Arterial Versus Plethysmographic Dynamic Indices to Test Responsiveness for Testing Fluid Administration in Hypotensive Patients: A Clinical Trial

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In the present study, we compared indices of respiratory-induced variation obtained from direct arterial blood pressure measurement with analogous indices obtained from the plethysmogram measured by the pulse oximeter to assess the value of these indices for predicting the cardiac output increase in response to a fluid challenge. Thirty-two fluid challenges were performed in 22 hypotensive patients who were also monitored with a pulmonary artery catheter. Hemodynamic and plethysmographic data were collected before and after intravascular volume expansion. Patients were classified as nonresponders if their cardiac index did not increase by 15% from baseline. Nonresponding patients had both lower arterial pulse variation ([10 ± 4]% vs [19 ± 13]%, $P = 0.020$) and lower plethysmographic pulse variation ([12 ± 7]% vs [21 ± 14]%, $P = 0.034$) when compared with responders. Fluid responsiveness was similarly predicted by arterial and plethysmographic pulse variations (area under ROC curve 0.74 vs 0.72, respectively, $P = 0.90$) and by arterial and plethysmographic systolic variation (area under ROC curve 0.64 vs 0.72, respectively, $P = 0.50$). Nonresponders were identified by changes in pulse variation both on arterial and plethysmographic waveform (area under ROC curve 0.80 vs 0.87, respectively, $P = 0.40$) and by changes in arterial and plethysmographic systolic variations (area under ROC curve 0.84 vs 0.80, respectively, $P = 0.76$). In the population studied, plethysmographic dynamic indices of respiratory-induced variation were just as useful for predicting fluid responsiveness as the analogous indices derived from direct arterial blood pressure measurement. These plethysmographic indices could provide a noninvasive tool for predicting the cardiac output increase by administering fluid.

(Anesth Analg 2006;103:1478–84)

Intravascular fluid administration is often the first step in resuscitating hypotensive patients (1–3). Unfortunately only half of these patients significantly increase cardiac output after intravascular volume expansion (4), while the remaining patients are at risk for pulmonary and peripheral edema because of excessive intravascular volume (5).

Dynamic indices derived from arterial blood pressure changes during mechanical ventilation can accurately predict "fluid responsiveness," defined as an increased cardiac index after fluid administration (6–8). Pulse pressure variation, systolic blood pressure variation and δDown (systolic blood pressure decrease to apnea value) have been shown to be more accurate indicators of fluid responsiveness than right atrial pressure, pulmonary artery occlusion pressure, and left ventricular end-diastolic area (6–8).

Pulse oximetry is a noninvasive monitoring tool routinely used to assess oxygenation. Pulse oximeters use photoelectric plethysmography to detect changes in blood volume at the site of measurement (9). Although the photoplethysmographic waveform differs from the arterial pressure waveform by measuring volume rather than pressure changes in both arterial and venous vessels (9,10), pulse plethysmographic variation showed significant correlation and good agreement with pulse pressure variation and accurately identified pulse pressure variation values associated with fluid responsiveness (11,12). Moreover, systolic blood pressure variation and δDown correlated with similar indices derived from the photoplethysmographic waveform after blood withdrawal (13).

These relationships between arterial and plethysmographic pulse variation suggest that photoplethysmography could be useful to predict fluid responsiveness. The result would be a simple, inexpensive, noninvasive alternative to more aggressive monitoring for

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Accepted for publication September 8, 2006.

Supported by departmental funding.

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DOI: 10.1213/01.ane.0000246811.88524.75

assessing fluid responsiveness of critically ill mechanically ventilated patients.

Changes in dynamic indices after intravascular volume expansion showed inverse correlation with cardiac index changes (7,14). For most patients, a single fluid challenge is not harmful, and the change in plethysmographic indices after a fluid challenge could help to assess the intravascular volume status.

The goals of the present study were to compare the diagnostic accuracy of arterial and plethysmographic dynamic indices, both as predictors and markers of fluid responsiveness, in hypotensive mechanically ventilated patients.

METHODS

Patients

The study protocol was approved by the institutional ethics committee (Comitato Etico Istituzioni Ospedaliere Cattoliche), and written informed consent was obtained from the closest relative of each patient. The study was conducted in the Intensive Care Unit of Poliambulanza Foundation Hospital from March 1, 2005 to October 31, 2005. The study population included consecutive patients who met the following inclusion criteria: mean arterial blood pressure lower than 65 mm Hg; controlled mechanical ventilation; pulse oximetry, arterial catheter, and pulmonary artery catheter monitoring. Patients were not admitted to the study if any of the following criteria were present: 1) spontaneous breathing activity detectable on airway pressure–time and flow–time curves, 2) arrhythmias, 3) clinical signs of excessive intravascular volume. Patients' characteristics are shown in Table 1. Septic shock was defined according to the International Sepsis Definitions Conference (15).

Table 1. Patients' Characteristics (32 Observations, 22 Patients)

Age (yr)	67 ± 11 (67, 58–81)
Weight (kg)	72 ± 18 (69, 49–90)
Pao_2/FIo_2	254 ± 124 (220, 114–434)
SAPS II (20)	57 ± 11 (58, 41–72)
SOFA (21) (calculated at the study day)	9 ± 2 (9, 7–12)
Mixed venous blood oxygen saturation (%)	64 ± 14 (65, 53–76)
Tidal volume/body weight (ml/kg)	8 ± 2 (8, 6–10)
Positive end-expiratory pressure (cm H_2O)	11 ± 4 (10, 10–12)
Septic shock	24 (75%)
Dobutamine $(mcg \cdot kg^{-1} \cdot min^{-1})^a$	8 ± 4 (5, 5–11)
Norepinephrine $(mcg \cdot kg^{-1} \cdot min^{-1})^b$	0.46 ± 0.56 (0.30, 0.09–1.26)
Epinephrine $(mcg \cdot kg^{-1} \cdot min^{-1})^c$	0.1
Dopamine $(mcg \cdot kg^{-1} \cdot min^{-1})^d$	5 ± 0 (5, 5–5)
Nitric oxide (ppm)[e]	14 ± 5 (13, 10–19)

Data are shown as mean ± SD; values inside parentheses indicate median and 10th–90th percentiles.

SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.

[a] data from 10 patients.

[b] from 19 patients.

[c] from 1 patient.

[d] from 2 patients.

[e] from 4 patients.

Measurements and Calculations

Electrocardiography, pulse oximetry, capnography, airway pressure, and flow at the airway opening were all continuously monitored for every patient (Datex-Engstrom CS/3 Critical Care Monitor, Datex-Engstrom Division, Instrumentarium, Helsinki, Finland). Arterial blood pressure and heart rate were continuously monitored via an arterial catheter introduced into either the radial or femoral artery. Correct placement of the pulmonary artery catheter was confirmed by the appropriate pressure traces on insertion and by chest radiography. Transducers were referenced to the midaxillary line, and all pressures were taken at end-expiration. Cardiac output was measured by thermodilution. Three consecutive cardiac output measurements within 10% were required, and their mean value was used for analysis and calculation.

Systolic and diastolic blood pressures were measured on a beat-to-beat basis, and pulse pressure was calculated as the difference between systolic and diastolic blood pressure. Maximal and minimal values for systolic (SP_{max} and SP_{min}, respectively) and pulse pressure (PP_{max} and PP_{min}, respectively) were determined over a single respiratory cycle. The percent variation in pulse arterial pressure (PV_{AP}) was calculated as $100 \times \{(PP_{max} - PP_{min})/[(PP_{max} + PP_{min})/2]\}$ (14). Similarly, the percent variation in systolic arterial blood pressure (SV_{AP}) was calculated as $100 \times \{(SP_{max} - SP_{min})/[(SP_{max} + SP_{min})/2]\}$ (7). Measurements and calculations were independently performed on five consecutive respiratory cycles, and mean values were used for analysis. Arterial and plethysmographic waveforms of a representative patient are shown in Figure 1.

Dynamic indices of respiratory-induced variation were derived from the photoplethysmographic waveforms in a fashion analogous to the indices derived from the arterial waveforms. The pulse amplitude of the photoplethysmographic wave was calculated as the difference between systolic and diastolic values. Percent changes over a single respiratory cycle of pulse (PV_{PLT}) and systolic (SV_{PLT}) amplitude were calculated similarly to PV_{AP} and SV_{AP}, respectively.

Percentage changes of these variables after intravascular volume expansion relative to the baseline value were indicated with the Greek letter "δ" before the corresponding variables.

Protocol

All patients were mechanically ventilated using a volume-controlled mode of ventilation (Servo 300

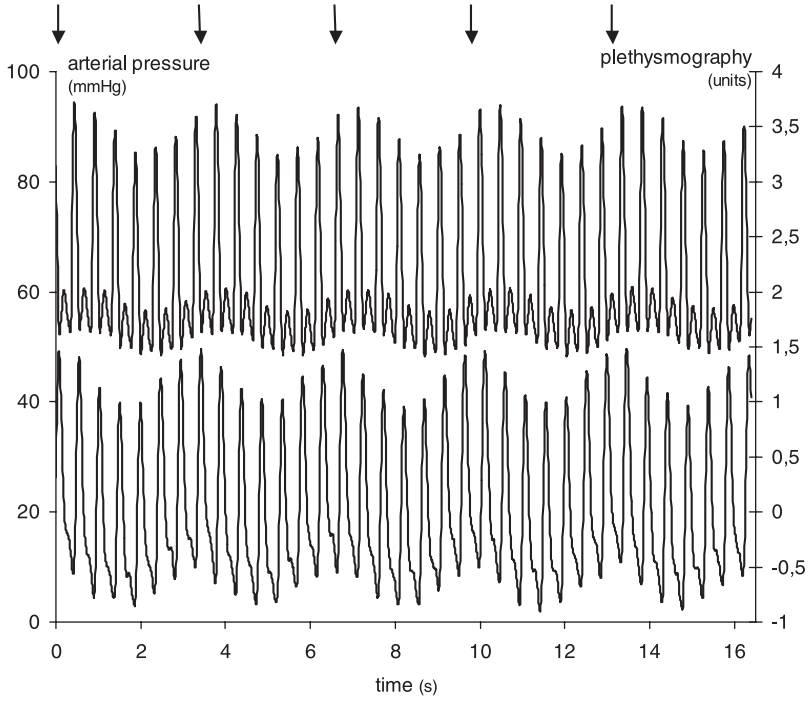

Figure 1. Simultaneous record of arterial pressure (upper curve) and plethysmographic waveform (lower curve) in a representative patient. Arrows indicate the beginning of inspiration.

Ventilator, Siemens-Elema AB, Solna, Sweden). Ventilator variables were maintained as set by the attending physician throughout the study. Baseline waveforms of the electrocardiogram, arterial blood pressure, photoplethysmogram, and flow at the airway opening were continuously recorded for 120 s at the sampling rate of 100 Hz and converted to ASCII files (Datex-Ohmeda S/5 Collect, Datex-Ohmeda Division, Instrumentarium, Helsinki, Finland). The autogain function of the pulse oximeter was disabled. Data were imported to a worksheet (Excel 2000, Microsoft Corporation, USA) and instantaneous absolute values of arterial blood pressure, photoplethysmography, flow, and pressure at airway opening were plotted against time. Arterial and pulmonary artery blood samples were obtained for blood gases (AVL OMNI 1–9 Modular System, AVL LIST Medizintechnik, Graz, Austria). Right atrial pressure and pulmonary artery occlusion pressure were measured from the proximal and distal port of the pulmonary arterial catheter respectively, and cardiac output was measured. After baseline data were obtained, intravascular volume expansion was performed by infusing hetastarch 6% 500 mL over 30 min and then collecting new data for comparison to the baseline. Patients were classified as nonresponders to intravascular fluid administration if after intravascular volume expansion cardiac index did not increase by at least 15% relative to the baseline value.

Study Outcomes

The main study outcomes were to compare arterial and plethysmographic dynamic indices as predictors (PV_{AP} vs PV_{PLT}, SV_{AP} vs SV_{PLT}) or markers (δPV_{AP} vs δPV_{PLT}, δSV_{AP} vs δSV_{PLT}) of nonresponsiveness to intravascular volume expansion.

A secondary outcome was to evaluate if nonresponding patients could be identified by hemodynamic variables, which have shown differences between responders and nonresponders.

Statistical Analysis

In the literature, pulse pressure variation has been shown to accurately predict fluid responsiveness (7,8) when the variability among observers can be considered small (it is a objective measurement) and the responders/nonresponders ratio is about 1/1 (4). Data in the present study were analyzed by six observers and a sample size of 20 patients was needed to detect differences of 0.15 between areas under receiver operating characteristic (ROC) curve (5% Type I error rate, 80% power, two-tailed test). A sample size of 31 observations was needed to detect differences of 0.10 between areas under ROC curve (16). The study was planned to have at least 20 patients and 31 observations. The main analysis was performed considering all observations.

Descriptive statistical data were shown as mean ± SD (median, 10th–90th percentiles). A comparison between responder and nonresponder patients was performed by *t*-test for unpaired data and 95% confidence intervals were calculated.

To assess the ability of measured/calculated parameters to identify nonresponders to intravascular fluid administration, ROC curves were generated, varying the discriminating threshold of each parameter. The optimal threshold value (the value that maximizes the sum of the sensitivity and specificity) was also determined. The areas under the ROC curves were calculated and compared as previously described (17).

Table 2. Baseline Hemodynamic and Plethysmographic Data for Responder and Nonresponder Patients

	Nonresponders ($n = 13$)	Responders ($n = 19$)	P
Mean arterial blood pressure (mm Hg)	55 ± 8 (51–60)	55 ± 8 (52–58)	0.874
Cardiac index ($l \cdot min^{-1} \cdot (m^2)^{-1}$)	3.3 ± 1.3 (2.6–4)	2.1 ± 0.5 (1.9–2.4)	0.001
Heart rate (bpm)	98 ± 19 (88–109)	87 ± 22 (77–97)	0.147
Right atrial pressure (mm Hg)	12 ± 3 (10–14)	10 ± 8 (6–13)	0.259
Pulmonary artery occlusion pressure (mm Hg)	13 ± 4 (11–16)	11 ± 5 (9–13)	0.149
Mean pulmonary artery pressure (mm Hg)	26 ± 6 (23–29)	23 ± 5 (20–25)	0.150
PV_{AP} (%)	10 ± 4 (7–12)	19 ± 13 (13–25)	0.020
PV_{PLT} (%)	12 ± 7 (8–15)*	21 ± 14 (15–27)	0.034
SV_{AP} (%)	8 ± 3 (6–9)	12 ± 8 (9–15)	0.070
SV_{PLT} (%)	40 ± 27 (25–55)*	60 ± 37 (43–76)	0.121

Data are shown as mean± SD; values inside parentheses indicate 95% confidence intervals.

PV_{AP} = arterial pressure pulse variation; SV_{AP} = arterial pressure systolic variation; PV_{PLT} = plethysmographic pulse variation; SV_{PLT} = plethysmographic systolic variation.

* data from 12 observations (see text for explanation).

Table 3. Percentage Changes in Hemodynamic and Plethysmographic Data for Responder and Nonresponder Patients after Intravascular Volume Expansion

	Nonresponders ($n = 13$)	Responders ($n = 19$)	P
Mean arterial blood pressure (%)	11 ± 9 (6–16)	23 ± 11 (19–28)	0.003
Cardiac index (%)	2 ± 9 ((−3)–7)	33 ± 13 (28–39)	<0.001
Heart rate (%)	−4 ± 4 ((−6)–(−2))	−6 ± 8 ((−10)–(−3))	0.429
Right atrial pressure (%)	32 ± 31 (15–49)	79 ± 230 ((−24)–183)	0.470
Pulmonary artery occlusion pressure (%)	29 ± 27 (15–44)	49 ± 78 (14–84)	0.382
Mean pulmonary artery pressure (%)	24 ± 42 (1–47)	21 ± 20 (12–30)	0.793
PV_{AP} (%)	−34 ± 30 ((−51)–(−18))	−61 ± 14 ((−67)–(−55))	0.002
PV_{PLT} (%)	11 ± 22 ((−1)–23)*	−27 ± 64 (−56–2)	0.056
SV_{AP} (%)	−30 ± 19 (−41)–(−20)	−51 ± 11 ((−56)–(−46))	0.001
SV_{PLT} (%)	−5 ± 30 ((−21)–12)*	−41 ± 37 ((−58)–(−25))	0.007

Data are shown as mean± SD; values inside parentheses indicate 95% confidence intervals.

PV_{AP} = arterial pressure pulse variation; SV_{AP} = arterial pressure systolic variation; PV_{PLT} = plethysmographic pulse variation; SV_{PLT} = plethysmographic systolic variation.

* data from 12 observations (see text for explanation).

For all comparisons, a P value <0.05 was considered significant.

RESULTS

Thirty-two intravascular volume expansions were performed in 22 patients. In one patient who was a nonresponder, the plethysmographic signal was not detectable and the data from that patient were excluded from ROC curve comparisons between arterial and plethysmographic dynamic indices. Intravascular volume expansion increased cardiac index (15% or more) in 19 cases (59%). Baseline hemodynamic data and arterial and plethysmographic indices in responder and nonresponder patients are shown in Table 2. In responders, cardiac index was lower, and both PV_{AP} and PV_{PLT} were higher than in nonresponders. The remaining hemodynamic and plethysmographic variables were not significantly different between the two groups.

Percentage changes relative to baseline after intravascular volume expansion are shown in Table 3. By definition, cardiac index variation was higher in responder patients than in nonresponder patients. Dynamic index changes were different between groups with the exception of PV_{PLT}, which did not reach statistical significance. Moreover, mean arterial blood pressure showed a larger percentage increase in responder than in nonresponder patients.

Table 4 and Figure 2 show the diagnostic performance of arterial and plethysmographic dynamic indices by comparing the area under the ROC curve using each arterial dynamic index relative to the corresponding plethysmographic index. Both pulse and systolic variations of baseline arterial and plethysmographic dynamic indices had similar areas under the ROC curve. All indices showed moderate accuracy to predict a lack of fluid responsiveness (ROC curve area between 0.64–0.74). This was mainly because low positive predictive value counterbalanced high negative predictive value. In other words, values higher than threshold accurately predicted cardiac index increase after intravascular volume expansion whereas values lower than threshold were not helpful for fluid responsiveness prediction.

The percentage decrease of dynamic indices after intravascular volume expansion with respect to baseline identified nonresponder patients with higher positive predictive value and higher ROC curve area than baseline dynamic indices (although these differences did not reach statistical significance). Again

Table 4. Prediction and Identification of Nonresponder Patients: Comparison Between Arterial and Plethysmographic Indices

	Threshold Value (%)	PPV (%)	NPV (%)	Area under ROC curve	*P*
PV_{AP} (%)	15	55	100	0.74	0.90
PV_{PLT} (%)	15	56	86	0.72	
SV_{AP} (%)	11	48	88	0.64	0.50
SV_{PLT} (%)	70	53	91	0.72	
ΔPV_{AP} (%)	−50	75	84	0.80	0.40
ΔPV_{PLT} (%)	−25	69	100	0.87	
ΔSV_{AP} (%)	−46	77	89	0.84	0.76
ΔSV_{PLT} (%)	−40	63	93	0.80	

PPV = positive predictive value; NPV = negative predictive value; PV_{AP} = arterial pressure pulse variation; SV_{AP} = arterial pressure systolic variation; PV_{PLT} = plethysmographic pulse variation; SV_{PLT} = plethysmographic systolic variation; Δ = percentual variation from baseline after intravascular volume expansion.

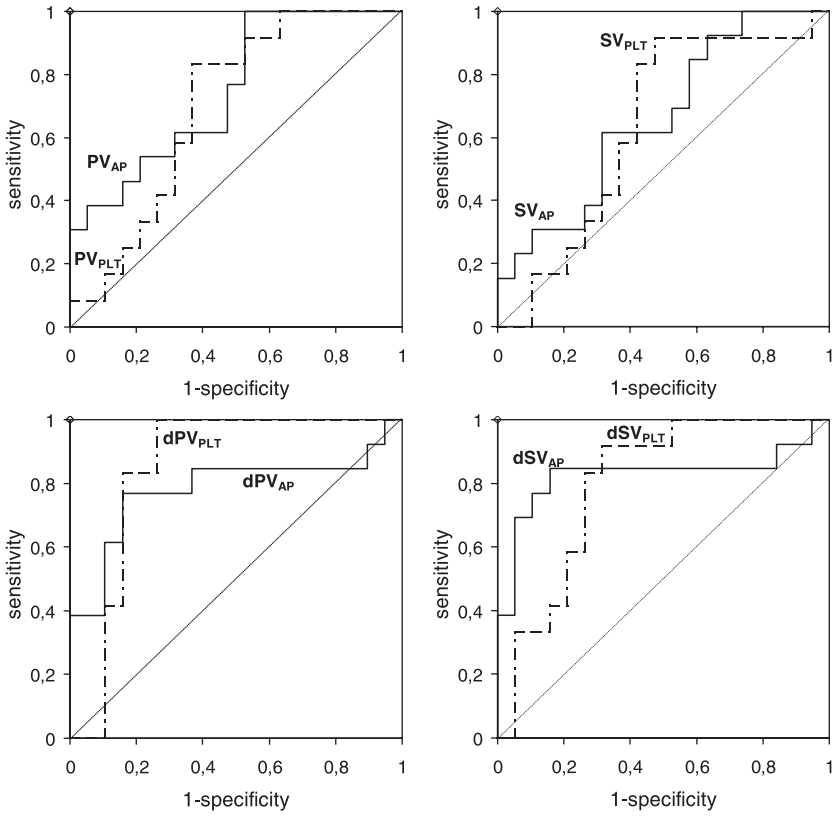

Figure 2. ROC curves of arterial (continuous line) and plethysmographic (broken line) dynamic indices. PV_{AP} = arterial pressure pulse variation; SV_{AP} = arterial pressure systolic variation; PV_{PLT} = plethysmographic pulse variation; SV_{PLT} = plethysmographic systolic variation; *d* = variation from baseline after intravascular volume expansion.

there were no differences between the areas under ROC curve of arterial indices and their corresponding plethysmographic indices.

Differently from dynamic indices, baseline cardiac index accurately predicted nonresponder status (area under ROC curve 0.83) with an optimal positive predictive value (100%): all patients with a cardiac index higher than 2.8 $L \cdot min^{-1} \cdot (m^2)^{-1}$ were nonresponders. Nonresponder status is also excluded by increase of mean arterial blood pressure more than 18% after intravascular volume expansion (negative predictive value = 86%, area under ROC curve = 0.73).

Results were substantially confirmed when analysis was conducted on the first fluid challenge for all patients. In particular, areas under the ROC curve were similar for baseline arterial and plethysmographic indices (PV_{AP} = 0.72 vs PV_{PLT} = 0.81, *P* = 0.52; SV_{AP} = 0.64 vs SV_{PLT} = 0.72, *P* = 0.70) and for their changes after intravascular volume expansion (δPV_{AP} = 0.91 vs δPV_{PLT} = 0.88, *P* = 0.76; δSV_{AP} = 0.97 vs δSV_{PLT} = 0.84, *P* = 0.20). Results did not change when areas under ROC curve were calculated for cardiac index (0.80) and for percentage changes of mean arterial blood pressure after the fluid challenge (0.84). Threshold and predictive values were similar to that presented in Table 4 for all measurements.

DISCUSSION

The present study showed that noninvasive dynamic indices of respiratory-induced variation derived from the plethysmographic signal assessed fluid responsiveness similar to pulse and systolic pressure variations derived from the arterial pressure signal in hypotensive, mechanically ventilated patients. Almost all patients with arterial or plethysmographic pulse variation above the threshold value were responders,

whereas dynamic indices were not useful for predicting fluid responsiveness when they were below the threshold value. In these patients, when the cardiac output measurement was not available, nonresponders could be identified by the amount of dynamic indices decrease after intravascular volume expansion from baseline. However, the most accurate predictor of the nonresponders status was high baseline cardiac index.

Previous studies on fluid responsiveness predicted by dynamic indices used more than one assessment in the same patient (6) or presented a single observation for each patient (7,8,18). In clinical practice, intravascular volume expansion often has to be decided in a single patient many times during the intensive care unit stay. Moreover, the response to intravascular volume expansion can change because of concurrent variation of intravascular volume status, infusion rate of vasoactive and inotropic drugs, mechanical ventilation, and finally the disease course. In the present study, 10 measurements were collected in previously enrolled patients (median 2 days after the first measurement) and six responders changed into nonresponders. We tailored the sample size to have sufficient statistical power without multiple observations in each patient. However, we presented more detailed data, including more than one measurement from the same patient, to reproduce daily practice when fluid responsiveness had to be evaluated both in different patients and in the same patient on different occasions. The results were similar both with and without multiple observations.

The plethysmographic waveform is generated by blood volume changes in both arterial and venous vessels (9,10). Its amplitude depends on intravascular pulse pressure as well as on distensibility of the vascular wall (9) and signal processing is complex (12). Despite the difference between plethysmography and arterial blood pressure monitoring, previous studies showed significant relationships between arterial and plethysmographic dynamic indices. A clinical trial compared arterial and photoplethysmographic ventilation-induced systolic blood pressure variations in 12 patients undergoing posterior spine fusion involving hemodilution. Systolic variation and δDown showed a significant correlation between arterial and plethysmographic calculations during hypovolemia, but not during intravascular volume replacement (13). Moreover, plethysmographic pulse variation accurately identified patients whose pulse pressure variation value suggested fluid responsiveness (11,12). Systolic blood pressure variation had significant relationship when calculated on arterial and plethysmographic waveforms, but plethysmographic variation was higher than arterial variation with a systematic increase of the difference over the range of measurement (12). Finally no relationship was found between arterial and plethysmographic δDown (12).

All pulse oximeters process the raw data in different ways, and this could generate some concerns about reproducibility of results when different devices are used to measure the plethysmogram. This could be true when signal amplitude is measured, but it should not be a problem when percentage changes of signal are considered. In fact, the relationship between arterial and plethysmographic dynamic indices is confirmed by three clinical trials conducted with devices from different manufacturers (11–13).

The present study showed similar diagnostic accuracy of arterial and plethysmographic dynamic indices. Fluid responsiveness prediction has been evaluated in three studies for pulse pressure variation (6,7,18) and in three studies for systolic blood pressure variation (6–8). In all but one study, dynamic indices showed excellent diagnostic performance with areas under the ROC curve from 0.91 to 0.94 for systolic blood pressure variation and from 0.98 to 0.99 for pulse pressure variation (6–8). Similar findings were not confirmed by our data, nor by the study by De Backer et al. (18) that showed areas under ROC curve of 0.74 and 0.76, respectively. The main difference between studies with optimal fluid responsiveness prediction (6–8) and those with less exciting results was the lower tidal volume in these last studies. The studies with areas under ROC curve more than 0.9 used tidal volume ranging from 8 to 12 mL/kg, whereas ours and De Backer et al.'s studies used a tidal volume <7–8 mL/kg for half of the patients. It has been shown that pulse pressure variation is a reliable indicator of fluid responsiveness only when tidal volume is at least 8 mL/kg (18). Our results confirm that prediction of fluid responsiveness by pulse pressure variation should be performed with caution in critically ill patients with low-to-normal tidal volume.

Moreover, patients in our and De Backer et al.'s studies had baseline cardiac index [median 2.5 and 2.7 $L \cdot min^{-1} \cdot (m^2)^{-1}$, respectively] less than in the previous studies [mean ranging from 3.4 to 3.7 $L \cdot min^{-1} \cdot (m^2)^{-1}$]. Furthermore, in our study, patients were more severely hypotensive (mean arterial blood pressure in all patients lower than 65 mm Hg, mean 54 mm Hg) than in other studies (mean or median value of mean arterial blood pressure ranging from 68 to 71 mm Hg). Probably most patients with more than 65 mm Hg and high cardiac output (usually associated with normal-to-high mixed venous oxygen saturation) should not require further hemodynamic support (19). In the clinical setting, patients who need to be evaluated for fluid challenge should probably be more similar to those enrolled in the current study and De Backer et al.'s studies than in studies reporting a better fluid responsiveness prediction by pulse pressure variation. Finally, data from our and De Backer et al.'s studies were collected from heterogeneous populations, whereas other studies analyzed homogeneous diagnostic groups, such as septic (6,7) or coronary artery bypass grafting patients (8). We believe that

fluid responsiveness prediction by pulse pressures variation (and systolic blood pressure variation) shows a high accuracy in only mildly hypotensive patients with high cardiac output and ventilated with normal-to-high tidal volume.

Previous studies showed a significant relationship between cardiac index variation and dynamic indices changes after intravascular volume expansion (7,14), but this property of dynamic indices was not considered as a possible marker of cardiac index increase. In the clinical setting, this should be only slightly less important than fluid responsiveness prediction. Most hypotensive patients without clinical contraindication to intravascular volume expansion can tolerate a single fluid challenge without significant complications, even if the fluid challenge does not result in an increased cardiac output. Excessive intravascular volume and its complications would be the consequence of more aggressive fluid administration. Changes in arterial and plethysmographic dynamic indices after a single fluid challenge performed well as indicators of fluid responsiveness and their use in clinical practice could limit ineffective fluid administration to only a single colloid bolus. Arterial and plethysmographic indices and their changes after intravascular volume expansion correctly classified patients as responders above the threshold value, but were inaccurate for separating responders and nonresponders when they were below the threshold value. In the present study, only an invasive measurement, cardiac index, accurately predicted nonresponders. This finding was not confirmed by previous studies (6–8,18). Indeed, there were substantial differences among these studies. Moreover, the predictive value of cardiac index was not a main outcome of the present study, and it should be considered as the result of an explorative procedure. Further studies should evaluate whether cardiac output measurement is indeed the best tool to identify nonresponders to intravascular volume expansion.

In conclusion, arterial and plethysmographic pulse and systolic blood pressure variation were found to be equally accurate for fluid responsiveness prediction. When dynamic indices are below their threshold value, the change after intravascular volume expansion can improve fluid responsiveness evaluation. The analysis of the waveform derived by pulse oximetry, a widely available technology, could become the first step to guide intravascular fluid administration in hypotensive mechanically ventilated patients.

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