Chapter 3

Assessment of venous return curve and mean systemic filling pressure in postoperative cardiac surgery patients

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Abstract

With the determination of the relationship between blood flow and central venous pressure (Pcv) mean systemic filling pressure (Pmsf), circulatory compliance and stressed volume can be estimated in patients in the intensive care unit (ICU). We measured the relationship between blood flow and Pcv using 12-second inspiratory hold maneuvers transiently increasing Pcv to three different steady-state levels and monitored the resultant blood flow via the pulse contour method during the last 3 seconds in twelve mechanically ventilated postoperative cardiac surgery patients in the intensive care unit. Inspiratory holds were performed during normovolemia in supine position (baseline), relative hypovolemia by placing the patients in 30° head-up position (hypo), and relative hypervolemia by volume loading with 0.5 l colloid (hyper). The Pcv to blood flow relation was linear for all measurements with a slope unaltered by relative volume status. Pmsf decreased with hypo and increased with hyper (18.8 ± 4.5 mmHg, to 14.5 ± 3.0 mmHg, to 29.1 ± 5.2 mmHg [baseline, hypo, hyper, respectively, $p < 0.05$)]. Baseline total circulatory compliance was 0.98 $ml \cdot mmHg^{-1} \cdot kg^{-1}$ and stressed volume was 1677 ml. In conclusion, Pmsf can be determined in intensive care patients with an intact circulation with use of inspiratory pause procedures, making serial measures of circulatory compliance and circulatory stressed volume feasible.

Introduction

The cardiovascular system is a closed circuit with varying blood flow out of the heart into the arterial system (cardiac output [CO]) and flow back to the heart from the venous system (venous return [VR]), which may not be equal at any point in time owing to ventilation-induced changes in venous return, but which over time must be equal.[1,2] Thus, under steady-state apneic conditions CO and VR become equal. Guyton *et al.*[3,4] showed that the relationship between stepwise changes in right atrial pressure (Pra) and the resulting changes in VR describes a VR curve, which itself is a function of the circulating blood volume, vasomotor tone and blood flow distribution. Importantly, Pra at the extrapolated zero-flow pressure intercept reflects mean systemic filling pressure (Pmsf) and the slope of this relation describes the resistance for venous return (Rvr).[3,5] This relationship between Pra and VR was well described in animal models with an artificial circulation[4], in patients during stop-flow conditions[6], and in animals with an intact circulation using invasive hemodynamic monitoring.[7-10] However, it has never been evaluated in humans with an intact circulation. If such VR curves could be easily calculated at the bedside, then complex cardiovascular analysis would be feasible, thereby, augmenting greatly our understanding of the dynamic determinants of circulatory insufficiency states and their responses to therapies. Intravascular blood volume can be divided in unstressed volume (the blood volume necessary to fill the blood vessels without generating an intravascular pressure) and stressed volume (the blood volume which generates the intravascular pressure, which is Pmsf in no-flow conditions).

Previously, Pinsky[7] constructed instantaneous VR curves based on the beat-to-beat changes in Pra and simultaneously measured right ventricular output during a single mechanical breath, neglecting possible transient effects of increasing Pra on VR.[1,2] Versprille and Jansen[8] prevented these transient changes by measuring Pra and right ventricular output during steady-state conditions generated by ventilator-applied inspiratory pause periods at different inflation volumes. Unfortunately, it is difficult to measure pulmonary blood flow on a beat-to-beat basis at the bedside. We hypothesized that if inspiratory hold maneuvers that increase Pra create a new steady state, then VR and CO would again be equal and direct measures of left-sided CO could be used to estimate steady-state VR.

Thus, we studied the effect of 12-second inspiratory hold maneuvers on the relation between central venous pressure (Pcv), as a surrogate for Pra, and arterial pulse contour-derived cardiac output (COmf), as a surrogate for VR, as Pcv was varied by inspiratory hold maneuvers and intravascular volume status altered by a head-up tilt body position (relative hypovolemia) and intravascular volume loading (hypervolemia).

Materials and methods

Patients. Twelve postoperative patients after elective coronary artery bypass surgery

or aortic valve replacement were included in the study after approval by the university medical ethics committee and patient's informed consent was obtained. All patients had symptomatic coronary artery disease without previous myocardial infarction and were on beta-adrenergic blocking medication. Patients with congestive heart failure (New York Heart Association class 4), aortic aneurysm, extensive peripheral arterial occlusive disease, or postoperative valvular insufficiency, were not considered for this study. Patients with postoperative arrhythmia or the necessity for artificial pacing, or use of a cardiac assist device were also excluded.

Anesthesia during surgery was maintained with sufentanil and propofol and patients were ventilated in synchronized intermittent mandatory ventilation mode (Evita 4 servo ventilator Dräger, Lübeck, Germany) adjusted to achieve normocapnia (arterial pCO_2 between 40 and 45 mmHg) with tidal volumes of 6-8 $ml \cdot kg^{-1}$ and a respiratory rate of 12-14 $breaths \cdot min^{-1}$. Fraction of inspired oxygen (FiO_2) was 0.4 and a positive end-expiratory pressure of 5 cmH_2O was applied. A hemodynamic stability was achieved using fluids and catecholamines. During the study interval all subjects were hemodynamically stable and no changes were made in their vasoactive drug therapy. Every patient experienced full recovery from anesthesia within 8 hours following surgery and was discharged from intensive care unit on the first postoperative day.

Measurements. Arterial blood pressure (Pa) was monitored via a 20-G, 3.8-cm long radial arterial catheter inserted by Seldinger technique and connected to a pressure transducer (PX600F, Edwards Lifesciences). Pcv was measured with a central venous catheter inserted through the right internal jugular vein (MultiCath 3 venous catheter, Vigon GmbH & Co, Aachen, Germany) and connected to a pressure transducer (PX600F, Edwards Lifesciences). Both Pa and Pcv transducers were referenced to the intersection of the anterior axillary line and the fifth intercostal space. Airway pressure (Pvent) was measured at the entrance of the endotracheal tube. Pvent was balanced at zero level against ambient air. Standard electrocardiogram leads were used to monitor heart rate. Beat-to-beat CO was obtained by Modelflow (COmf) pulse contour analysis as previously described by us.[11-13] We calibrated the pulse contour CO measurements with 3 thermodilution CO measurements equally spread over the ventilatory cycle.[12]

Experimental protocol. Before starting the protocol, the mechanical ventilation mode was switched to airway pressure release ventilation with the same rate, FiO_2, and positive end-expiratory pressure level. Inspiration pressure was adapted to have the same gas exchange as in SIMV mode. This change in ventilation mode allowed external control of the ventilatory process. We developed a computer program to drive the ventilator. During the observation period ventilator settings, sedation and vasoactive medications remained unchanged. No spontaneous breathing movements were observed during the study. Pa, Pcv and Pvent were recorded on computer disk for offline data analysis at a sample frequency of 100 Hz and 0.2 mmHg resolution.

We constructed VR curves by measuring steady-state Pa, Pcv and COmf over the final 3 seconds for a set of four 12-second inspiratory hold maneuvers at Pvent plateau pressures of 5, 15, 25, 35 cm H_2O. The inspiratory hold maneuvers were separated by 1-minute intervals to reestablish the initial hemodynamic steady state. An example of the hemodynamic changes during an inspiratory hold is presented in figure 3.1. When Pvent increases, Pcv increases concomitantly, whereas COmf and Pa decrease with a delay of three-four beats, reaching a steady state between 7 and 12 seconds after start of inflation. From the steady-state values of Pcv and COmf during the four inspiratory pause periods, a VR curve was constructed by fitting a linear regression line through these data points (figure 3.2).

The four inspiratory hold maneuvers were performed under three sequential volumetric conditions: initial baseline conditions (baseline) with the subject lying supine, relative hypovolemia by rotating the bed to a 30 degree head-up (anti-Trendelenburg) position (hypo) and after administration of 500 ml hydroxyethyl starch (130/0.4) in supine position (hyper). Measurements were done 2 minutes after head-up tilt and 2-5 minutes after the fluid bolus, which was given in 15-20 minutes.

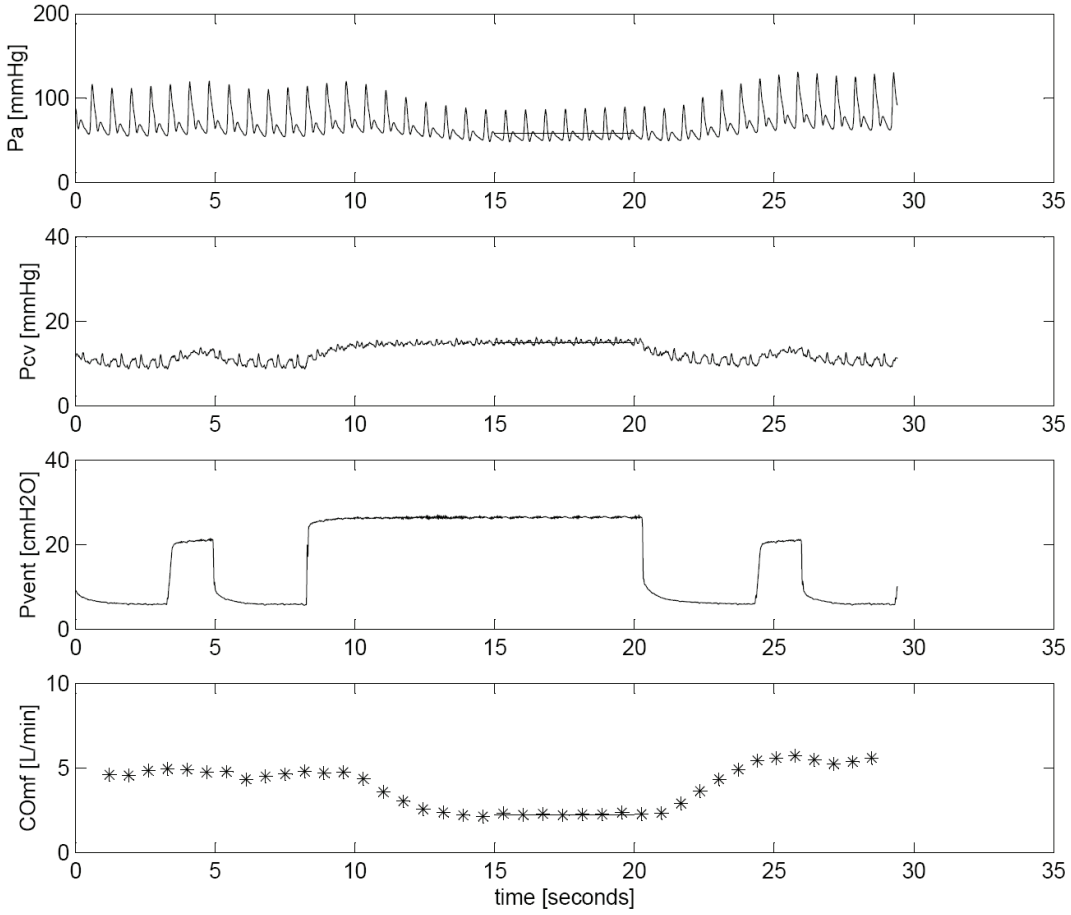

Figure 3.1 Example of an inspiratory hold maneuver

Effects of an inspiratory hold maneuver on arterial pressure (Pa), 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.

Data analysis and statistics. We fitted the set of four data points of Pcv and COmf by linear regression for each volume state to define the VR curve. We defined Pmsf as the extrapolation of this linear regression to zero flow (figure 3.2), assuming that Pvent does not affect Pmsf. We have previously validated this extrapolation in piglets.[8-10] Total systemic vascular resistance (Rsys) was calculated as the ratio of the pressure difference between mean Pa and mean Pcv and COmf (Rsys = (Pa - Pcv)/COmf). The resistance downstream of Pmsf was taken to reflect the Rvr and was calculated as the ratio of the pressure difference between Pcv and Pmsf and COmf (Rvr = (Pmsf-Pcv)/COmf). Systemic arterial resistance (Ra) was taken to be the difference between systemic and venous resistance. The ratio of Rvr and Rsys describes the location within the circulation where Pmsf exists. A higher ratio implies a more upstream Pmsf location. Systemic compliance (Csys) was calculated by dividing the amount of fluid (Vload) administrated to induce the hyper state by the Pmsf difference between baseline and hyper (Csys = Vload /($Pmsf_{Hyper}$ –$Pmsf_{Baseline}$). We assume Csys to be constant for the three volemic conditions studied. Stressed vascular volume (Vs) was calculated as the product of Csys and Pmsf. We calculated Vs for all three relative volume conditions. Data are presented as mean ± SD. Linear regressions were fitted using a least-squares method. The changes between the three conditions were tested by a paired Student's *t* test, with differences corresponding to a $p < 0.05$ considered significant. We compared baseline to both hypo and hyper.

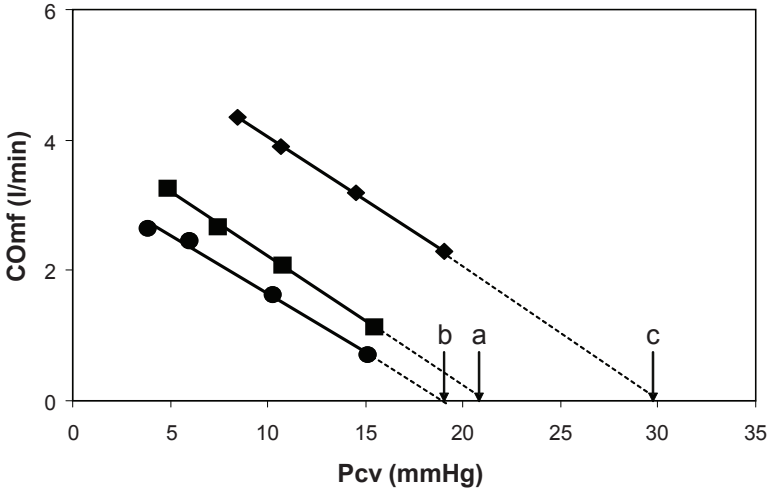

Figure 3.2 Venous return curves
Relationship between venous return (COmf) and central venous pressure (Pcv) for an individual patient. Venous return curves are plotted for three conditions, baseline (a), hypovolemia (b) and hypervolemia (c).

Results

Sixteen patients were recruited into the study, but four were excluded from analysis because they could not receive an additional volume challenge. Table 3.1 shows the patient characteristics and table 3.2 shows the pooled data of the 12 subjects who completed all three steps of the protocol.

Table 3.1 Patient Characteristics

No	Gender	Age (years)	Weight (kg)	Length (cm)	HR (min^{-1})	Pcv (mmHg)	CO ($l \cdot min^{-1}$)	mean Pa (mmHg)	Temp (˚C)	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	85	8.2	4.6	72	36.8	CABG		300	15
2	M	57	78	169	119	9.9	5.7	73	36.9	CABG	D 2	300	15
3	M	79	78	174	86	7.5	6.3	88	36.9	AVR	D 5	200	10
4	M	50	90	190	93	7.4	3.2	138	36.3	AVR	NPN 0.25	300	15
5	M	80	90	172	99	8.0	6.1	80	36.7	CABG	N 0.01	200	10
6	F	64	83	167	76	7.1	5.8	88	37.4	CABG	N 0.04, D 3	200	10
7	M	50	112	183	83	4.0	5.7	85	37.0	CABG	N 0.06	500	15
8	M	57	91	177	63	4.9	6.4	78	35.1	CABG		300	10
9	M	71	73	179	93	8.0	8.8	91	37.1	CABG	N 0.09, D 4	120	5
10	M	66	88	178	69	3.0	7.4	71	35.8	CABG	N 0.02	200	10
11	M	75	95	173	77	9.0	4.4	130	36.5	CABG		300	10
12	F	60	74	158	89	3.7	5.3	86	36.6	CABG	N 0.04, E 2	150	5
mean		64	86	174	86	6.7	5.8	90	36.6			256	11
SD		10	11	8	15	2.3	1.4	22	0.6			101	4

HR, heart rate; Pcv, central venous pressure; CO, cardiac output; mean Pa, mean arterial pressure; Temp, body temperature; CABG, coronary artery bypass grafting; AVR, aortic valve replacement; D, dobutamine; NPN, nitroprusside sodium; N, norepinephrine; E, enoximone.

Venous return curve analysis. Pcv and COmf decreased during hypo and increased during hyper. Similarly, Pmsf decreased during hypo and increased during hyper, whereas the slope of the VR (conductance) was not significantly different for the three conditions of baseline, hypo and hyper. The pressure gradient for VR did not change with hypo but increased with hyper such that Rvr was unchanged by hypo but increased with hyper. Importantly, Rsys, did not change. Thus, the estimated location of Pmsf was unchanged by hypo but migrated upstream with hyper.

Table 3.2 Hemodynamic data of patients during baseline, hypo- and hypervolemic condition

	Baseline Mean	SD	Hypo Mean	SD	p1	Hyper Mean	SD	p2
Pa (mmHg)	89.9	21.6	75.7	17.3	0.001	96.5	14.9	0.170
Pcv (mmHg)	6.72	2.26	4.02	2.12	0.001	9.67	2.63	0.007
COmf ($l \cdot min^{-1}$)	5.82	1.44	4.76	1.30	0.001	6.83	1.36	0.002
HR (min^{-1})	86.0	14.7	85.7	15.1	0.456	84.3	10.7	0.401
Slope ($l \cdot min^{-1} \cdot mmHg^{-1}$)	-0.465	0.151	-0.429	0.160	0.388	-0.389	0.135	0.134
Pmsf (mmHg)	18.76	4.53	14.54	2.99	0.005	29.07	5.23	0.001
Pvr (mmHg)	12.04	3.70	10.52	2.27	0.106	19.40	6.88	0.003
Rvr ($mmHg \cdot min \cdot l^{-1}$)	2.18	0.86	2.41	1.14	0.184	2.91	1.10	0.037
Rsys ($mmHg \cdot min \cdot l^{-1}$)	15.89	9.00	16.95	10.27	0.379	13.52	5.60	0.122
Rvr/Rsys (%)	14.94	5.00	14.84	2.37	0.931	22.62	8.07	0.006

Values are means ± SD; n = 12 patients. Pa, arterial pressure; Pcv, central venous pressure; COmf, cardiac output; HR, heart rate; Slope, slope of venous return curve; Pmsf, mean systemic filling pressure; Pvr, pressure difference between Pmsf and Pcv; Rvr, resistance for venous return; Rsys, resistance of the systemic circulation. Statistical comparison, p1, paired t-test between baseline and hypovolemic condition (hypo) and p2, paired t-test between baseline and hypervolemic condition (hyper).

Systemic compliance and stressed volume. The change in stressed volume vs. Pmsf is shown in figure 3.3. Assuming a constant compliance, the loss of stressed volume due to hypo is approximately 200 ml. On average, Csys was 80 ± 62 ml·mmHg^{-1} (0.98 ± 0.82 ml·mmHg^{-1}·kg^{-1} body weight) and stressed volume during baseline was 1677 ± 1643 ml (19.5 ± 12.1 ml·kg^{-1} body weight).

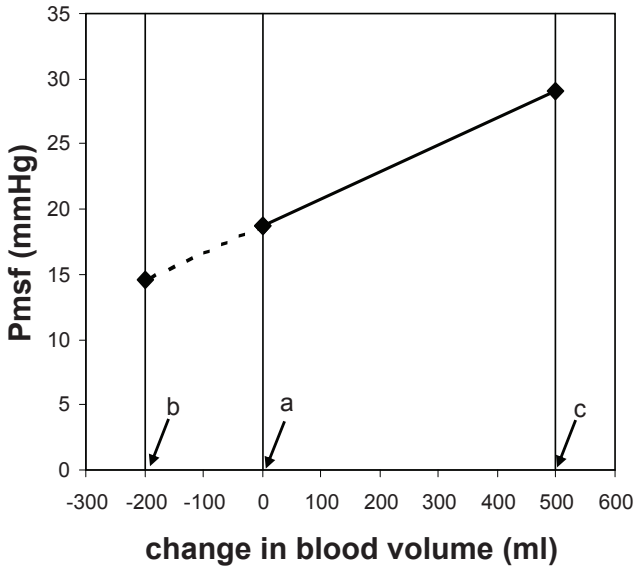

Figure 3.3 Pressure - volume curve
Relationship between change in blood volume and mean systemic filling pressure (Pmsf) for three conditions, baseline (a), hypovolemia (b) and hypervolemia (c). See text for discussion.

Discussion

Our study demonstrates that by using a simple inspiratory hold maneuver while simultaneously measuring Pcv and Pa, one can generate VR curves and derive their associated vascular parameters at the bedside. Our data suggest that volume-altering maneuvers (hypo and hyper) do not alter vascular conductance (slope of the VR curve). These clinical data are concordant with the long-described experimental data introduced by Guyton *et al.* over 50 years ago.[4,14] Importantly, our novel approach to assessing VR allows these analyses to be done at the bedside in patients after coronary artery bypass surgery or aortic valve replacement. Patients with congestive heart failure (New York Heart Association class 4), aortic aneurysm, extensive peripheral arterial occlusive disease, postoperative valvular insufficiency, postoperative arrhythmia, or the necessity for artificial pacing or use of a cardiac assist device were excluded from this study. It will be interesting to see how these vascular parameters change in different disease states, such as septic shock and heart failure, and how treatments alter them further because these analyses allow for the repetitive estimation of circulatory vascular compliance and effective circulatory blood volume.

Methodological issues. During an inspiratory pause period a new steady state was attained, which can be concluded from the plateau phase in the COmf, Pa and Pcv

(figure 3.1). In this example, the time needed to reach the plateau was approximately 7 seconds. This duration is too short to be associated with changes in autonomic tone which would otherwise occur owing to the decrease in Pa-induced baroreceptor-mediated increase in sympathetic tone. Samar and Coleman[15] showed in rats that a total circulatory stop, by pulmonary occlusion, caused a simultaneous decrease of arterial pressure and a rise in central pressure to an equal plateau pressure within 4-5 seconds. This was followed by a second rise in Pcv after 10-12 seconds of circulatory arrest in rats[15,16] and after 12-15 seconds in dogs.[17] The second rise was seen in unanesthetized rats and during methoxyflurane anesthesia, however, seldom seen with pentobarbital and inhibited by hexamethonium or spinal cord transaction.[18] Thus, any secondary increase in heart rate or Pcv was due to sympathetic reflex activation. We did not observe an increase in Pcv or heart rate during the last phase of our inspiratory pause, not even during pause pressures of 35 cm H_2O. Furthermore, all Pa values rapidly reached steady-state conditions within 7 seconds, making our analysis relatively free of the confounding effects of varying autonomic tone. However, our subjects were also receiving neurosuppressive agents (propofol and sufentanil) during the study interval, thus sympathetic responsiveness may have been blunted. Propofol depresses the baroreflex responses to hypotension and inhibits sympathetic nerve activity in healthy volunteers[19,20], whereas sufentanil might depress baroreceptor reflexes.[21] Thus, these studies will need to be repeated in nonanesthetized subjects to validate their usefulness in that population. Still, in the setting of general anesthesia, these findings appear valid.

During inflation venous capacitance is loaded due to an increase in Pcv, which leads to a transient reduction in VR, in right ventricular output and consequently in left ventricular output.[1,2] To avoid this effect on the relationship between VR and Pcv we measured Pcv and COmf during short periods of steady state following these initial non-steady-state conditions (figure 3.1). Our Pmsf estimation method by extrapolating the values of four pairs of Pcv and COmf obtained from four levels of inspiratory plateau pressures has several advantages. First, it allows the construction of Guyton-type VR curves with an intact circulation, an opportunity not presently available. Second, Pmsf can be determined without creating stop-flow conditions, such as stopping the heart by electrical fibrillation or injection of acetylcholine or by blocking the circulation. And third, Pmsf is not influenced by changes in lung or thorax compliance. Lung or thorax compliance affects the transfer of the applied Pvent to intra-thoracic pressures. Thus, during an inspiratory hold the resulting Pcv depends on these compliances. But, indeed, the measured Pcv and CO will always be on the same line in the VR plot. For instance, in a patient with stiffer lungs, during an inspiratory hold the transfer from Pvent to intra-thoracic pressure will be less, resulting in a smaller increase in Pcv and a smaller decrease in CO.

We assumed a linear relation between Pcv and COmf to extrapolate to the condition of

COmf is zero (figure 3.2). This assumption is based on the observation of linearity of the VR curves presented by Guyton and colleagues[4,14] and expressed by the mathematical relation VR = CO = (Pmsf – Pcv)/Rvr. Furthermore, this linearity has been confirmed in the intact circulation in several animal studies.[7-10,22,23] Our VR curves were best fitted with straight lines allowing extrapolating the venous return curve to flow zero. This linearity was neither affected by hypo nor hyper.

Our estimated Pmsf values are higher than those described in highly instrumented animals, which are in dogs 7-12.5 mmHg[4,7,14,17,24,25], rats 7-9 mmHg[15,16], pigs 10-12 mmHg[8-10], and as high as 20-30 mmHg in conscious calves implanted with an artificial heart.[26] We report baseline Pmsf values of 18.8 mm Hg in our cardiovascular surgical patients. A primary difference between the prior animal studies and our patient observations is the difference in baseline Pcv. In the animal studies, this value is close to zero whereas Pcv in our patient population is on average 6.7 mm Hg. If one assumes a similar Rvr, this Pcv pressure difference would extrapolate to a Pmsf of 12 mm Hg for our subjects if their Pcv was zero (see table 3.2). Thus, our Pmsf values are coupled with the increased Pcv.

Our present data seem to be in conflict with those of our previous study, wherein we demonstrated that inspiratory hold maneuvers did not decrease blood flow, as estimated by thermodilution pulmonary artery flow[27] despite an increase in Pcv. There were no differences between the two studies in terms of Pa (75 ± 15 versus 88 ± 18 mmHg), Pcv (9 ± 4 versus 8 ± 2 mmHg) and CO (5.7 ± 1.52 versus 5.6 ± 1.6 l·min^{-1}, previous to present mean pooled data, respectively). However, two major differences in the protocols exist. First, the inspiratory hold maneuver used by van den Berg *et al.*[27] had a temporarily higher inflation pressure at the beginning of the maneuver which was decreased to the steady-state plateau value, and second, the bolus thermodilution method was applied during the inspiratory pause in the first study whereas we used the Modelflow pulse contour CO method to measure instantaneous flow in the present one. Reexamination of the data of van den Berg *et al.*[27] suggests that the thermodilution injections might have been performed before the plateau in blood flow had been reached. If this were the case, then the thermodilution CO values would overestimate steady-state values, resulting in an underestimation of the slope of the VR curve. Furthermore, in their study[27] plateau pressures from 0 up to 19 cm H_2O were used whereas we used plateau pressures from 5 up to 35 cm H_2O, which are comparable to those used by Versprille and Jansen[8] in their animal experiments. The limited range of applied plateau pressures in the van den Berg study[27] might have hampered the construction of proper VR curves. Jellinek *et al.*[28] estimated in ten patients during episodes of apnea and ventricular fibrillation, induced for defibrillator testing, a mean Pmsf value of 10.2 mmHg and Schipke *et al.*[6] estimated a mean Pmsf value of 12 mm Hg in a similar group of 85 patients. However, both studies were done on highly anesthetized nonvolume resuscitated subjects. Our method

of estimation of Pmsf differs considerably from stopping flow by defibrillation of the heart and our method allows an estimation of Pmsf with intact circulation, applicable in the intensive care unit. Still, until paired comparisons of Pmsf are made using the two techniques (i.e., stop-flow and our method) in the same subjects direct comparisons and interpretation of the data can not be made.

Using these maneuvers to assess cardiovascular status. Moving patients from supine into a head-up tilt position shifts blood from the central compartment to the legs, creating a relative hypovolemic state as manifest by a decreasing Pmsf, Pcv and CO. Potentially, other conflicting processes could also be occurring simultaneously. As the blood volume shifted to the legs increase femoral venous pressure, venous vascular diameter will increase decreasing vascular resistance from the legs. The impact of the intra-abdominal volume shift off the diaphragm is less clear but may increase hepatic resistance if chest wall movement compresses the subdiaphragmatic liver. The results of these effects lead to no change in Rvr and a decrease in COmf, Pa, Pcv and Pmsf (table 3.2).

Volume loading creates relative hypervolemia which results in an increase of Pmsf, Pcv, CO and Pa. The higher CO can only be generated by a higher filling of the right atrium reflected in an increase of Pcv. Because the pressure gradient for VR is increased more than Rvr, CO increases (table 3.2).
Pmsf is the pressure at the midpoint of the vascular pressure drop from the aorta to the right atrium. In practice, it is usually located in the venules and is less than arteriolar pressure and more than Pcv but close to capillary-venule tissue pressure.[8,18] The localization of Pmsf within the circulation is a conceptual model at best, since it reflects a lumped parameter of all the vascular beds. However, its position in the pooled vascular beds will shift depending on changes in arterial and venous resistances as was pointed out by Versprille and Jansen.[8] Our data suggests that the vascular site for Pmsf exists in the range of the capillary-venule pressures, i.e. Rvr/Rsys = 15% (table 3.2). And, indeed, this site shifted upstream (Rvr/Rsys = 23%) with hyper, whereas hypo had no effect on the site of Pmsf (Rvr/Rsys = 15%). These data suggest that in the immediate postoperative period increased sympathetic tone keeps Pmsf in the venular side but with volume loading and a presumed reduction of vasomotor tone, this point shifts retrograde toward the arterial system. It will be interesting to see how this location changes with the use of vasoactive drug therapy and in patients with either sepsis or heart failure. We also saw that Rvr increased during hypervolemic conditions whereas conductance (conductance = 1/Rvr) was constant. We are not sure why this would be the case, because anatomically and physiologically speaking, the same factors affect both resistance and conductance. Potentially, our technique systematically overestimated Pmsf, and thus pressure gradient for VR under hypervolemic conditions due to squeezing of blood volume out of the lung, or the associated increase in Pcv

decreased the flow through the more dependent venous conduits. Our study design does not allow us to speculate further on these Rvr changes.
Whole body vascular compliance is calculated as the ratio of the change of volume to the change in estimated Pmsf ($\Delta V/\Delta P$). Using our inspiratory hold technique we found a vascular compliance, Csys, of 0.98 $ml \cdot mmHg^{-1} \cdot kg^{-1}$ body weight. The administration of 500 ml of colloid can expand plasma volume with more than 500 ml, because of fluid recruitment of the extravascular space and fluid loss (urine and blood loss), contribute to the volume expansion. Previous studies in instrumented anesthetized animals have reported a linear relation between Pmsf and blood volume over a Pmsf of 5-20 mmHg.[18] Thus, vascular compliance over this Pmsf range may be considered constant. From this constant total systemic vascular compliance and the change in Pmsf from baseline to hypo we calculated an effective volume loss to be about 200 ml. This loss is due to a shift of blood from stressed to unstressed blood volume.

The stressed volume can be estimated from the compliance and Pmsf. In normovolemic patients in supine position we estimated an averaged stressed volume of 1677 ml or 19.5 $ml \cdot kg^{-1}$. To our surprise, this calculated stressed volume is close to the stressed volume of 20.2 $ml \cdot kg^{-1}$ reported by Magder and De Varennes[29] in patients undergoing hypothermic circulatory arrest for surgery on major vessels. They measured stressed volume as the volume that drained from the patient into the reservoir of the pump when the pump was turned off.

Previously reported values for Csys ranged from 1.4 to 2.6 $ml \cdot mmHg^{-1} \cdot kg^{-1}$ in dogs[17,30-33] and from 1.5 to 2.4 $ml \cdot mmHg^{-1} \cdot kg^{-1}$ in rats.[15,16,34] The lower compliance (0.98 $ml \cdot mmHg^{-1} \cdot kg^{-1}$) observed in our patients may reflect species differences or differences in methodology used. The main difference in methodology is related to the time between volume loading and the determination of Pmsf. In animal studies, the Pmsf measurement is performed 30 seconds after volume loading, whereas we finished our measurements after > 20 minutes following volume loading. According to Rothe[18], it is virtually impossible to measure the vascular capacitance characteristics, and thus passive V/P curves and stressed volume of the total body in reflex-intact animals and humans. This limitation is because one cannot change blood volume and measure Pmsf in < 7-10 seconds, which is the maximal delay before reflex venoconstriction normally becomes evident, unless these reflexes are blocked. In our patients, the use of propofol and sufentanil might have blocked these reflexes[19-21] and might be the explanation for the corresponding stressed volume results of our study and the study of Magder and De Varennes.[29]

Conclusions

Pmsf can be determined in intensive care patients with an intact circulation with use of inspiratory pause procedures, making estimations of circulatory compliance and serial measures of circulatory stressed volume feasible.

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