid loading					
No	Slope Pmsf ($l \cdot min^{-1} \cdot mmHg^{-1}$)	R^2	Pmsf (mmHg)	Slope Pcc ($l \cdot min^{-1} \cdot mmHg^{-1}$)	R^2	Pcc (mmHg)	Slope Pmsf ($l \cdot min^{-1} \cdot mmHg^{-1}$)	R^2	Pmsf (mmHg)	Slope Pcc ($l \cdot min^{-1} \cdot mmHg^{-1}$)	R^2	Pcc (mmHg)
1	-0.548	0.996	15.5	0.145	0.949	38.7	-0.371	0.983	28.7	0.284	0.987	60.6
2	-0.440	0.995	21.2	0.195	0.894	37.3	-0.612	0.999	24.4	0.245	0.995	42.5
3	-0.663	0.989	16.0	0.132	0.997	38.4	-0.469	0.987	27.4	0.168	0.995	45.5
4	-0.198	0.997	19.6	0.054	0.990	66.1	-0.193	0.999	29.0	0.064	0.941	61.8
5	-0.454	0.994	19.2	0.170	0.996	36.4	-0.429	0.988	19.6	0.164	0.987	43.3
6	-0.587	0.937	15.3	0.166	0.997	58.2	-0.482	0.972	24.3	0.138	0.973	62.5
7	-0.565	0.995	14.1	0.130	0.996	38.5	-0.434	0.769	27.8	0.186	0.736	46.4
8	-0.459	0.971	28.0	0.262	0.978	53.8	-0.491	0.985	30.5	0.542	0.977	59.0
9	-0.257	0.997	19.2	0.091	0.956	52.4	-0.373	0.956	24.2	0.169	0.965	53.9
10	-0.211	0.911	18.6	0.055	0.992	35.3	-0.224	0.997	27.0	0.089	0.881	39.5
mean	-0.438	0.978	18.7	0.140	0.974	45.5	-0.408	0.964	26.3	0.205	0.944	51.5
SD	0.164	0.030	4.0	0.064	0.033	11.1	0.125	0.070	3.2	0.135	0.081	9.0

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

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 ($l \cdot min^{-1} \cdot mmHg^{-1}$) and of 0.140 ± 0.064 ($l \cdot min^{-1} \cdot mmHg^{-1}$), respectively. In table 8.3, 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 16.1–46.48 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, total systemic vascular resistance (Rsys) would have been calculated as 16.56 ± 8.57 $mmHg \cdot min \cdot l^{-1}$. However, considering a waterfall, Ra was 8.27 ± 4.45 $mmHg \cdot min \cdot l^{-1}$, Rvr was 2.75 ± 1.23 $mmHg \cdot min \cdot l^{-1}$, and the sum of Ra and Rvr was 11.01 ± 5.52 $mmHg \cdot min \cdot l^{-1}$, which is significantly different from Rsys ($p = 0.005$) and reflects at least a 30% hydrodynamic energy loss across the vascular waterfall.

Table 8.3 Hemodynamic data of patients during baseline condition and after intravascular volume expansion

	Baseline Mean	SD	Hyper Mean	SD	p
Pa (mmHg)	85.5	15.4	91.4	13.5	0.059
Pcv (mmHg)	4.8	1.8	7.1	2.6	0.011
COmf ($l \bullet min^{-1}$)	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
Pcc (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 ($l \bullet min^{-1} \bullet mmHg^{-1}$)	0.140	0.064	0.205	0.135	0.046
Slope VR ($l \bullet min^{-1} \bullet mmHg^{-1}$)	-0.438	0.164	-0.408	0.125	0.450
Pcc-Pmsf (mmHg)	26.8	10.7	25.2	8.2	0.454
Pmsf-Pcv (mmHg)	13.8	4.0	19.2	3.1	< 0.0001
Rsys ($mmHg \bullet min \bullet l^{-1}$)	16.56	8.57	13.49	5.77	0.028
Ra ($mmHg \bullet min \bullet l^{-1}$)	8.27	4.45	6.54	3.67	0.008
Rvr ($mmHg \bullet min \bullet l^{-1}$)	2.75	1.23	3.00	1.01	0.350

Values are means ± SD; n = 10 patients. Pa, mean arterial pressure; Pcv, central venous pressure; CO, cardiac output; HR, heart rate; SV, stroke volume; PP, pulse pressure (systolic pressure – diastolic pressure); Pcc, critical closing pressure Pmsf, mean systemic filling pressure; VO, ventricular output curve; VR, venous return curve; Rsys, total systemic vascular resistance; Ra, arterial vascular resistance Rv, venous vascular resistance. Statistical comparison, p, paired t-test between baseline and volume expansion; [a] Wilcoxon signed rank test.

Volume loading. Pmsf, Pcv, Pcc and CO increased with intravascular volume administration as did the pressure gradient for venous return (Pmsf-Pcv) (table 8.3). 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, whereas the slope of the venous return curve and its calculated Rvr

did not change significantly.
We investigated a possible relation between Rsys and Ra, because Rsys and Ra significantly changed whereas Rvr did not change with intravascular fluid administration. The results of individual data are indicated in figure 8.3. The relation between Ra and Rsys (Ra = 0.52(95%CI 0.44-0.62) • Rsys–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 seconds[7] 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-Assenmacher *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 on heart beating data, i.e. on the aortic pressure decay, these authors found a significant higher value (53 ± 15.6 mmHg). The Pcc value of 45.5 ± 11.1 mmHg in our study is in the range Kottenberg-Assenmacher *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-Assenmacher *et al.* report.[6-8] In animal stop-flow studies, the pressure gap between arterial and venous pressure was already well known and the reason for using a pump or large arteriovenous fistula to move blood from the arterial compartment to the venous compartment 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.

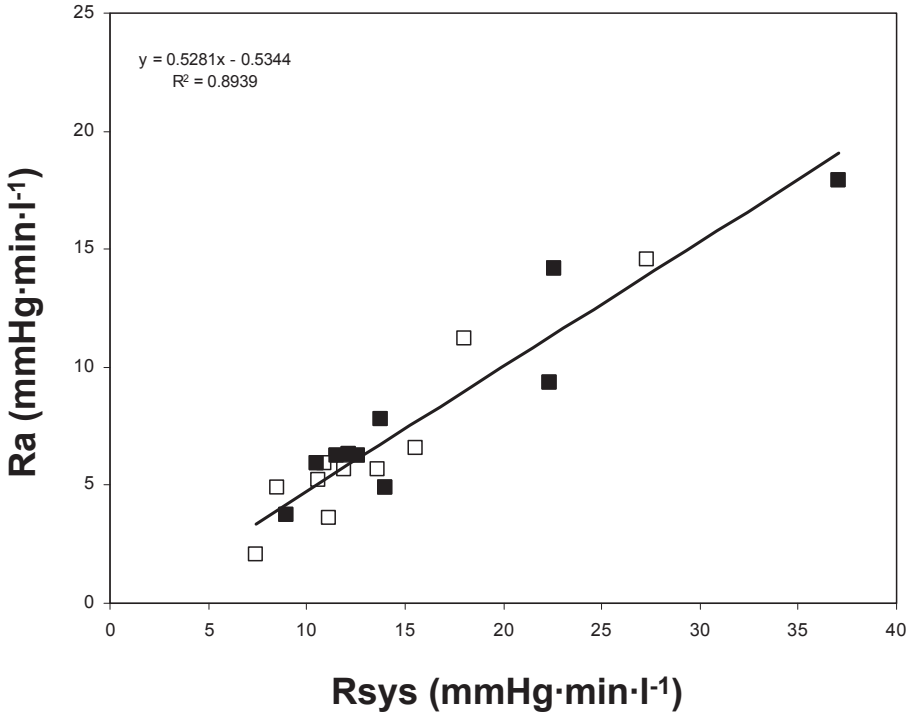

Figure 8.3 Relationship between arterial vascular resistance (Ra) and total systemic vascular resistance (Rsys)
Ra is calculated as (mean arterial pressure - critical closing pressure)/cardiac output. Rsys is calculated as (mean arterial pressure – central venous pressure)/cardiac output. The filled squares represent measurements at baseline, the open squares represent measurements after volume loading.

Vascular resistance. Classically, Rsys is calculated as the ratio of the pressure difference between mean Pa and mean Pcv, and CO. Kottenberg-Assenmacher *et al.*[8] already pointed out that Rsys has to be partitioned into an Ra and an Rvr, 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 Rvr = [Pmsf-Pcv]/CO. Based on our findings, we conclude that Rsys is an entity that does not exist in vascular physiology and calculated Rsys overestimates the sum of Ra and Rvr. In figure 8.4, a dotted line is plotted directly after the waterfall, because it is not known whether the waterfall ends directly in vascular lacunae (where Pmsf is located). Furthermore, we have no information about the presence of parallel blood streams to the waterfall. However, if the clinician at the bedside wants to understand if 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 8.3). Measurement of Pcc and Pmsf and calculation of Ra and Rvr allows us to understand physiology and the point of action of vasoactive medication and in future could guide the clinician in the hemodynamic treatment of critically ill patients.

Influence of volume expansion. The response to volume loading 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 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 finding are also consistent with baroreceptors-induced arterial vasodilation.

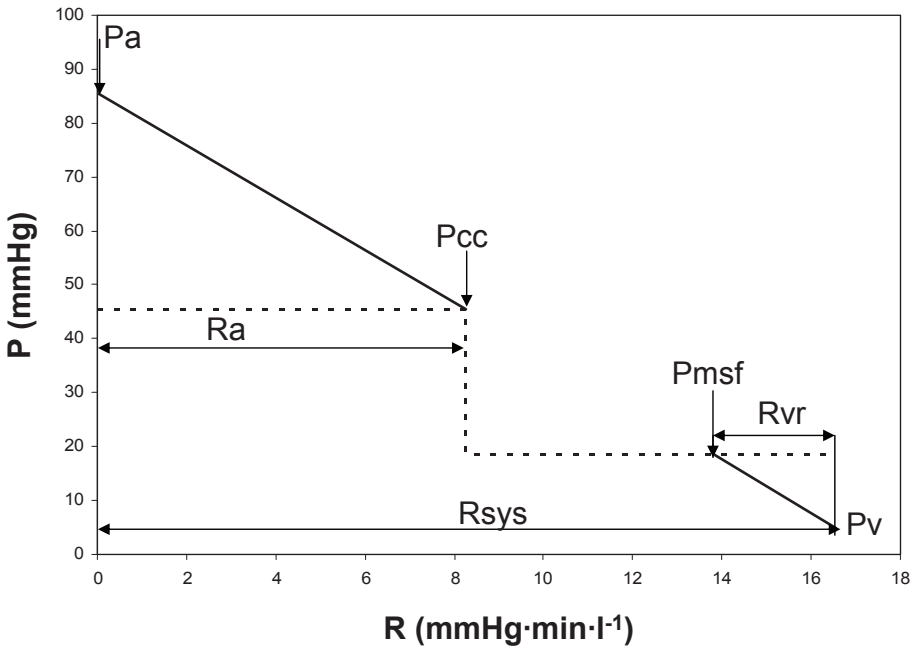

Figure 8.4 Schematic graph of the pressure trend from arterial blood pressure (Pa) to critical closing pressure (Pcc), mean systemic filling pressure (Pmsf) to venous pressure (Pv)
The pressure drop between Pcc and Pmsf (the vascular waterfall) shows that total systemic vascular resistance (Rsys) does not exist. Instead vascular resistance can be divided in a resistance upstream of the waterfall (arterial resistance Ra) and downstream (venous resistance Rvr). The dotted line between the waterfall and Pmsf indicates that it is unknown how close to the waterfall Pmsf is located.

Methodological issues. 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 8.1 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 be 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 Guyton[1], 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 8.2). However, during the inspiratory holds of 35 cmH_2O in some patients cardiac output 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.

Waterfalls, where are they 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], kidneys[29], and coronaries.[8] Importantly, the organ-specific Pcc values are often different, reflecting organ specific vascular flow control.
Why are there vascular waterfalls,and what is their purpose? First, because 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]

Limitations. Although the size of the study group was small, the gap between Pmsf and Pcc was large in every patient during baseline conditions and following intravascular volume expansion. Because only cardiac surgery patients with relative intact ventricular function were included, these conclusions may not carry the same magnitude of inter-

relation 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 Rvr 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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