

Passive leg raising predicts fluid responsiveness in the critically ill*

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Objective: Passive leg raising (PLR) represents a “self-volume challenge” that could predict fluid response and might be useful when the respiratory variation of stroke volume cannot be used for that purpose. We hypothesized that the hemodynamic response to PLR predicts fluid responsiveness in mechanically ventilated patients.

Design: Prospective study.

Setting: Medical intensive care unit of a university hospital.

Patients: We investigated 71 mechanically ventilated patients considered for volume expansion. Thirty-one patients had spontaneous breathing activity and/or arrhythmias.

Interventions: We assessed hemodynamic status at baseline, after PLR, and after volume expansion (500 mL NaCl 0.9% infusion over 10 mins).

Measurements and Main Results: We recorded aortic blood flow using esophageal Doppler and arterial pulse pressure. We calculated the respiratory variation of pulse pressure in patients without arrhythmias. In 37 patients (responders), aortic blood

flow increased by $\geq 15\%$ after fluid infusion. A PLR increase of aortic blood flow $\geq 10\%$ predicted fluid responsiveness with a sensitivity of 97% and a specificity of 94%. A PLR increase of pulse pressure $\geq 12\%$ predicted volume responsiveness with significantly lower sensitivity (60%) and specificity (85%). In 30 patients without arrhythmias or spontaneous breathing, a respiratory variation in pulse pressure $\geq 12\%$ was of similar predictive value as was PLR increases in aortic blood flow (sensitivity of 88% and specificity of 93%). In patients with spontaneous breathing activity, the specificity of respiratory variations in pulse pressure was poor (46%).

Conclusions: The changes in aortic blood flow induced by PLR predict preload responsiveness in ventilated patients, whereas with arrhythmias and spontaneous breathing activity, respiratory variations of arterial pulse pressure poorly predict preload responsiveness. (Crit Care Med 2006; 34:1402–1407)

KEY WORDS: fluid responsiveness; leg raising; pulse pressure variation; aortic blood flow

It is important to be able to predict which hemodynamically unstable patients will increase their systemic blood flow in response to volume expansion, because fluid loading in a non-volume-responsive patient delays definitive therapy and may be detrimental. In this regard, respiration-induced changes in arterial pulse pressure (ΔPP) have been demonstrated to accurately predict preload responsiveness in mechanically ventilated patients who are making no inspiratory efforts (1). However, not studied is whether such respiration-induced pulse

pressure variation may not accurately predict preload responsiveness when the patients are triggering the ventilator or in the presence of arrhythmias (2).

We hypothesized that the transient hemodynamic effect of passive leg raising (PLR) on left ventricular stroke volume or its surrogates could be an alternative method to detect preload responsiveness in all categories of patients receiving mechanical ventilation because the effect persists over several breaths. PLR induces a translocation of venous blood from the legs to the intrathoracic compartment (3, 4), resulting in a transient increase in right ventricular (5) and left ventricular (6, 7) preload. PLR as a “reversible-volume challenge” (8) is attractive because it is easy to perform at the bedside, induces a reversible volume challenge that is proportional to body size, and does not result in volume overload in non-preload-responsive subjects. The effects of PLR on cardiac output are variable (5, 8, 9), presumably depending on the existence of cardiac preload reserve. In this regard, our group previously proposed to predict fluid responsiveness in patients fully synchronized to their ven-

tilator by examining the effects of PLR on pulse pressure, taken as a surrogate for stroke volume (10). However, the predictive value of PLR in that previous study was only fair, presumably because stroke volume was estimated from peripheral pulse pressure, which also depends on arterial compliance and vasomotor tone (11). Estimating stroke volume by a more reliable surrogate, such as descending aortic flow, may improve the predictive value of PLR for preload-responsiveness.

Esophageal Doppler is a minimally invasive method allowing real-time monitoring of the descending aortic blood flow, an estimate of cardiac output (12–16). Esophageal Doppler tracks changes in cardiac output induced either by inotropic drugs (17) or by volume replacement (18).

We performed the present study in patients receiving mechanical ventilation. We hypothesized that changes in aortic blood flow during PLR a) could predict fluid responsiveness as reliably as ΔPP and better than changes in mean pulse pressure during PLR in patients well synchronized to the ventilator and in sinus rhythm; and b) would be better

***See also p. 1559.**

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than ΔPP in cases of persistent breathing activity and/or arrhythmias. Thus, we tested the ability of three parameters to predict fluid response: the PLR-induced changes in aortic blood flow, the PLR-induced changes in pulse pressure and ΔPP . These parameters were tested in two groups of patients: patients with perfect adaptation to the ventilator and with sinus rhythm and patients assisting the ventilator and/or with irregular cardiac rhythm.

PATIENTS AND METHODS

Patients. We studied mechanically ventilated patients for whom the attending physician decided to perform a fluid challenge. This decision was based on the presence of at least one clinical sign of inadequate tissue perfusion in the absence of contraindication for fluid infusion. Clinical signs of inadequate tissue perfusion were defined as a) systolic blood pressure <90 mm Hg (or a decrease >50 mm Hg in previously hypertensive patients) or the need for vasoactive drugs (dopamine >5 $\mu\text{g}/\text{kg}/\text{min}$ or norepinephrine); b) urine output <0.5 mL/kg/hr for ≥ 2 hrs; c) tachycardia (heart rate $>100/\text{min}$); or d) presence of skin mottling. Some patients exhibited spontaneous breathing activity, as assessed by visual observation of the airway pressure/time curve, and/or had an irregular cardiac rhythm. Subjects were recruited from our general intensive care unit service. No subjects who met the previous criteria were excluded from this study if identified before volume resuscitation.

This observational study was submitted for approval to three committees: the Institutional Review Board for Human Subjects of Bicêtre hospital, the Institutional Board of the University of Pittsburgh, and the Ethics Committee of the Société de Réanimation de Langue Française. All approved the protocol and considered it a part of routine practice. Patients were informed that they participated in this study.

Measurements. All hemodynamic data were continuously collected using the HEM3.5 software (Notocord, Croissy-sur-Seine, France). Heart rate and arterial pressure were averaged over 10 secs. In patients with an arterial catheter, ΔPP was calculated as follows (19):

$$\Delta PP (\%) = \frac{(PP_{\max} - PP_{\min})}{[(PP_{\max} + PP_{\min})/2]} \times 100 \quad [1]$$

where PP_{\max} and PP_{\min} are the maximal and minimal values of pulse pressure over one respiratory cycle, respectively. The ΔPP value was averaged over five respiratory cycles.

Doppler measurements were obtained using Hemosonic100 (Arrow Intl, Everett, MA) (20). The position of the esophageal probe was adjusted to obtain the best

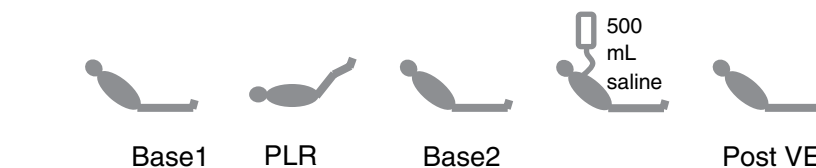


Figure 1. Study design. PLR, passive leg raising; VE, volume expansion.

signals of descending aorta blood velocity and diameter. Once positioned, the esophageal probe was not moved unless the flow signal drifted due to patient movement. Aortic blood flow was continuously and automatically calculated from these signals by the acquisition software and averaged over 10 secs.

Study Design. We measured pressures and flow during four sequential steps (Fig. 1). A first set of measurements was obtained in the semirecumbent position (45°) (designated base 1). Using an automatic bed elevation technique, the lower limbs were then raised to a 45° angle while the patient's trunk was lowered in supine position. Thus, the angle between the trunk and the lower limbs was unchanged (135°). A second set of measurements (designated PLR) were obtained during leg elevation, at the moment when aortic blood flow reached its highest value. In all patients, the maximal effect of PLR on aortic blood flow was observed within 1 min. The body posture was then returned to the base 1 position and a third set of measurements was recorded (base 2). Finally, measurements were obtained after a 10-min infusion of 500 mL of saline (designated post-VE). The ventilator settings and vasoactive therapy were kept constant throughout the study period.

Statistical Analysis. Patients with an increase in aortic blood flow $\geq 15\%$ and $<15\%$ with fluid infusion from base 2 were classified as responders and nonresponders, respectively. This cutoff value was chosen by reference to previous studies (19, 21, 22) assessing fluid responsiveness on the basis of cardiac index. Initially, this cutoff value was admitted as the minimal difference between two measures of cardiac output by thermodilution to suggest clinical significance (23). All the analyzed variables were normally distributed (Kolmogorov-Smirnov test for normality). Comparisons of hemodynamic variables before vs. after intervention were assessed using a paired Student's *t*-test, and the comparisons between responders vs. nonresponders were assessed using two sample Student's *t*-test. Results are expressed as mean \pm SD. Linear correlations were tested using the linear regression method. The area under the receiver operating characteristic (ROC) curves (\pm SE) for PLR-induced changes of aortic blood flow and of pulse pressure were compared in all patients using a Hanley-McNeil test (24). Patients for whom ΔPP was available were divided in two subgroups: one including only

patients with no spontaneous breathing activity and the other including patients with spontaneous breathing activity. Area under ROC curves for ΔPP and PLR-induced changes of aortic blood flow and of pulse pressure were compared in each subgroup. We considered $p \leq .05$ as statistically significant. The statistical analysis was performed using Statview 5.0 software (Abacus Concepts, Berkeley, CA) for all tests except the Hanley-McNeil test, which was performed with the MedCalc 8.1.0.0 software (Mariakerke, Belgium).

RESULTS

Patient Characteristics. Seventy-four patients were initially included in the study. Three of these subjects (4%) were excluded because satisfactory Doppler signals could not be obtained. The final pool of patients comprised 44 men and 27 women who were 58 ± 16 yrs old. Sixty-six patients were ventilated in the assist-controlled mode (tidal volume, 558 ± 96 mL) and five patients with pressure support. Respiratory rate was $23 \pm 5/\text{min}$, and positive expiratory pressure was 6 ± 2 cm H_2O . Thirty-nine patients were sedated. Spontaneous ventilator triggering was observed in 22 patients and arrhythmias in 11 patients (frequent ventricular extra-systoles in four patients, atrial fibrillation in three, and frequent atrial extrasystoles in four). Two patients had both spontaneous ventilator triggering and arrhythmia. The insertion and positioning of the Doppler probe took 4 ± 1 mins. This insertion or the PLR maneuver did not induce any adverse effect.

Table 1 summarizes the origin of the hemodynamic disturbance in responders and nonresponders. Thirty-six patients received vasoactive drugs (norepinephrine in 29, dopamine in five, dobutamine in two, and epinephrine in one).

Effects of PLR and Volume Expansion on Aortic Blood Flow. For the group as a whole, aortic blood flow significantly increased from 3.3 ± 2.0 to 3.7 ± 1.9 L/min during PLR. After returning to baseline (base 2) following repositioning, aortic blood flow increased again to 3.9 ± 2.0 L/min after volume expansion ($p < .05$ vs. base 2).

Table 1. Origin of hemodynamic disturbance in responders and nonresponders suspected before fluid administration

	Responders (n)	Nonresponders (n)
Septic shock	19	27
Cardiogenic shock	4	2
Non-septic hypovolemic shock	4	3
Shock resulting from a severe brain injury	6	0
Drug poisoning	1	1
Unknown origin	3	1
Total	37	34

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

	Base 1	PLR	Base 2	Post VE
HR, beats/min				
Nonresponders	98 ± 18	96 ± 19	96 ± 19	95 ± 19
Responders	107 ± 28 ^a	107 ± 28	107 ± 28	106 ± 26
SAP, mm Hg				
Nonresponders	116 ± 26	119 ± 27	115 ± 25	120 ± 29
Responders	99 ± 23 ^a	114 ± 25 ^b	100 ± 22 ^a	115 ± 29 ^c
DAP, mm Hg				
Nonresponders	59 ± 16	60 ± 16	58 ± 16	60 ± 17
Responders	54 ± 17	61 ± 16 ^b	53 ± 16	59 ± 18 ^c
MAP, mm Hg				
Nonresponders	79 ± 18	81 ± 20	77 ± 18	80 ± 20
Responders	69 ± 17 ^a	78 ± 17 ^b	68 ± 16 ^a	77 ± 20 ^c
PP, mm Hg				
Nonresponders	57 ± 18	59 ± 19	57 ± 18	60 ± 19
Responders	45 ± 14 ^a	53 ± 17 ^b	47 ± 14 ^a	56 ± 19 ^c
ABF, L/min				
Nonresponders	4.2 ± 2.2	4.3 ± 2.2	4.1 ± 2.1	4.2 ± 2.2
Responders	2.5 ± 1.3 ^a	3.1 ± 1.5 ^{a,b}	2.6 ± 1.3 ^a	3.5 ± 2 ^c
Aortic diameter, mm				
Nonresponders	23 ± 3	22 ± 3	22 ± 3	22 ± 3
Responders	22 ± 4	23 ± 4 ^b	22 ± 3	24 ± 4 ^c

PLR, passive leg raising; VE, volume expansion; HR, heart rate; SAP, DAP, MAP, and PP, systolic, diastolic, mean, and pulse arterial pressure, respectively; ABF, aortic blood flow.

^a*p* < .05, responders vs. nonresponders; ^b*p* < .05, PLR vs. base 1; ^c*p* < .05, post-VE vs. base 2. Mean ± SD. n = 71 patients.

Aortic blood flow was increased by ≥15% from base 2 value after volume expansion in 37 patients (responders) and by <15% in 34 patients (nonresponders, Table 2). The changes in aortic blood flow induced by either PLR or fluid loading were significantly greater in responders than in nonresponders. In responders, was aortic blood flow increased by 28 ± 21% from base 1 (*p* < .05) to PLR and by 40 ± 22% from base 2 to volume expansion (*p* < .05, Fig. 2). In all these patients, the effect of PLR on aortic blood flow occurred in the first 30 secs. In nonresponders, aortic blood flow did not change significantly, either with PLR or after volume expansion (Table 2, Fig. 2).

For the group as a whole, the increase in aortic blood flow induced by PLR (from base 1 value) correlated well with that induced by volume expansion (from base 2 value, *r*² = .69, *p* < .001). An increase in aortic blood flow induced by PLR

≥10% predicted the response to volume expansion (increase in aortic blood flow by ≥15%) with a sensitivity of 97% and a specificity of 94% (Fig. 3); that is, only one responder and two nonresponders out of 74 subjects were incorrectly classified by the method.

Effects of PLR and Volume Expansion on Pulse Pressure. In those patients who responded to fluid administration, PLR and volume expansion increased pulse pressure over the base 1 value by 19 ± 19% (*p* < .05) and 22 ± 32% (*p* < .05), respectively. In nonresponders, neither PLR nor volume expansion changed pulse pressure. The comparison of the effect of PLR on pulse pressure in these two groups was significant (*p* < .05, Table 2).

For the group as a whole, if PLR increased pulse pressure by ≥12%, the ensuing response to volume expansion could be predicted with a sensitivity of 60% and a specificity of 85%. However,

the area under the ROC curve (±SE) for the PLR-induced changes in aortic blood flow (0.96 ± 0.02) was significantly greater than that under the ROC curve for the PLR-induced changes in pulse pressure (0.75 ± 0.06, Fig. 4).

Respiratory Variation of Pulse Pressure. ΔPP was assessed in 30 patients in whom both no inspiratory effort occurred and their cardiac rhythm was regular sinus rhythm. Sixteen were responders and 14 were nonresponders. As shown in Table 3, in this population of 30 patients, ΔPP at base 2 was significantly greater in responders than in nonresponders (18 ± 10% vs. 7 ± 4%, respectively). In responders, ΔPP significantly decreased to 14 ± 15% after fluid infusion, whereas it was not altered by fluid infusion in nonresponders. The changes in ΔPP induced by fluid infusion were significantly different between responders and nonresponders.

If ΔPP at base 2 was ≥12%, the ensuing response to volume expansion could be predicted with a sensitivity of 88% and a specificity of 93%.

The areas under the ROC curves (±SE) for the PLR-induced changes in aortic blood flow (0.91 ± 0.06), for ΔPP (0.91 ± 0.05), and for the PLR-induced changes in pulse pressure (0.74 ± 0.09) were not significantly different in those patients making no inspiratory effort and with sinus cardiac rhythm.

Nineteen patients with regular sinus rhythm had spontaneous breathing activity. ΔPP was not different between responders (eight patients) and nonresponders (11 patients) in this subgroup (16 ± 17% vs. 15 ± 11%, respectively, Table 3). A ΔPP ≥8% predicted fluid responsiveness with a sensitivity of 88% and a specificity of 46%. If a ΔPP ≥12% was considered (i.e., the threshold found for the patients with sinus rhythm and no spontaneous breathing activity), the sensitivity was 75% and the specificity 46%. In this subgroup, the area under the ROC curves (±SE) for the PLR-induced changes in aortic blood flow (1.00 ± 0.00) and for the PLR-induced changes in pulse pressure (0.69 ± 0.13) were not statistically different, but both were significantly greater than the area under the ROC curve for ΔPP (0.56 ± 0.14).

In the 11 patients without sinus rhythm, ΔPP could not be calculated. In these patients, the predictive value of PLR-induced changes in aortic blood flow was evaluated. All 11 patients were correctly classified in terms of volume responsiveness.

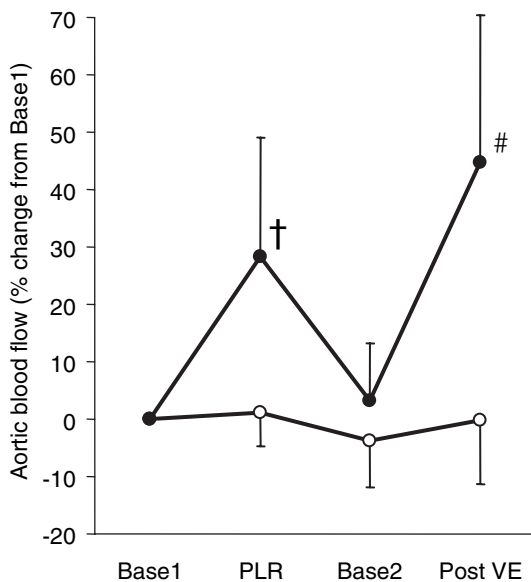


Figure 2. Evolution of aortic blood flow at the four steps of the study, expressed as percent change from base 1. *Open circles*, evolution in the subgroup of nonresponders, in whom neither volume expansion (VE) nor passive leg raising (PLR) changed aortic blood flow; *filled circles*, evolution in the subgroup of responders, in whom the increase of aortic blood flow induced by fluid infusion was preceded by an increase induced by passive leg raising. †*p* < .05 vs. base 1; #*p* < .05 vs. base 2.

By definition, fluid loading should increase left ventricular stroke volume if the heart is preload responsive. Therefore, the effects of small variations in preload should induce proportional changes in stroke volume or its estimates, making these changes markers of preload responsiveness. Accordingly, positive-pressure ventilation-induced changes in stroke volume predict preload responsiveness in ventilator-dependent patients (1). Respiratory variation of surrogates of left ventricular stroke volume, including arterial pulse pressure (19), subaortic outflow (21), and arterial pulse contour-estimated left ventricular stroke volume (22, 25), have also been reported to be reliable parameters for predicting preload responsiveness in mechanically ventilated patients who are making no inspiratory effort and with regular cardiac rhythm. We confirmed that ΔPP is of poor value to predict fluid responsiveness in patients triggering the ventilator, as it has been previously assumed (2). This is also emphasized by the observation that the value of ΔPP in these patients was much higher at base 1 than at base 2, although all other hemodynamic variables (namely heart rate, arterial pressure, and aortic blood flow) confirmed that the hemodynamic status was unchanged. In these patients, the specificity of the respiratory variation in stroke volume for predicting fluid response was reduced because it might be related not only to the effects of preload variation over one respiratory cycle but also to the heterogeneity of the intrathoracic pressure variation from one respiratory cycle to the other.

PLR represents a simple method of transiently increasing systemic venous return (3, 4) by transferring blood from the legs to the intrathoracic compartment (3). PLR can be considered as a “self fluid challenge” since the phenomenon reverses once legs are returned to the supine position and does not persist if the legs are held elevated for extended intervals. Thus, PLR allows for a rapid and reversible preload challenge without needing to infuse fluid. In our study, we did not perform a classic PLR because leg elevation was associated with trunk lowering from 45° to 0°. The volume of blood transferred to the central compartment by this body postural maneuver might be greater than that induced by the classic PLR and our results may not be directly applicable if the legs are merely elevated in a supine patient. Since heart rate was unchanged during PLR, suggesting an

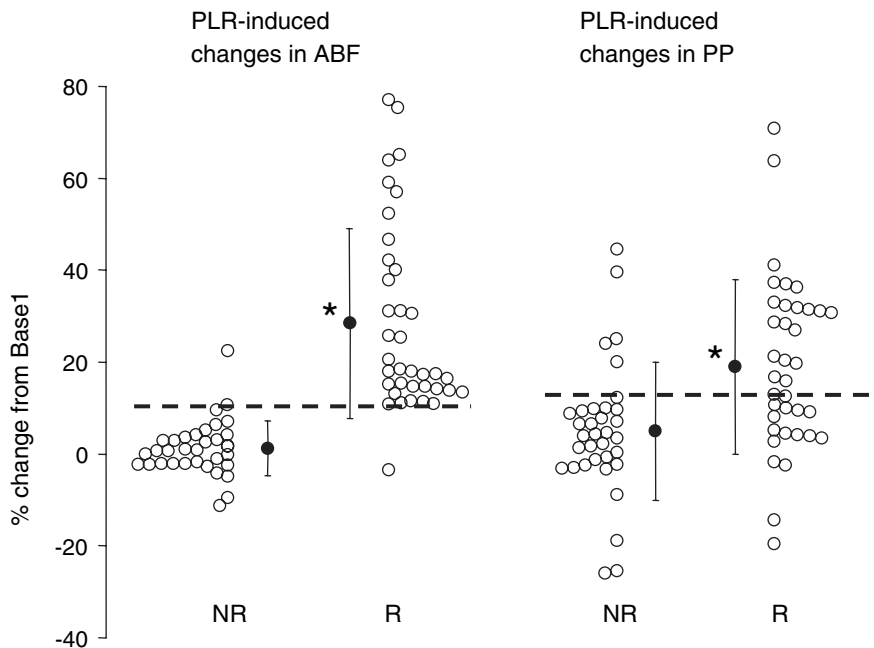


Figure 3. Individual values (*open circles*) and mean \pm SD (*filled circles*) of changes of aortic blood flow (ABF) and of changes of pulse pressure (PP) induced by passive leg raising (PLR) (both expressed as percent variation from base 1) in responders (R) and nonresponders (NR). **p* < .05 vs. nonresponders.

DISCUSSION

Our study demonstrates that the transient hemodynamic changes induced by PLR afford an excellent prediction of preload responsiveness in the critically ill. An increase in aortic blood flow $\geq 10\%$ by PLR predicted a volume expansion-induced increase in aortic blood flow

$\geq 15\%$ with a sensitivity of 97% and specificity of 94%. This predictive value was demonstrated in a wide variety of patients including subjects with spontaneous breathing activity or irregular cardiac rhythm in which the respiratory changes of hemodynamic signals could not be used to predict preload responsiveness.

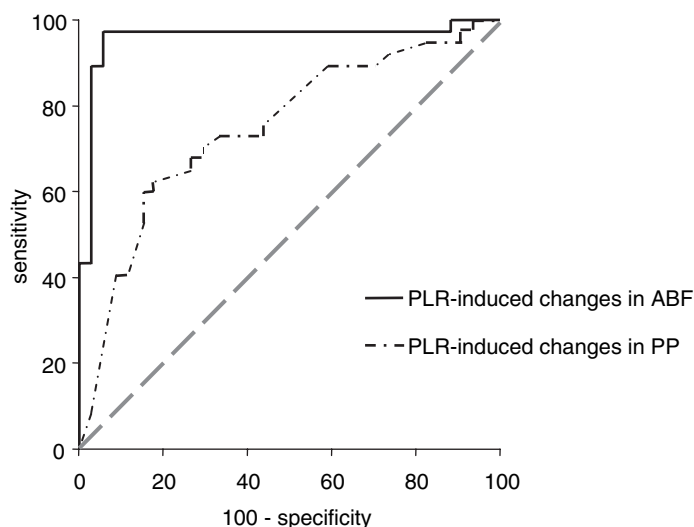


Figure 4. Receiver operating curves comparing the ability of variations in aortic blood flow (*ABF*) and pulse pressure (*PP*) induced by passive leg raising (*PLR*) (both expressed as percent variation from base 1) to discriminate responders and nonresponders to volume expansion in the whole population.

unaltered sympathetic tone, *PLR* likely induced a simple shift of blood to the central compartment. The effects of *PLR* on hemodynamics occurred rapidly after starting the maneuver since in all responders, the highest value of aortic

blood flow and pulse pressure were observed within the first 30 secs. Our study confirms that *PLR* could be used as a reversible fluid challenge since aortic blood flow values at base 1 and base 2 data were similar.

In a previous study, our group tested the value of the changes in arterial pulse pressure induced by classic *PLR* to predict fluid responsiveness in a population of patients under controlled mechanical ventilation (10). However, the prediction of fluid responsiveness in that study by the *PLR*-induced changes in pulse pressure was only fair. Our present findings confirmed these previous results but extended them to a wider population including patients with inspiratory efforts, in whom respiratory variations of hemodynamic signals are unhelpful for predicting fluid responsiveness.

Interestingly, this study suggests that measuring changes in aortic blood flow rather than pulse pressure during *PLR* is more robust parameter of preload responsiveness in a general population of mechanically ventilated patients. Unlike pulse pressure, aortic blood flow is not influenced by complex changes in pulse wave propagation and reflection along the arterial tree (26) that might occur during the change in stroke volume induced by *PLR*. Furthermore flow is less influenced by arterial compliance (11).

Table 3. Hemodynamic parameters at different times of the study according to the presence of spontaneous activity or arrhythmias

	Base 1	PLR	Base 2	Post VE
Patients with no ventilator triggering and no arrhythmia (n = 41)				
PP, mm Hg (n = 41)				
Nonresponders (n = 19)	63 ± 14	63 ± 17	64 ± 15	65 ± 16
Responders (n = 22)	41 ± 13 ^a	48 ± 16 ^{a,b}	42 ± 12	56 ± 18 ^c
ABF, L/min (n = 41)				
Nonresponders (n = 19)	5.1 ± 2.0	5.2 ± 2.0	4.9 ± 1.8	5.2 ± 2.0
Responders (n = 22)	2.4 ± 0.9 ^a	3.1 ± 1.0 ^{a,b}	2.5 ± 0.9 ^a	3.6 ± 1.1 ^{a,c}
ΔPP, % (n = 30)				
Nonresponders (n = 14)	7 ± 4	6 ± 4	7 ± 4	6 ± 5
Responders (n = 16)	16 ± 9 ^a	13 ± 8 ^{a,b}	18 ± 10 ^a	14 ± 15 ^c
Patients with spontaneous breathing activity and no arrhythmia (n = 19)				
PP, mm Hg				
Nonresponders (n = 11)	53 ± 22	57 ± 23	52 ± 19	55 ± 23
Responders (n = 8)	52 ± 12 ^a	62 ± 14 ^b	54 ± 10	55 ± 25
ABF, L/min				
Nonresponders (n = 11)	3.2 ± 1.6	3.3 ± 1.7	3.1 ± 1.7	3.2 ± 1.8
Responders (n = 8)	3.0 ± 1.9	3.6 ± 2.2 ^b	3.2 ± 2.0	4.1 ± 2.7 ^c
ΔPP, %				
Nonresponders (n = 11)	13 ± 11	25 ± 36	15 ± 11	14 ± 11
Responders (n = 8)	53 ± 40 ^a	33 ± 29	16 ± 7 ^b	37 ± 56
Patients with arrhythmia (n = 11)				
PP, mm Hg				
Nonresponders (n = 4)	42 ± 13	47 ± 13	44 ± 12	49 ± 12
Responders (n = 7)	50 ± 15	59 ± 16	52 ± 18	57 ± 16
ABF, L/min				
Nonresponders (n = 4)	2.8 ± 2.6	2.8 ± 2.7	2.8 ± 2.6	2.9 ± 2.5
Responders (n = 7)	2.2 ± 1.5	2.6 ± 1.7 ^b	2.2 ± 1.5	2.8 ± 1.8 ^c

PLR, passive leg raising; *VE*, volume expansion; *PP*, pulse arterial pressure; *ABF*, aortic blood flow; *ΔPP*, pulse pressure respiratory variation.

^a*p* < .05, responders vs. nonresponders; ^b*p* < .05, *PLR* vs. base 1; ^c*p* < .05, post-*VE* vs. base 2. Mean ± SD.

Although esophageal Doppler has been criticized because it assesses the blood flow in the descending aorta but not the total blood flow, it correctly tracks the changes in thermodilution cardiac output in various clinical conditions (14–18). Potentially, PLR, by improving the hemodynamic status in responders, could have reduced sympathetic tone and hence altered the proportion of cardiac output sent through the descending aorta. However, this redistribution scenario seems unlikely because heart rate was unchanged, suggesting an unaltered sympathetic tone. Thus, the changes in aortic blood flow during PLR probably reflected proportionally similar changes in cardiac output. Furthermore, when the issue of hemodynamic response to volume is addressed, assessing blood flow in the descending aorta makes sense since it represents the major part of cardiac output (17, 20). Moreover, since the esophageal Doppler measures aortic blood flow on a real-time basis, its monitoring provides for tracking instantaneous changes in stroke volume induced by the transient PLR maneuver, mechanical ventilation, or volume infusion. All these reasons probably explained why the effects of PLR on aortic blood flow had a better predictive value than the effects on pulse pressure in our study. Finally, our data suggest that in the absence of available real-time blood flow monitoring methods, the simple monitoring of pulse pressure during PLR provides a fair prediction of volume responsiveness, even in mechanically ventilated patients with inspiratory efforts or arrhythmias.

Our study has some limitations. First, our study was not designed to specifically investigate the physiologic effects of PLR, in particular in terms of volume transfer. Second, we could not identify the precise reason why the effects of PLR on aortic blood flow were unable to predict fluid responsiveness in the three misclassified patients. Third, we defined fluid responsiveness as an increase in aortic blood flow $\geq 15\%$ with fluid infusion. This cutoff value was chosen by reference to previous studies assessing fluid responsiveness by means of changes in thermodilution cardiac output (1). Although this cutoff seems clinically relevant, the predictive value of the effects of PLR may be altered if another cutoff value would be chosen.

CONCLUSION

We demonstrated that the changes in aortic blood flow induced by PLR are highly predictive of preload responsive-

ness in ventilated patients, even in the presence of spontaneous respiratory efforts or arrhythmias. This simple observation greatly extends the spectrum of patients in whom a relatively noninvasive dynamic index might be used as a guide to fluid resuscitation.

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