

Ventilation-Induced Plethysmographic Variations Predict Fluid Responsiveness in Ventilated Postoperative Cardiac Surgery Patients

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BACKGROUND: It has been shown that ventilation-induced pulse pressure variation (PPV) is a better variable than central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP) for predicting cardiac output changes after fluid administration. The plethysmographic wave form measured with a fingertip pulse is very similar to the arterial blood pressure curve.

METHODS: We investigated whether this widely used, noninvasive instrument could predict fluid responsiveness by conducting an observational study in 32 patients who had undergone cardiac surgery. We compared PPV, CVP, PAOP, diastolic pulmonary artery pressure, and ventilation-induced plethysmographic variation (VPV) for predicting the cardiac output change after the administration of 500 mL 6% hydroxyethylstarch.

RESULTS: We found a good correlation between cardiac output changes and both PPV and VPV ($P < 0.05$). Receiver operating characteristic analysis revealed an area under the curve of 0.937 for PPV and 0.892 for VPV. The optimal thresholds were a variation of 11.3% for both PPV and VPV in predicting a 15% increase in cardiac output.

CONCLUSION: This study shows that VPV, like PPV, is a more reliable predictor of fluid responsiveness than CVP and PAOP.

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There is growing evidence that dynamic markers, e.g., pulse pressure variation (PPV) (1,2), systolic pressure variation (3), aortic blood flow velocity (1), and vena cava superior collapsibility (4), more accurately predict the response to a fluid challenge, i.e., fluid responsiveness, than the classic static parameters of preload, such as central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP). The dynamic indices are based on the fact that mechanical ventilation induces cyclic changes in cardiac filling status (2).

We investigated whether ventilation-induced plethysmographic variation (VPV) can be used as a new dynamic parameter to predict fluid responsiveness. Pulse oximeter plethysmography is a standard monitor in the intensive care unit (ICU) and operating room (OR) for detecting hypoxemia (5). Ventilation-induced plethysmographic wave form changes have been shown to correlate with intravascular volume status in

humans (6). This parameter could act as a “poor man’s solution” for PPV in areas with fewer resources, or as a back-up system when there is a perioperative failure of the arterial line.

To evaluate this potential, we conducted an observational study comparing PPV, VPV, CVP, PAOP, and diastolic pulmonary arterial pressure (PAP_{dia}) as predictors for fluid responsiveness in patients admitted to the ICU after cardiac surgery.

METHODS

After obtaining protocol approval from our institutional ethics committee and written informed consent from patients or their relatives, we conducted an observational study on patients who underwent cardiac surgery and were admitted to the ICU in the periods from March 2005 to July 2005 and from May 2006 to July 2006. Patients were recruited consecutively during periods of staff availability, usually during the daytime on weekdays.

All patients needed to be fully monitored with a pulmonary artery catheter (CCoMboV774HF75; Edwards Lifesciences, Irvine, CA) and a Vigilance monitor (Edwards Lifesciences), central venous line, arterial line, and finger pulse oximeter (Monitor Hewlett Packard M1166A model G65). They had to be fully sedated and ventilated (with a tidal volume of 8–10 mL/kg). Finally, all patients had to have a sinus rhythm without extra systoles.

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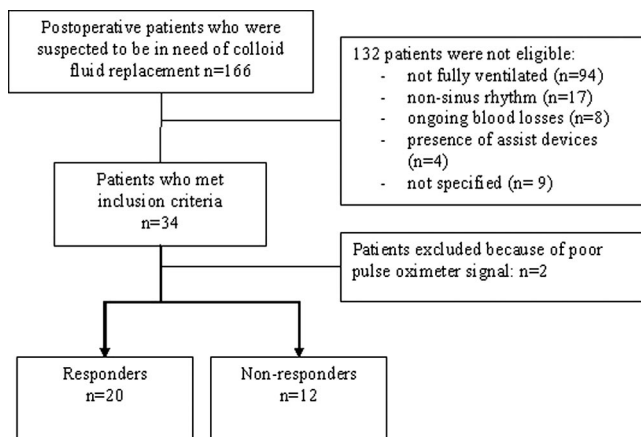


Figure 1. Enrollment flowchart.

Exclusion criteria were: (a) manifest excessive intravascular volume assessed by transesophageal echocardiography and/or PAOP >18 mm Hg; (b) presence of an assist device such as an intraaortic balloon pump; (c) major blood loss preceding or during registration, i.e., >200 mL/h; (d) administration of noradrenaline of >0.2 µg/kg/min; (e) known allergies to hetastarch products; (f) severe hypoxemia (defined as $P_{aO_2}/F_{iO_2} < 100$).

As this was an observational study, the decision to perform a fluid challenge was based on usual clinical parameters such as hypotension (systolic blood pressure <100 mm Hg), decreasing arterial blood pressure, previous blood loss, and low cardiac output. The decision was left to the discretion of the attending anesthesiologist. An enrollment flowchart is shown in Figure 1.

After inclusion, a set of measurements was taken before and after the administration of 500 mL 6% hydroxyethylstarch (Voluven®, Fresenius Kabi, Graz, Austria), which was administered over 20 min.

The cardiac index (CI) used was defined as the mean of three consecutive measurements of the CI, displayed on the VIGILANCE monitor in STATmodus. Arterial blood pressure, PAP, and CVP were noted. PPV was defined as $100 \times (PP_{max} - PP_{min}) / [(PP_{max} + PP_{min}) / 2] (\%)$ in accordance with published definitions (1,3,6). Likewise, the VPV was defined as $100 \times (\text{Max amplitude} -$

$\text{Min Amplitude}) / [(\text{Max amplitude} + \text{Min amplitude}) / 2] (\%)$ (Fig. 2). Both parameters were measured off-line and by hand from a printout containing the curves of the arterial line and the plethysmograph taken over a period of three ventilation cycles. All the curves had a height of at least 25 mm.

Patients were divided into groups of “responders” and “nonresponders” according to the change of CI after the fluid challenge. In accordance with other authors (6), we defined a change of 15% of CI as the cut-off for fluid responsiveness.

Baseline and postchallenge data are given (median and range), and were compared using a Wilcoxon’s signed rank test. For each subject the difference between baseline and postchallenge values was calculated. These differences were compared between the two groups using a Wilcoxon’s ranked sum test (7). Linear correlation was tested using a Spearman rank correlation test for PPV, VPV, CVP, PAOP, and PAPdia with change in CI (%) (8). A value of 0.05 was considered significant. Receiver operating characteristics (ROC) were generated for PPV, VPV, CVP, PAOP, and PAPdia. The area under the curve (AUC) was calculated (SD) and compared (9).

As there are a few data in the literature concerning VPV, we conducted a power analysis as follows: for single ROC values, the minimum required sample size, with a Type 1 error of 0.05, Type 2 error of 0.10, and null hypothesis of 0.5, is 37, 29, 26, and 20 for ROC = 0.800, 0.833, 0.850, and 0.900, respectively. The ROC values of CVP (0.51) and PAOP (0.41 and 0.67) were taken from Michard and Teboul (1) and Tavernier et al. (3) for the comparison of two ROC curves (VPV versus CVP or PAOP). The value of 8.333 for VPV was calculated from our own data after the first 16 patients were included. Rank correlations between the parameters were also calculated from our own data ($n = 16$). The minimum required sample size with a Type 1 error of 0.05 and a Type 2 error of 0.10 was 26 and 85 for the null hypothesis CVP = VPV and PAOP = VPV, respectively.

Statistical analysis was performed using MedCalc software 9.0.1.0 (MedCalc Inc., Mariakerke, Belgium).

Figure 2. The wave form changes were measured off-line and by hand from a printout containing the curves of the arterial line and the plethysmograph, taken over a period of three ventilation cycles. All the curves had a height of at least 25 mm. As the curve obtained by the pulse oximeter does not have a dimension, we quantified the wave form changes as $100 (\text{Max amplitude} - \text{Min Amplitude}) / [(\text{Max amplitude} + \text{Min amplitude}) / 2]$ expressed in % and similar to the definition of pulse pressure variation (1,3,7).

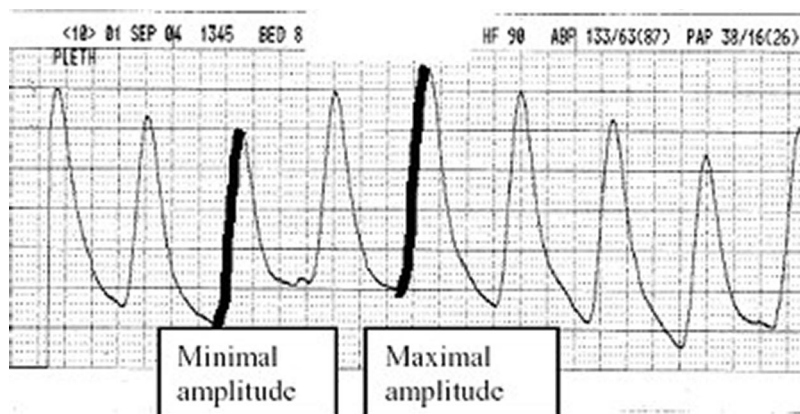


Table 1. Demographic Characteristics and Type of Surgery of Included Patients

Characteristic	All included patients
Demographic characteristic	
Female sex (<i>n</i> /total <i>n</i>)	10/32 (31.3%)
Age in years, median (range)	70 (78–46)
Caucasian (<i>n</i> /total <i>n</i>)	32/32 (100%)
Type of surgery (<i>n</i> /total <i>n</i>)	
Coronary artery bypass graft	9/32 (38.1%)
Off-pump coronary artery bypass graft	14/32 (43.8%)
Aortic valve replacement	2/32 (6.3%)
Combined aortic valve replacement with coronary bypass	4/32 (12.5%)
Mitral valve repair	3/32 (9.4%)

RESULTS

We included 32 patients. Demographic characteristics are shown in Table 1. Twenty were responders and 12 were nonresponders. Baseline and postchallenge data are shown in Table 2. There was a significant difference between the responders' and nonresponders' baseline PPV (17.1% [9.1–70] vs 7.7% [3.8–19.4], $P < 0.0001$) and VPV (25.5% [7.8–47.6] vs 9.9% [3.5–25.6], $P = 0.0003$). The differences between the median baseline CVP (7 mm Hg [2–12] vs 9 mm Hg [1–13]), PAPdia (14.5 mm Hg [9–22] vs 13.5 mm Hg [9–22]) and PAOP (8 mm Hg [5–15] vs 10 mm Hg [4–13]) of responders and nonresponders were not significant.

The Spearman rank correlation was calculated. Only PPV and VPV showed a fairly good correlation with the change in CI. Scatter plots with regression

lines were drawn (Fig. 3). The AUC of the ROC curves were as follows (95% confidence interval): PPV 0.937 (0.792–0.991); VPV: 0.892 (0.731–0.972); PAPdia 0.575 (0.389–0.747); CVP 0.602 (0.145–0.770); and PAOP 0.515 (0.327–0.700). A pairwise comparison was done; the AUC of PPV differed significantly from all parameters (all $P < 0.01$) except for VPV ($P = 0.413$). The AUC of VPV differed significantly from CVP ($P = 0.01$), PAOP ($P = 0.002$), and PAPdia ($P = 0.029$). Optimal cut-off points with corresponding sensitivity, specificity and predictive values are shown in Table 3.

DISCUSSION

A growing number of studies have demonstrated the usefulness of dynamic parameters, such as PPV and systolic pressure variation, over the classic static parameters, such as CVP and PAOP, for predicting a change in CI in response to a fluid challenge in ventilated patients (1–3,7). These parameters combine higher accuracy with reduced invasiveness. We demonstrated that the changes of the plethysmographic wave form measured with fingertip pulse oximeter can be regarded as a dynamic parameter with these two properties: high accuracy and noninvasiveness.

Our data show that PPV and VPV perform significantly better than CVP, PAOP, and PAPdia. These findings confirm data in other publications. For example, Shamir et al. (6) reported a correlation between blood volume status and plethysmographic wave form changes in patients undergoing spinal surgery involving hypotension and hemodilution. Others have demonstrated a close correlation between VPV and

Table 2. Baseline Data and Postchallenge Data, Broken Down by Responders and Nonresponders

	Baseline		Postchallenge		<i>P</i>	Changes	
	Median	Range	Median	Range		Median	<i>P</i>
CI all	2.5	1.5–3.6	3.0	1.9–5.3	<0.0001		<0.0001
Resp	2.6	1.5–3.6	3.0	1.9–5.3		32.1%	
Nonresp	2.4	2.0–3.3	2.9	2.0–3.9		3.1%	
PPV all	15.4	3.8–28.6	8.5	5.8–9.3	0.0003		0.0011
Resp	17.8	9.1–70	6.3	1.7–4.0		–9.8	
Nonresp	8.0	4.0–19.4	8.9	3.6–14.6		0.7	
VPV all	16	3.5–47.6	10.0	2.5–40.0	0.0027		0.0013
Resp	27.0	8.2–46.2	9.5	4.9–29.1		–14.5	
Nonresp	10.0	3.5–26.6	12.6	2.5–40.0		3.9	
CVP all	7.0	1.0–13.0	10.5	4.0–16.0	<0.0001		0.2058
Resp	7.0	2.0–12.0	10.5	5.0–16.0		3	
Nonresp	9.0	1.0–13.0	10.5	4.0–15.0		1	
PAPdia all	14.0	9.0–14.0	18.0	10.0–27.0	<0.0001		0.5081
Resp	14.0	9.0–22.0	17.5	12.0–27.0		4.5	
Nonresp	13.5	9.0–22.0	18.0	10.0–21.0		2.5	
PAOP all	9.5	4.0–15.0	12.0	5.0–18.0	0.0001		0.2004
Resp	10.0	4.0–13.0	12.0	7.0–15.0		2	
Nonresp	7.0	5.0–15.0	12.0	5.0–18.0		4.5	

The differences between the values of baseline and postchallenge data were calculated using a Wilcoxon signed rank test. For each subject the difference between baseline and postchallenge data was calculated. These changes were compared between responders and nonresponders using a Wilcoxon rank-sum test. (P values <0.05 were considered significant).

CI = cardiac index (L/min/m²); PPV = pulse pressure variation (%); VPV = ventilation-induced plethysmographic variation (%); CVP = central venous pressure (mm Hg); PAPdia = diastolic pulmonary arterial pressure (mm Hg); PAOP = pulmonary artery occlusion pressure (mm Hg).

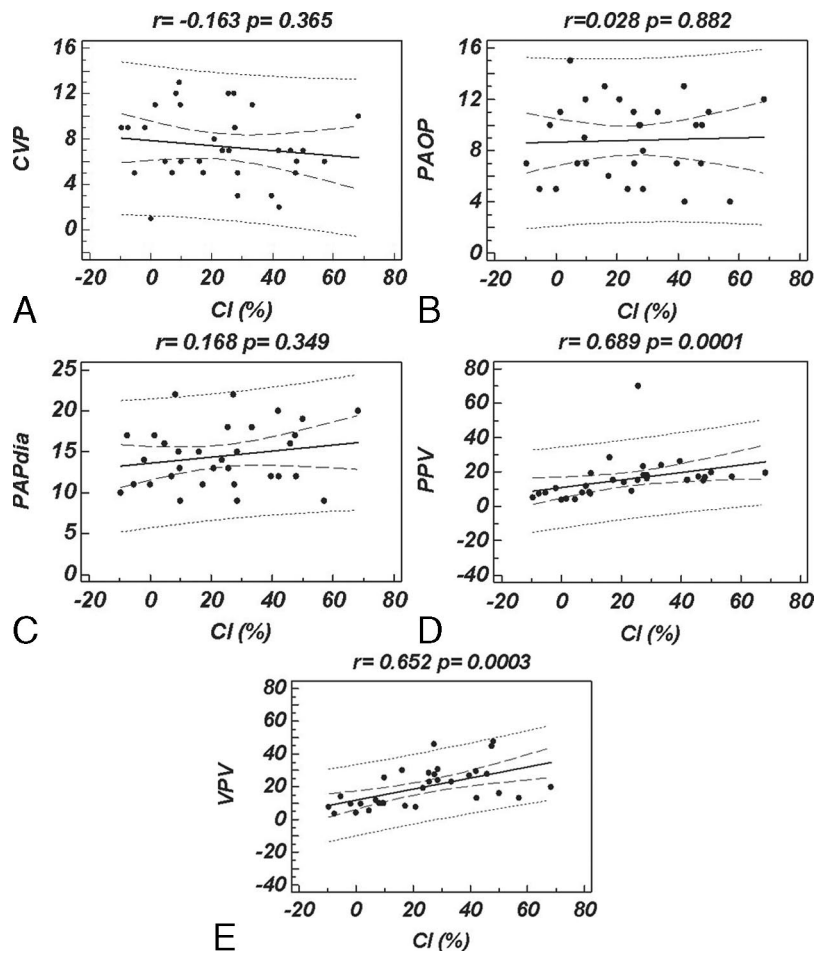


Figure 3. Scatter diagram with regression line for CVP (central venous pressure), PAOP (pulmonary artery occlusion pressure), PAPdia (diastolic pulmonary artery pressure), PPV (pulse pressure variation), and VPV (ventilation-induced plethysmographic variation) versus cardiac index change (CI in %). Spearman rank correlation is given with corresponding *P* value (*P* < 0.05 considered significant).

Table 3. Optimal Cut-offs of PPV and VPV with Corresponding Sensitivity, Specificity, and Predictive Values

Cut-off	Sensitivity	Specificity	Prevalence 0.625	Prevalence 0.100	Prevalence 0.900
PPV: >11.8	0.950	0.917	PoPV: 0.950 NPV: 0.917	PoPV: 0.560 NPV: 0.994	PoPV: 0.990 NPV: 0.671
VPV: >11.8	0.900	0.833	PoPV: 0.900 NPV: 0.833	PoPV: 0.374 NPV: 0.987	PoPV: 0.980 NPV: 0.481

PPV = pulse pressure variation (%); VPV = ventilation-induced plethysmographic variation (%); PoPV = positive predictive value; NPV = negative predictive value.

known dynamic parameters. Yamakage et al., (10) in a study of 22 patients with ASA1/2, showed a close correlation between VPV and vena cava superior collapsibility. And Cannesson et al. (11) found VPV to be a good predictor of the PPV value. To our knowledge, there is only one study which investigates the diagnostic usefulness of VPV in a fluid challenge-based protocol. Feissel et al. (12) studied 19 ventilated patients in septic shock. They found a VPV threshold of 12% to have a sensitivity of 100% and a specificity of 88%.

The differences we found between PPV and VPV characteristics were not significant, even after omitting case 15, the one outlier of PPV. This is due mainly to our study not being powered to detect such differences.

In addition to the small number of patients studied, some other elements may have influenced our data. First, although we tried to standardize our work as much as possible, some steps or measurements in the protocol may have flawed our findings. We conducted

the fluid challenge with 500 mL hydroxyethylstarch, but we were unable to correct for continuing silent blood loss. Therefore, the net effective fluid bolus administered could have differed among patients. Second, our CI determination was measured with a continuous cardiac method (12). Another aspect to be considered is the calculation of the PPV and VPV. We conducted an off-line and by-hand analysis of the wave forms on a printed strip. The curves were at least 25 mm, which is bigger than the height of the curves on standard monitors. When we consider the threshold found, namely 11.8% for VPV, this means a difference of 2.8 mm between the maximal and minimal amplitudes, when the maximal amplitude is 25 mm. We measured the amplitudes of the curves with an error of up to 0.5 mm. This corresponds to a measured error of maximum 1 mm between the minimum and maximum amplitudes. Therefore, if the real VPV was 11.8%, the measured one may range from 7.6% to 15.6%.

Aside from the effect on our results, this is important for everyday practice. Regular monitors in ICUs and ORs display their wave forms on a smaller scale, making the threshold almost invisible to the naked eye. Applying VPV in a clinical decision would require a digital calculation by the monitor (which is not difficult to accomplish). Finally, as this was an observational study, we could not standardize the indication for fluid administration, which was left to the discretion of the attending anesthesiologist. However, in daily clinical practice, most patients need fluid administration in the postoperative period.

Aside from the parameter-specific properties, applying VPV, one needs to know the test population properties, as Bayesian statistics show us. Our study was conducted on patients after cardiac surgery. Another study was conducted on septic patients (13). These patients differ from everyday patients in an OR. They (may) have different ages, comorbidities, medication use and, most importantly, a different prevalence of hypovolemia or fluid responsiveness. Table 3 shows the influence of different prevalences on the predictive values of a test with a characteristic sensitivity and specificity.

To summarize, our data suggest that the changes in plethysmographic wave forms induced by ventilation, like PPV, act as a more accurate parameter for fluid responsiveness than the more classic nondynamic parameters, such as CVP and PAOP. We conducted our study on fully sedated and ventilated patients after cardiac surgery. If our results are confirmed by other studies in other areas, such as ORs, a digital calculation of this new index could be integrated into our daily monitors.

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