Passive leg raising is predictive of fluid responsiveness in spontaneously breathing patients with severe sepsis or acute pancreatitis*

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Objective: **Rapid fluid loading is standard treatment for hypovolemia. Because volume expansion does not always improve hemodynamic status, predictive parameters of fluid responsiveness are needed. Passive leg raising is a reversible maneuver that mimics rapid volume expansion. Passive leg raising-induced changes in stroke volume and its surrogates are reliable predictive indices of volume expansion responsiveness for mechanically ventilated patients. We hypothesized that the hemodynamic response to passive leg raising indicates fluid responsiveness in nonintubated patients without mechanical ventilation.**

Design: **Prospective study.**

Setting: **Intensive care unit of a general hospital.**

Patients: **We investigated consecutive nonintubated patients, without mechanical ventilation, considered for volume expansion.**

Interventions: **We assessed hemodynamic status at baseline, after passive leg raising, and after volume expansion (500 mL 6% hydroxyethyl starch infusion over 30 mins).**

Measurements and Main Results: **We measured stroke volume using transthoracic echocardiography, radial pulse pressure using an arterial catheter, and peak velocity of femoral artery flow using continuous Doppler. We calculated changes in stroke volume, pulse pressure, and velocity of femoral artery flow induced by passive leg raising (respectively, Δstroke volume, Δpulse pressure, and Δvelocity of femoral artery flow). Among 34 patients included in this study, 14 had a stroke volume increase of ≥15% after volume expansion (responders). All patients included in the study had severe sepsis (n = 28; 82%) or acute pancreatitis (n = 6; 18%). The Δstroke volume ≥10% predicted fluid responsiveness with sensitivity of 86% and specificity of 90%. The Δpulse pressure ≥9% predicted fluid responsiveness with sensitivity of 79% and specificity of 85%. The Δvelocity of femoral artery flow ≥8% predicted fluid responsiveness with sensitivity of 86% and specificity of 80%.**

Conclusions: **Changes in stroke volume, radial pulse pressure, and peak velocity of femoral artery flow induced by passive leg raising are accurate and interchangeable indices for predicting fluid responsiveness in nonintubated patients with severe sepsis or acute pancreatitis.(Crit Care Med 2010; 38:819–825)**

KEY WORDS: fluid responsiveness; leg raising; stroke volume; pulse pressure; blood flow; Doppler; echocardiography; sepsis; pancreatitis.

Blood volume is a determinant of hemodynamic stability, which determines oxygen supplied to the tissues. Rapid infusion of crystalloids or colloids is the usual treatment for symptomatic hypovolemia. Because blood volume cannot easily be measured at the bedside, physicians need to know whether left ventricular stroke volume (SV) increases with volume expansion (VE) (1–3).

Cardiac preload estimation is not an accurate method for predicting fluid responsiveness in patients with acute circulatory failure (1). Dynamic indices, based on analysis of SV preload dependence, have been validated to predict fluid responsiveness in mechanically ventilated patients (3). Such indices are also needed for spontaneously breathing patients. Passive leg raising (PLR) is a reversible maneuver that mimics rapid VE by shifting venous blood from the lower limbs (4) toward the intrathoracic compartment (5, 6). Thus, PLR increases the cardiac preload and, by definition, increases SV if the heart is preload-dependent (7–9).

Recent studies demonstrated that PLR-induced changes in SV (ΔSV) and cardiac output are reliable predictive indices of VE responsiveness, whatever the breathing conditions (10–13). The ΔSV, measured by transthoracic echocardiography (11, 12), is an accurate index of fluid responsiveness, but its feasibility is variable and depends on patient echogenicity, hospital equipment, and physicians' skills in echocardiography.

PLR-induced change in systemic arterial pulse pressure (ΔPP) is another hemodynamic parameter that detects preload responsiveness (10, 14). Its measurement requires ordinary critical care equipment and expertise, but ΔPP has been demonstrated to be less accurate than PLR-induced change in aortic blood flow at detecting VE responsiveness in mechanically ventilated patients (14, 15). To our knowledge, no study has compared the accuracy of ΔPP with that of PLR-induced change in blood flow for predicting fluid-loading responsiveness in nonintubated patients.

Echo Doppler of peripheral arteries permits noninvasive measurement of changes in peripheral artery flow. Those measurements are independent of transthoracic echogenicity and the presence of

*See also p. 989.

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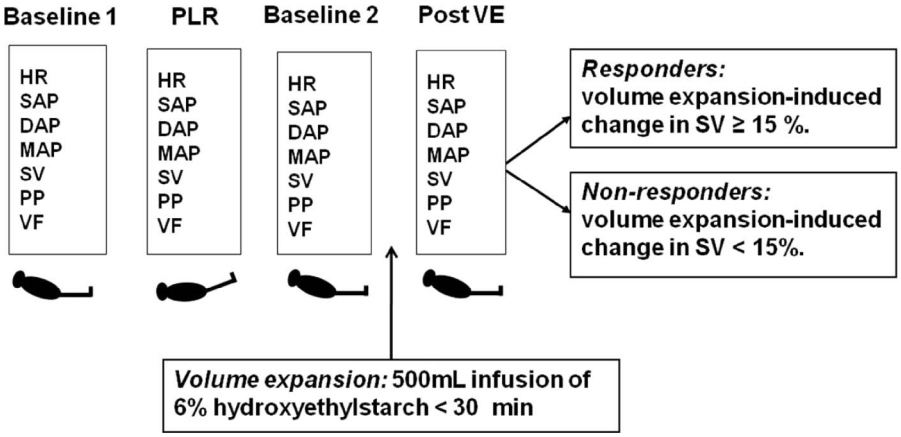

Figure 1. Study design. *PLR*, passive leg raising; *VE*, volume expansion; *HR*, heart rate; *SAP*, systolic arterial pressure; *DAP*, diastolic arterial pressure; *MAP*, mean arterial pressure; *PP*, radial pulse pressure; *SV*, stroke volume; *VF*, peak velocity of femoral artery flow; Δ*SV*, Δ*PP*, and Δ*VF*, PLR-induced changes in SV, PP, and VF, respectively.

an arterial catheter. Thus, when ΔSV and ΔPP are not available, PLR-induced change in peripheral artery flow could be measured. To our knowledge, no study has tested PLR-induced change in peripheral artery flow measured by echo Doppler to predict preload responsiveness.

The ΔSV as measured by transthoracic echocardiography, ΔPP as measured by radial catheter, and PLR-induced change in the peak velocity of femoral artery flow (ΔVF), as measured by echo Doppler, are three different methods for hemodynamic assessment. When one of these indices is not measurable, it can be replaced by another if accuracy for predicting fluid responsiveness is identical. However, their relative accuracy at predicting VE responsiveness is not clearly established.

The aim of this study was to test whether ΔSV, ΔPP, and ΔVF are equally accurate at predicting VE responsiveness in nonintubated patients with acute circulatory failure, thus rendering them interchangeable.

MATERIALS AND METHODS

This study was submitted to the Institutional Review Board for human subjects of our institutions. The protocol was approved and was considered to be part of routine practice. Patients were informed before participation in the study.

Patients

Two echocardiographists (S.P. and F.D.) prospectively assessed consecutive patients hospitalized in the critical care unit (21 beds) of the general hospital center in Valenciennes (France), from December 2004 to July 2006. We selected for inclusion in the study all nonintubated patients with sepsis or acute pancreatitis, with no amputation of lower limbs, for whom the attending physician decided to perform fluid challenge. This decision was based on the presence of at least one clinical sign of inadequate tissue perfusion and the absence of contraindications for fluid infusion. Clinical signs of inadequate tissue perfusion were defined as follows: acute circulatory failure defined as systolic arterial pressure (SAP) of <90 mm Hg (or a decrease of >40 mm Hg in previously hypertensive patients); urine output of <0.5 mL/kg per hour for at least 1 hr; tachycardia (heart rate >100/min); and mottled skin. Cardiac rhythm had to be regular and sinusal. Every patient had a 3-Fr radial catheter (Seldiflex Plastimed; Division Prodimed, Saint-Leu-La-Foret, France) in place before the study as part of their standard hemodynamic monitoring. Patients were not included in the study if they had high-grade aortic insufficiency, if transthoracic echogenicity was not satisfactory, or if noninvasive ventilation was warranted.

Measurements

For blood pressure and heart rate measurements, we used off-line recordings on a central monitor (Information Center M3155; Philips Medical System, Andover, MA) connected to bedside monitors (IntelliVue MP70; Philips Medical System, Boeblingen, Germany). SAP and diastolic arterial pressure (DAP) were measured. Mean arterial pressure (MAP) was calculated as MAP = (SAP + 2DAP)/3. Arterial PP was calculated as the SAP minus the DAP.

All echographic measurements were made on-line with commercially available echocardiographic HDI 3000 equipment (Philips Medical System; Bothell, WA) with a 2-MHz transthoracic transducer. Aortic blood flow was recorded with pulsed Doppler at the level of the aortic valve so that the click of the aortic closure was obtained. The velocity time integral of aortic blood flow was measured. The aortic valve area was calculated from the diameter of the aortic orifice, measured at the insertion of the aortic cusps, as aortic area = $\pi \times (\text{aortic diameter}/2)^2$. SV was calculated as SV = aortic valve area × the velocity time integral of aortic blood flow (16). Femoral blood flow was recorded with continuous Doppler at the level of the common femoral artery. One of the two common femoral arteries was identified with echographic two-dimensional and color Doppler modes. VF was measured with continuous Doppler.

Because hemodynamic values may vary within a respiratory cycle (17), an average of 10 consecutive cardiac cycles, over at least one respiratory cycle, was used for measurements of SAP, DAP, MAP, PP, SV, and VF. Measurements started at the lowest value of each index within a respiratory cycle.

Study Design

Figure 1 illustrates the design of the study. Hemodynamic measurements (heart rate, SAP, DAP, MAP, PP, VF, and SV) were recorded at each step of the protocol. Baseline 1 indicates that patients were in a semirecumbent position, with the trunk elevated 30° to 45° relative to the lower limbs, who were horizontal (baseline position). PLR indicates that patients were in a supine position with the lower limbs elevated 30° to 45° relative to the trunk, who was horizontal. Each hemodynamic measurement was recorded within the first 5 mins. Relative changes in hemodynamic indices induced by PLR are expressed in percentages as follows: change (%) = 100 × (PLR value − baseline 1 value)/baseline 1 value. Baseline 2 indicates that the lower limbs and trunk were returned to baseline position for at least 5 mins. After hemodynamic measurements, VE was performed within 30 mins by infusing 500 mL of 6% hydroxyethyl starch (Voluven; Fresenius Kabi, Sèvres, France). Post-VE indicates that after VE, patients remained in the baseline position. Relative changes in hemodynamic indices induced by VE are expressed in percentages as follows: change (%) = 100 × (post-VE value − baseline 2 value)/baseline 2 value. Patients were considered as responders to VE if their SV increased by ≥15%. Because the aortic valve area is not affected by VE, this 15% cut-off value was chosen before the beginning of the study as being twice the intraobserver variability of the velocity time integral of the aortic valve flow, measured by transthoracic echocardiography in previous studies (11, 12, 16, 17).

Table 1. Descriptive clinical data

	Responders, n = 14	Nonresponders, n = 20	p
Age, yrs	55 ± 20	52 ± 19	.61
Sex ratio, M/F	6/8	13/7	.30
SAPS II	33.7 ± 12.8	32.5 ± 12.6	.78
In-hospital mortality	2 (14%)	2 (10%)	1
ICU stay before inclusion, days[a]	1 (0–5)	0 (0–3)	.31
OALL	0 (0%)	1 (5%)	1
COPD	0 (0%)	2 (10%)	.50
Arterial hypertension	8 (57%)	5 (25%)	.46
LVEF <45%	3 (21%)	2 (10%)	.63
Indication for ICU stay (on the day of inclusion)			
Sepsis	13 (93%)	15 (75%)	.36
Pulmonary infections	7 (50%)	10 (50%)	1
Urine tract infections	3 (21%)	2 (10%)	.63
Abdominal infections	2 (14%)	1 (5%)	.56
Other infections	1 (7%)	2 (10%)	1
Nosocomial infections	6 (43%)	5 (25%)	.46
Acute pancreatitis	1 (7%)	5 (25%)	.36
Clinical hemodynamic parameters			
Arterial hypotension	8 (57%)	10 (50%)	1
Oliguria	8 (57%)	11 (55%)	1
Tachycardia	10 (71%)	13 (65%)	1
Mottled skin	6 (43%)	3 (15%)	.12
Vasoactive drugs	2 (14%)	4 (20%)	1

SAPS II, Simplified Acute Physiologic Score II; ICU, intensive care unit, OALL, obliterating arteriopathy of the lower limbs; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction.

[a]Values expressed as median and interquartile range (25^{th}–75^{th} percentiles). Values are expressed as number (%) or mean ± SD.

Statistical Analysis

Numerical data are given as mean ± SD except when otherwise indicated. The Shapiro-Wilk test was used to test for normal distribution. All numerical variables were normally distributed in responders and nonresponders except for the "ICU stay before inclusion." Comparisons before and after PLR, before and after VE, and between baseline 1 and baseline 2 were performed using a paired-sample Student's *t* test. The comparison between responder and nonresponder values was performed using an independent-sample Student's *t* test except for the "ICU stay before inclusion," which was compared using the Mann-Whitney *U* test. Qualitative variables were reported as number and percentage and compared between groups using a Fisher test. Linear correlations were tested using the Pearson test and linear regression method. The receiver-operating characteristic curves ± SE were compared using the Hanley-McNeil test (18). Cut-off values for ΔSV, ΔPP, and ΔVF were chosen to correspond to the best respective Youden's index (19) calculated as follows: Youden's index = sensitivity + specificity − 1. Threshold indicator values such as sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated for each hemodynamic indicator tested. A $p < .05$ was considered statistically significant. Statistical analysis was performed using SPSS 13.0.1 software (SPSS, Chicago, IL) for all tests except the Hanley-McNeil test.

RESULTS

Among 890 patients hospitalized in the critical care unit of the general hospital center in Valenciennes from December 2004 to July 2006, 39 (4.4%) were assessed for inclusion in the study. Among those 39 patients meeting inclusion criteria, five (12.8%) were excluded because of transthoracic poor insonation. Therefore, 34 patients (15 females and 19 males) with a mean age of 53 ± 19 yrs were included in the study because of the presence of hypotension (n = 19; 56%), oliguria (n = 19; 56%), tachycardia (n = 23; 68%), or mottled skin (n = 8; 24%). Mean Simplified Acute Physiologic Score II (20) was 33 ± 13, and four (12%) patients died during hospitalization. All patients had severe sepsis (21) (n = 28; 82%) or acute pancreatitis (22) (n = 6; 18%), and at least hypoperfusion or hypotension. Most patients had no vasoactive drugs (n = 34; 85%).

The variability of SV and VF measurements was tested. SV and VF were measured three times in 10 patients by the same observer (SP, intraobserver variability) and by a second observer (FD, interobserver variability). Intraobserver and interobserver variabilities for SV were, respectively, 3.7% ± 1.8% and 7.2% ± 4.7%. Intraobserver and interobserver variabilities for VF were, respectively, 2% ± 1.2% and 8.4% ± 9.2%.

The results were obtained with SAP, DAP, MAP, PP, SV, and VF measured over an average of 1.6 ± .2 respiratory cycles. For the group as a whole, SV was significantly increased by PLR from 47 ± 14 mL to 50 ± 14 mL ($p < .001$), and by VE from 47 ± 14 mL to 53 ± 15 mL ($p < .001$). The ΔPP and ΔVF were positively correlated with ΔSV with, respectively, $r^2 = .40$ ($\Delta SV = .69\Delta PP + 5$; $p < .001$) and $r^2 = .62$ ($\Delta SV = 1.01\Delta VF + 2.4$; $p < .001$). Fourteen (41%) patients were considered to be responders to VE. The general characteristics of the two groups were similar (Table 1). Within each group, hemodynamic parameters were identical at baseline 1 and baseline 2 (Table 2). The ΔSV (17 ± 7% vs. 4 ± 5%; $p < .001$), ΔPP (12 ± 8% vs. 3 ± 6%; $p < .01$), and ΔVF (12 ± 5% vs. 3 ± 5%; $p < .001$) were significantly higher in responders than in nonresponders, and each was positively correlated with a VE-induced increase in SV (Fig. 2).

A ΔSV of ≥10% predicted fluid responsiveness with a sensitivity of 86% and a specificity of 90% (Table 3, Fig. 3). Likewise, PLR-induced increases in surrogates of SV, ΔPP ≥9%, and ΔVF ≥8% were able to distinguish fluid responders from nonresponders (Table 3, Fig. 3). Areas under receiver-operating characteristic curves ± SE for ΔSV (area under the curve, .94 ± .04), ΔPP (area under the curve, .86 ± .08), and ΔVF (area under the curve, .93 ± .04) were not significantly different (Fig. 4).

SV at baseline (39 ± 15 mL vs. 52 ± 10 mL; $p < .01$) and changes in SAP (9% ± 9% vs. 2% ± 3%; $p < .05$) or MAP (8% ± 10% vs. 1% ± 4%; $p < .05$) induced by PLR differed between responders and nonresponders. They were all tested as fluid responsiveness indices, but with lower accuracy for predicting the hemodynamic response to VE than ΔSV, ΔPP, or ΔVF.

DISCUSSION

The main finding of this study was that ΔSV, ΔPP, and ΔVF enabled accurate bedside prediction of preload responsiveness in nonintubated patients with severe

Table 2. Hemodynamic parameters at different times of the study in responders and nonresponders

	Baseline 1	PLR	Baseline 2	Post-VE
HR, beats/min				
Nonresponders	100 ± 23	100 ± 24	101 ± 24	100 ± 23[c]
Responders	102 ± 19	102 ± 19	101 ± 19	99 ± 17[c]
SAP, mm Hg				
Nonresponders	117 ± 23	119 ± 22[b]	117 ± 22	122 ± 23[c]
Responders	109 ± 23	118 ± 23[b]	109 ± 24	122 ± 26[c]
DAP, mm Hg				
Nonresponders	59 ± 14	60 ± 14	60 ± 14	62 ± 12[c]
Responders	57 ± 12	61 ± 13[b]	56 ± 11	62 ± 12[c]
MAP, mm Hg				
Nonresponders	79 ± 15	79 ± 14	79 ± 15	82 ± 14[c]
Responders	74 ± 13	80 ± 14[b]	74 ± 13	82 ± 14[c]
PP, mm Hg				
Nonresponders	58 ± 19	59 ± 20	57 ± 19	60 ± 20[c]
Responders	53 ± 20	58 ± 19[b]	53 ± 21	60 ± 24[c]
SV, mL				
Nonresponders	52 ± 10	54 ± 11[b]	52 ± 11	55 ± 12[c]
Responders	39 ± 15[a]	45 ± 17[b]	40 ± 16[a]	49 ± 20[c]
CI, L/min/m^2				
Nonresponders	2.73 ± .77	2.81 ± .71[b]	2.75 ± .75	2.85 ± .72[c]
Responders	2.32 ± 1.05[a]	2.70 ± 1.21[b]	2.36 ± 1.09[a]	2.89 ± 1.30[c]
VF, cm/s				
Nonresponders	78 ± 19	80 ± 19[b]	78 ± 19	82 ± 21[c]
Responders	77 ± 25	86 ± 25[b]	78 ± 25	90 ± 28[c]
SV/PP				
Nonresponders	.90 ± .35	.92 ± .33	.91 ± .33	.92 ± .34
Responders	.74 ± .23[a]	.78 ± .24[b]	.75 ± .24[a]	.82 ± .25[c]
SV/VF				
Nonresponders	.67 ± .20	.68 ± .20	.67 ± .19	.67 ± .21
Responders	.51 ± .18[a]	.52 ± .19[b]	.51 ± .20[a]	.54 ± .21[c]

CI, cardiac index; PLR, passive leg raising; VE, volume expansion; HR, heart rate; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; PP, radial pulse pressure; SV, stroke volume; VF, peak velocity of femoral artery flow.

[a]$p < .05$ vs. nonresponders; [b]$p < .05$ vs. baseline 1; [c]$p < .05$ vs. baseline 2. Values given as mean ±SD.

sepsis or acute pancreatitis and can be considered interchangeable for predicting preload responsiveness. A ΔSV of >10%, a ΔPP of >9%, and a ΔVF of >8% were predictive of a positive hemodynamic response to VE induced by rapid fluid infusion.

Rapid fluid loading is the usual treatment for hypovolemia. The search for predictive factors of fluid responsiveness in spontaneously breathing patients was justified, because fluid responsiveness occurred in only 41% of patients. Thus, as previously described in spontaneously breathing patients, VE does not consistently improve hemodynamics (12, 17). Interestingly, VE-induced changes in heart rate in responders and nonresponders were not different and the decrease in heart rate (−2 ± 4%; $p < .05$) in responders was statistically significant but very small. Likewise, previous studies described no significant change in heart rate with VE despite a SAP increase in responder patients (12–14). Desensitizing of baroreflexes was described in patients with sepsis syndrome, septic shock, and even in healthy volunteers in a recumbent position (23). This suggests autonomic failure in patients in our study, all in cases of severe sepsis or systemic inflammatory response syndrome (24).

The effect via which hemodynamic status is enhanced after VE is related to increased venous return and cardiac preload. Thus, a practical way of ascertaining preload responsiveness is to determine whether the heart responds positively to rapid fluid loading. PLR was recently proposed as a simple reversible fluid-loading test, avoiding fluid infusion in patients in whom it would be harmful (1, 2, 25). Previous studies demonstrated that PLR effects on SV were correlated with VE effects, whatever the breathing conditions, and that hemodynamic effects induced by PLR were completely reversible (10–13). Because ΔSV was positively correlated with a VE-induced increase in SV, and because hemodynamic parameters did not differ between baselines 1 and 2, this study confirms that PLR mimics reversible rapid fluid loading in nonintubated patients. In addition, heart rate was unaltered by PLR, suggesting that efferent activity of the autonomic nervous system was not significantly altered. Considering its hemodynamic effects, PLR was proposed to detect responders to VE (1, 2, 25). Because ΔSV enables prediction of VE-induced change in SV ≥15% with positive and negative likelihood ratios of 8.6 and .16, respectively, this study confirms that PLR effects on SV permit accurate detection of nonintubated patients who will respond positively to VE (11, 12).

To our knowledge, our study is the first to compare, in nonintubated patients, the accuracy of ΔSV and PLR-induced changes in surrogates of SV (ΔPP and ΔVF) for detecting fluid responsiveness. In this particular population of patients with severe sepsis or acute pancreatitis, we did not find any difference between the accuracy of ΔSV, ΔPP, and ΔVF at predicting fluid responsiveness; therefore, to this end, they can be considered as interchangeable. The use of ΔPP and ΔVF as preload responsiveness markers is based on the hypothesis that they depend on SV and that their relationships with SV are not altered by PLR. During each systole, the left ventricle ejects a variable amount of blood through the systemic arterial circulation. Thus, each heartbeat generates a PP wave along the arterial tree that leads to arterial blood flow (26). Both PP and VF are influenced by complex properties of the systemic arterial tree, such as compliance, wave propagation, and wave reflexion (27, 28). Previous studies demonstrated that PLR-induced changes in surrogates of SV may be used in clinical practice to predict VE responsiveness in patients with mechanical ventilation (14, 15). They also found that the use of proximal substitutes of SV, such as aortic blood flow, may be more accurate markers of fluid responsiveness than the use of more distal markers such as radial PP (14). In this study, PLR induced significant increases in SV/PP and SV/VF in responders, but not in nonresponders. However, ΔPP and ΔVF were significantly correlated with ΔSV. Therefore, we conclude that the relationships between SV and its surrogates, PP and VF, are weakly but significantly altered by PLR. However, whatever the specific changes induced by PLR, ΔPP, and ΔVF, they were strongly correlated with the effects of VE on SV. Furthermore, ΔPP ≥9% and ΔVF ≥8% are able to discriminate between responders and nonresponders with very good accuracy (Table 3). Thus, physicians can choose between two devices, echo Dopp-

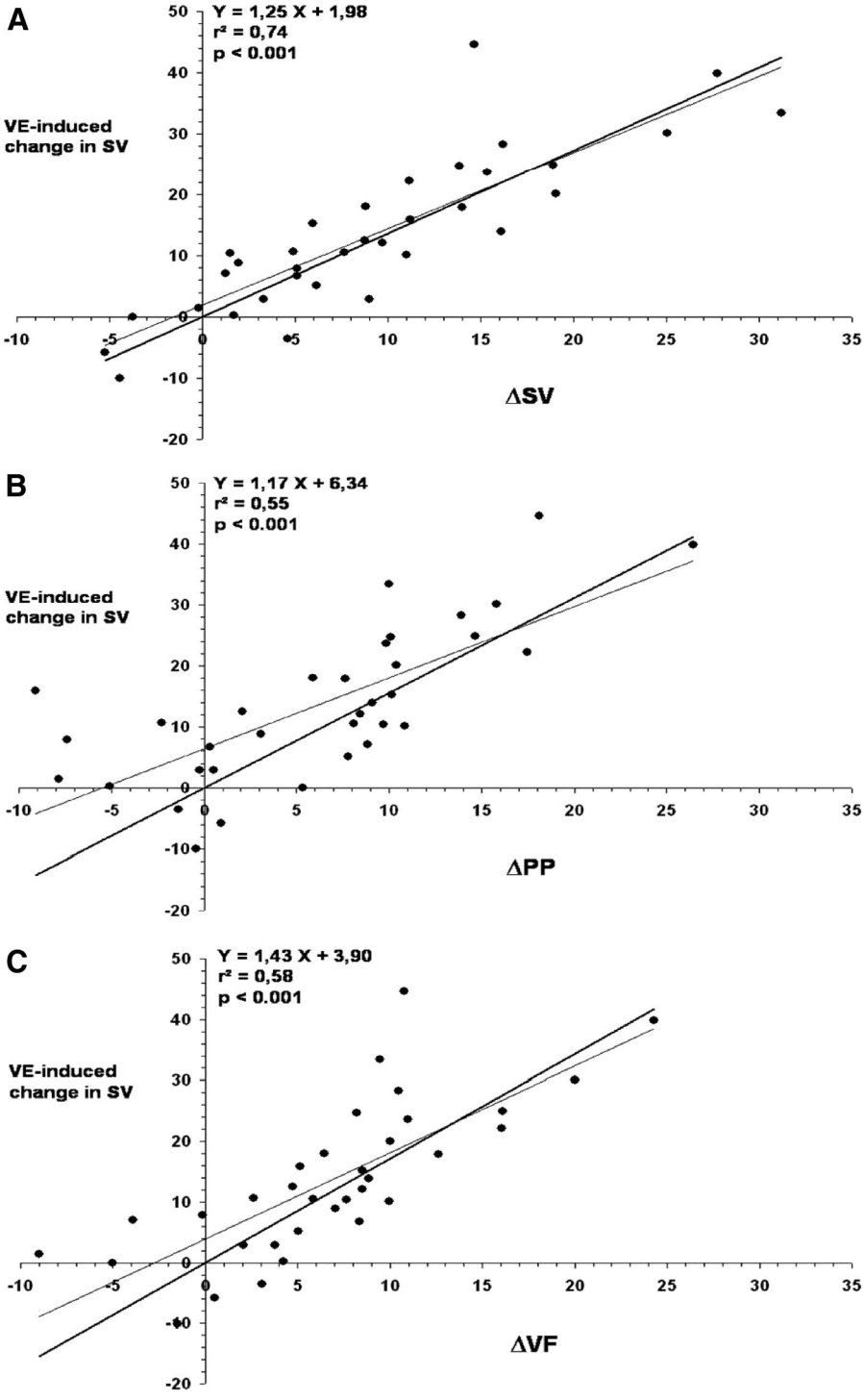

Figure 2. *A*, Linear correlation between change in stroke volumne (*SV*) induced by passive leg raising (Δ*SV*) and volume expansion (*VE*)-induced change in stroke volume. *B*, Linear correlation between change in radial pulse pressure induced by passive leg raising (Δ*PP*) and VE-induced change in stroke volume. *C*, Linear correlation between change in peak velocity of femoral artery flow induced by passive leg raising (Δ*VF*) and VE-induced change in stroke volume.

ler or artery catheter, and three sites of measurement, radial artery, femoral artery, or aortic valve, to detect spontaneously breathing patients who will respond to VE. Finally, changes in SAP and MAP induced by PLR and SV at baseline were all tested as fluid-responsiveness indices, but with lower accuracy for predicting a hemodynamic response to VE than ΔSV, ΔPP, or ΔVF. Because changes in SAP and MAP induced by PLR and SV at baseline are not greater than ΔSV, ΔPP, or ΔVF in terms of feasibility, and because their accuracy at predicting preload responsiveness is lower, they should not be used to this end.

Attention should be directed to the specific PLR maneuver providing such results (25). Contrary to the classic PLR maneuver (9, 10, 15), this specific PLR maneuver combined trunk lowering and lower limb raising. The correlation obtained between ΔSV and VE-induced change in SV in mechanically ventilated patients suggests that classic lower limb raising mimics a 300-mL VE (10). Given that trunk lowering may induce a 150-mL increase in intrathoracic blood volume (29), we suggest that the PLR maneuver used in our study may mimic a VE of approximately 450 to 500 mL. The correlation between ΔSV and effects on SV induced by infusion of 500 mL 6% hydroxyethyl starch supports this hypothesis. Consequently, the threshold values for ΔPP and ΔVF proposed in this study to detect responders to VE may not be extrapolated to a classic PLR maneuver that might transfer a smaller amount of blood to the central compartment.

Our study has some limitations. First, it was not designed to specifically investigate physiologic effects of PLR, in particular, in terms of volume transfer and kinetics. Second, we measured SV using a modified standard left ventricular outflow track Doppler method (16). Patients were not in a lateral recumbent position, as described previously, but in a semirecumbent or PLR position. This method was previously tested (11, 12) for discriminating responders to VE in spontaneously breathing patients with low intraobserver and interobserver variabilities (12). Third, we defined the positive response to VE as an increase in SV of ≥15% with rapid fluid loading. This cut-off value seems clinically relevant, because it was chosen in reference to previous studies (11, 17) and was at least twice the intraobserver variability of the velocity time integral of aortic blood flow measured in this study: $2 \times 3.7\% \pm 1.8\% = 7.4\% \pm 3.6\%$. Fourth, echo-derived SV was used both as a predictor and as a method to measure fluid responsiveness. Therefore, accuracy of ΔSV for predicting response to VE might be less reliable than ΔPP or ΔVF. To our knowledge, SV was not measured with two independent methods for predicting and measuring fluid responsiveness in previous studies. Finally, the study population comprised few or no patients with low left ventricular ejection fraction

Table 3. Accuracy of hemodynamic parameters for predicting fluid responsiveness

	Threshold Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio
ΔSV	10%	86%	90%	86%	90%	8.6	.16
ΔPP	9%	79%	85%	79%	85%	5.2	.25
ΔVF	8%	86%	80%	75%	89%	4.3	.18

ΔSV, passive leg raising induced-change in stroke volume; ΔPP, passive leg raising induced-change in radial pulse pressure; ΔVF, passive leg raising induced-change in the peak velocity of femoral artery flow.

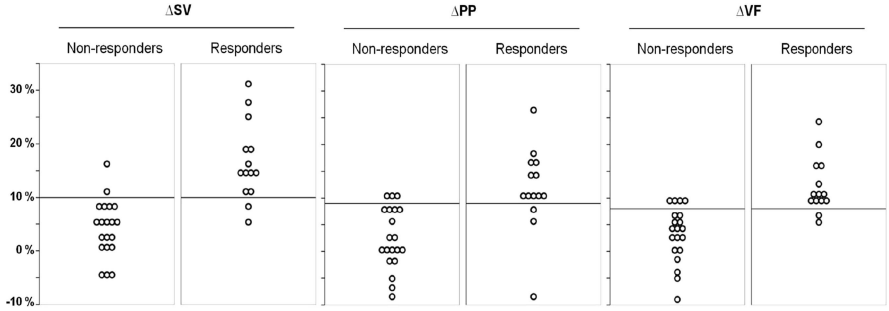

Figure 3. Individual baseline values for each indicator, passive leg raising-induced changes in stroke volume (Δ*SV*), radial pulse pressure (Δ*PP*), and peak velocity of femoral artery flow (Δ*VF*) in patients with volume expansion-induced changes in SV ≥15% (responders) and <15% (nonresponders).

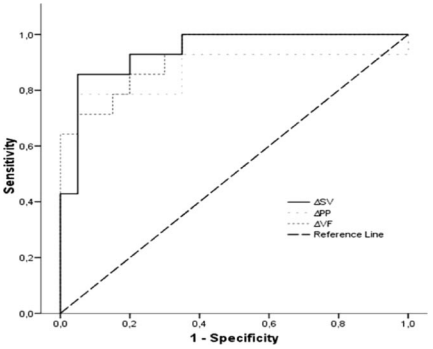

Figure 4. Receiver-operating characteristics curves comparing the capacity of changes induced by passive leg raising in stroke volume (Δ*SV*), radial pulse pressure (Δ*PP*), and peak velocity of femoral artery flow (Δ*VF*) to discriminate responders from nonresponders regarding volume expansion in the overall population.

(<45%) or reduced right ventricular function using vasoactive (inotropic, vasopressor, vasodilator) drugs, nonsinusal rhythm, or peripheral arterial occlusive disease. Thus, results need to be confirmed in further studies before they can be generalized to an unselected critically ill population.

CONCLUSIONS

We demonstrate that changes in left ventricular SV, radial PP, and VF are accurate and interchangeable indices of fluid-loading responsiveness in spontaneously breathing patients with sepsis or acute pancreatitis. This finding extends the feasibility of preload responsiveness assessment by passive leg raising in spontaneously breathing patients.

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