Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance

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Objectives: **We tested whether the poor ability of pulse pressure variation to predict fluid responsiveness in cases of acute respiratory distress syndrome was related to low lung compliance. We also tested whether the changes in cardiac index induced by passive leg-raising and by an end-expiratory occlusion test were better than pulse pressure variation at predicting fluid responsiveness in acute respiratory distress syndrome patients.**

Design: **Prospective study.**

Setting: **Medical intensive care unit.**

Patients: **We included 54 patients with circulatory shock (63 ± 13 yrs; Simplified Acute Physiology Score II, 63 ± 24). Twenty-seven patients had acute respiratory distress syndrome (compliance of the respiratory system, 22 ± 3 mL/cmH_2O). In nonacute respiratory distress syndrome patients, the compliance of the respiratory system was 45 ± 9 mL/cmH_2O.**

Measurements and Main Results: **We measured the response of cardiac index (transpulmonary thermodilution) to fluid administration (500 mL saline). Before fluid administration, we recorded pulse pressure variation and the changes in pulse contour analysis-derived cardiac index induced by passive leg-raising and end-expiratory occlusion. Fluid increased cardiac index ≥15% (44% ± 39%) in 30 "responders." Pulse pressure variation was significantly correlated with compliance of the respiratory system ($r = .58$), but not with tidal volume. The higher the compliance of the respiratory system, the better the prediction of fluid responsiveness by pulse pressure variation. A compliance of the respiratory system of 30 mL/cmH_2O was the best cut-off for discriminating patients regarding the ability of pulse pressure variation to predict fluid responsiveness. If compliance of the respiratory system was >30 mL/cmH_2O, then the area under the receiver-operating characteristics curve for predicting fluid responsiveness was not different for pulse pressure variation and the passive leg-raising and end-expiratory occlusion tests (0.98 ± 0.03, 0.91 ± 0.06, and 0.97 ± 0.03, respectively). By contrast, if compliance of the respiratory system was ≤30 mL/cmH_2O, then the area under the receiver-operating characteristics curve was significantly lower for pulse pressure variation than for the passive leg-raising and end-expiratory occlusion tests (0.69 ± 0.10, 0.94 ± 0.05, and 0.93 ± 0.05, respectively).**

Conclusions: **The ability of pulse pressure variation to predict fluid responsiveness was inversely related to compliance of the respiratory system. If compliance of the respiratory system was ≤30 mL/cmH_2O, then pulse pressure variation became less accurate for predicting fluid responsiveness. However, the passive leg-raising and end-expiratory occlusion tests remained valuable in such cases. (Crit Care Med 2012; 40:000–000)**

Key Words: ●●●

Predicting fluid responsiveness in critically ill patients, i.e., whether fluid administration will result in a significant increase in cardiac output, has become one of the major topics of research in hemodynamics in recent years (1). Predicting fluid responsiveness might be of particular importance in patients with acute respiratory distress syndrome (ARDS), because excessive fluid overload is deleterious and because a restrictive fluid strategy might be preferred in this context (2). Among the different methods that are currently available for detecting preload dependence, the variation of arterial pulse pressure (PP) induced by mechanical ventilation (PPV) has received much attention (3).

Nevertheless, PPV might be of lower predictive value in cases of ARDS, as suggested by some studies (4–9). To explain this limitation, it is usually hypothesized that the low tidal volume (Vt) used for ARDS patients is insufficient to generate significant changes in cardiac preload (6–9) and, thus, to test preload responsiveness through PPV. However, this reasoning might be debatable. PPV depends on the degree of preload dependency and on the change in intracardiac pressure induced by mechanical ventilation. This change in intracardiac pressure itself is not only related to Vt (10). First, it depends on the change in airway pressure induced by Vt (i.e., it is inversely related to lung compliance). Second, it depends on the degree to which the change in airway pressure is transmitted to the pleural or pericardial spaces (i.e., it is directly related to lung compliance). Thus, it is plausible that PPV might depend not only on Vt but also on lung compliance. We conducted the present study to test this hypothesis.

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Table 1. Characteristics of patients depending on the compliance of the respiratory system

	Compliance of the Respiratory System ≤ 30 cmH_2O/mL (n = 28)	Compliance of the Respiratory System >30 cmH_2O/mL (n = 26)
Age (mean ± SD, yrs)	63 ± 12	66 ± 10
Gender (male/female, No. of patients)	17/11	16/10
Simplified Acute Physiology Score II (mean ± SD)	64 ± 23	63 ± 20
Acute respiratory distress syndrome (No. of patients)	25	4
Tidal volume (mean ± SD, mL/kg of predicted body weight)	7.1 ± 0.8	8.8 ± 1.5[a]
Total positive end-expiratory pressure (mean ± SD, cmH_2O)	7 ± 3	6 ± 2[a]
Plateau pressure (mean ± SD, cmH_2O)	27 ± 3	18 ± 3[a]
Driving pressure (plateau pressure − positive end-expiratory pressure) (mean ± SD, cmH_2O)	19 ± 3	12 ± 2[a]
Compliance of the respiratory system (mean ± SD, mL/cmH_2O)	23 ± 3	44 ± 9[a]
PaO_2/FIO_2 (mean ± SD, mm Hg)	185 ± 18	290 ± 24[a]
Lactate (mean ± SD, mmol/L)	2.4 ± 1.4	2.1 ± 1.1
Left ventricular ejection fraction (mean ± SD, %)	51 ± 4	52 ± 5
Patients receiving norepinephrine (No. of patients)	23	18
Dose of norepinephrine, median (25%–75% interquartile range, μg/kg/min)	1.7 (0.9–2.2)	1.1 (0.3–1.7)

[a] $p < .05$ vs. compliance of the respiratory system ≤30 cmH_2O/mL.

In addition, we attempted to evaluate whether two alternative tests known to predict fluid responsiveness could replace PPV in patients with ARDS. First, the passive leg-raising (PLR) test acts like a self-volume challenge (11). This postural test might act independently of mechanical ventilation and might be valuable in the case of ARDS. Second, the end-expiratory occlusion (EEO) test consists of interrupting tidal ventilation at end-expiration for a few seconds. This provokes an increase in venous return and, in cases of preload responsiveness, an increase in cardiac output and PP (12).

PATIENTS AND METHODS

Patients. As approved by the Institutional Review Board of our institution, patients were included if they met all the following criteria: presence of circulatory failure defined by a systolic arterial pressure ≤90 mm Hg (or decline of systolic arterial pressure ≥50 mm Hg in known hypertensive patients) and one or more of the following signs of urinary flow ≤0.5 mL/kg/min for ≥2 hrs, tachycardia ≥100 beats/min, or) presence of skin mottling; need for a fluid challenge, as decided by the attending physician; mechanical ventilation in the assist control mode; and absence of cardiac arrhythmias and of spontaneous triggering of the ventilator, as assessed by two investigators using the airway pressure curve.

Patients were excluded if they were younger than 18 yrs old, if they were moribund, and if PLR was contraindicated (head trauma, venous compression stockings). All patients were sedated and five patients were paralyzed. They were all monitored by a PiCCO2 device (Pulsion Medical Systems, Munich, Germany) and ventilated by an Evita 4 (Dräger Medical, Lübeck, Germany). ARDS was defined by the presence of lung infiltrates on chest radiograph, a ratio of partial arterial oxygen over inspired oxygen fraction ≤200 mm Hg, and the absence of elevated left cardiac filling pressures (13). In this study, the left cardiac filling pressures were evaluated by echocardiography (14). In patients with ARDS, Vt was 6–7 mL/kg of predicted body weight and positive end-expiratory pressure was set to reach a plateau pressure of 28–30 mm Hg (15).

Study Design. At baseline, respiratory measurements were obtained, including Vt, respiratory rate, positive end-expiratory pressure, and the plateau pressure. Compliance of the respiratory system (Crs) was measured by dividing Vt by the driving pressure. At this time, heart rate, arterial pressure, cardiac index (CI; transpulmonary thermodilution), global end-diastolic volume, and PPV were recorded. A PLR test was performed as previously described (16). Heart rate, arterial pressure, and pulse contour analysis-derived CI were measured when the changes induced by PLR were maximal, i.e., within 1 min (17). The patient was then returned to the semirecumbent position. Another baseline measurement of the same hemodynamic variables was performed again 1 min after the end of PLR. An EEO test was performed by interrupting the ventilator at end-expiration over 15 secs using the automatic device of the ventilator (12). During EEO, the absence of spontaneous triggering of the ventilator was assessed by two different investigators by observing the airway pressure curve displayed by the ventilator. Heart rate, arterial pressure, and pulse contour analysis-derived CI were measured at the end of EEO. Another baseline measurement of the same hemodynamic variables was performed again 1 min after the end of EEO.

After the PLR and EEO tests, 500 mL of saline was infused over 20 mins (18). At the end of fluid infusion, heart rate, arterial pressure, CI (transpulmonary thermodilution), global end-diastolic volume, and PPV were recorded.

Statistical Analysis. Data are expressed as mean ± SD or as median (25%–75% interquartile range). Data before and after fluid challenge were compared using a paired Student *t* test or a Wilcoxon paired test, as appropriate. The comparison of data between different groups of patients was performed using a two-sample Student *t* test or a Mann-Whitney *U* test, as appropriate.

The sensitivity, specificity, and positive and negative predictive values are expressed as mean and 95% confidence interval. Receiver-operating characteristics curves were constructed to test the ability of PPV, the percent change in CI during the PLR test, and the EEO test to predict fluid responsiveness, and they were compared using the Hanley-McNeil test. A $p < .05$ was considered statistically significant. The statistical analysis was performed with MedCalc 8.1.0.0 (Mariakerke, Belgium).

RESULTS

Study Population

Fifty-four patients were included in the study (Table 1). The source of circulatory shock was sepsis in 44 patients (pneumonia in 40), mesenteric ischemia in four patients, hemorrhage in two patients, hypovolemia in six patients (ketoacidosis in two, diarrhea in four), and two patients experienced shock after resuscitated cardiac arrest. No patient exhibited acute cor pulmonale on echocardiography performed at study inclusion. Fluid challenge significantly increased the global end-diastolic volume index from 691 ± 201 to 800 ± 296 mL/m^2 and increased CI by 27% ± 35%. Fluid challenge increased CI ≥15% (+44% ± 39%) in 30 "volume responders" (3). Twenty-seven patients had ARDS (16 responders and 11 nonresponders) and Crs was 22 ± 3 mL/cmH_2O in these patients. In non-ARDS patients (14 responders and 13 nonresponders), the Crs was 45 ± 9 mL/cmH_2O.

PPV Before the Fluid Challenge

In volume responders, PPV before the fluid challenge was 10% ± 6%. PPV was significantly correlated with Crs ($r = .55$; $p = .0001$), but not with Vt ($r = .21$; $p =$

.13). The relative performance of PPV in predicting fluid responsiveness depended on the value of Crs (Fig. 1). A Crs of 29–30 mL/cmH_2O was the value for which the predictive value of PPV differed most between patients with lower and with higher Crs. The difference between receiver-operating characteristic curve areas of patients with lower and higher Crs was greater than for any other Crs threshold (0.69 ± 0.10 vs. 0.98 ± 0.03, respectively). PPV was significantly higher in volume responders with a Crs >30 mL/cmH_2O (18% ± 5%) than in volume responders with a Crs ≤30 mL/cmH_2O (7% ± 3%; Table 2). In four volume responders, Vt was <8 mL/kg (7.0 ± 0.6 mL/kg) but Crs was >30 mL/kg and PPV was 17% ± 7%. In three volume responders, Vt was >8 mL/kg but Crs was <30 mL/kg and PPV was 5% ± 1%. In nonvolume responders, PPV did not differ between patients with a Crs >30 mL/cmH_2O and patients with a Crs ≤30 mL/cmH_2O (Table 2).

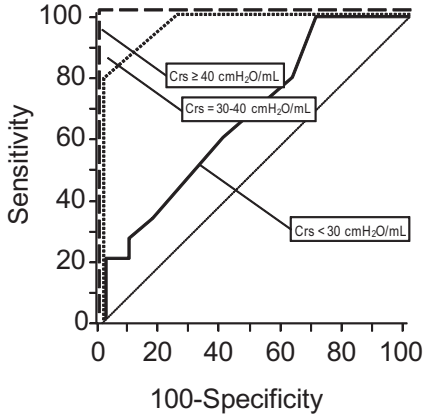

Figure 1. Receiver-operating characteristic curves describing the ability of the pulse pressure variation to predict an increase in cardiac index ≥15% induced by the fluid challenge depending on the level of compliance of the respiratory system (*Crs*).

Effects of PLR on CI

The changes in CI induced by PLR were not significantly correlated with Crs ($r = -0.09$) or with Vt ($r = .14$). In volume responders, PLR significantly increased CI by 26% ± 18% (Table 2). In nonvolume responders, CI did not significantly change during PLR (Table 2).

Effects of EEO on CI

The changes in CI induced by EEO were significantly correlated with Crs ($r = .34$; $p = .01$), but not with Vt ($r = .06$; $p = .64$). In volume responders, EEO significantly increased CI by 9% ± 5%. It did not differ between volume responders with a Crs >30 mL/cmH_2O (10% ± 9%) and volume responders with a Crs ≤30 mL/cmH_2O (9% ± 5%). In nonvolume responders, CI did not significantly change during EEO (Table 2).

Prediction of Fluid Responsiveness

In patients with a Crs >30 mL/cmH_2O, fluid responsiveness was predicted by a PPV ≥12%, by a PLR-induced increase in CI ≥10%, and by an EEO-induced increase in CI ≥5% with a similar predictive value (Table 3, Fig. 2). For PPV, if a cut-off of 12.5% was fixed, i.e., the PPV value that can be considered as established by previous data (3), then the sensitivity and specificity were similar for a 12% cut-off value.

In patients with a Crs ≤30 mL/cmH_2O, fluid responsiveness was predicted by a PPV ≥4%, with a significantly lower predictive value than by a PLR-induced increase in cardiac index of ≥10% and by an EEO-induced increase in CI ≥5% (Table 3, Fig. 3). For PPV, if a cut-off of 12.5% was fixed (3), then the sensitivity was 12% (95% confidence interval, 2%–38%) and the specificity was 100% (95% confidence interval, 75%–100%).

DISCUSSION

This study confirms that PPV is of limited value in predicting fluid responsiveness in the case of ARDS. The ability of PPV to predict fluid responsiveness was poorer in patients with low Crs. By contrast, the predictive value of the PLR and EEO tests was not affected by the value of Crs, such that these tests should be considered as better alternatives to PPV in the case of ARDS with a low Crs.

PPV is the predictor of fluid responsiveness that has the largest evidence base (3), but it is limited by the fact that it cannot be used in many instances (19) such as cardiac arrhythmias (17) and spontaneous breathing activity (17, 20). During open chest conditions, the predictive value of PPV has also been reported to be limited (21), although there are conflicting results (22). In the present

Table 2. Hemodynamic variables before and after volume expansion

	Compliance of Respiratory System ≤30 cmH_2O/mL (n = 28)				Compliance of Respiratory System >30 cmH_2O/mL (n = 26)			
	Responders (n = 15)		Nonresponders (n = 13)		Responders (n = 15)		Nonresponders (n = 11)	
	Before VE	After VE	Before VE	After VE	Before VE	After VE	Before VE	After VE
Heart rate (mean ± SD, beats/min)	79 ± 15	76 ± 14	85 ± 22	85 ± 22	96 ± 21	92 ± 20	87 ± 13	84 ± 14
Mean systemic arterial pressure (mean ± SD, mm Hg)	62 ± 18	81 ± 25[a]	85 ± 24[b]	87 ± 19	76 ± 24	90 ± 25[a]	69 ± 17	69 ± 20
Global end-diastolic volume index (mean ± SD, mL/m^2)	734 ± 200	875 ± 364[a]	746 ± 199	823 ± 282[a]	596 ± 236	734 ± 326[a]	696 ± 126	769 ± 157[a]
Cardiac index (mean ± SD, L/min/m^2)	3.2 ± 2.8	4.3 ± 2.7[a]	4.2 ± 2.7	4.4 ± 2.7	3.1 ± 2.2	4.4 ± 2.1[a]	3.6 ± 2.6	3.7 ± 2.6
Positive predictive value (mean ± SD, %)	8 ± 3	6 ± 3	6 ± 2	7 ± 7	18 ± 5	10 ± 4[a]	6 ± 3[b]	8 ± 5
Changes in cardiac index during passive leg-raising (mean ± SD, %)	28 ± 21	—	3 ± 3[b]	—	24 ± 16	—	4 ± 9[b]	—
Changes in cardiac index during end-expiratory occlusion (mean ± SD, %)	9 ± 5	—	2 ± 1[b]	—	10 ± 9	—	2 ± 2[b]	—

VE, volume expansion.
[a]$p < .05$ vs. before volume expansion; [b]$p < .05$ vs. responders.

Table 3. Diagnostic ability of the pulse pressure variation and the global end-diastolic volume at baseline, of the passive leg-raising test, and of the end-expiratory occlusion test to detect a fluid-induced increase in cardiac index ≥15%

Variable	Area Under the Curve	*p* vs. 0.500	Best Cut-Off Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Youden Index
Compliance of the respiratory system >30 cmH_2O/mL (n = 26)								
Pulse pressure variation at baseline	0.98 ± 0.03	<.0001	12%	85 (57–98)	100 (71–100)	100 (73–100)	84 (53–98)	0.85
Passive leg-raising–induced changes in CI	0.91 ± 0.06	<.0001	10%	93 (66–100)	91 (59–100)	93 (66–100)	91 (57–100)	0.84
End-expiratory occlusion-induced changes in CI	0.97 ± 0.03	<.0001	5%	93 (68–99)	91 (59–100)	93 (68–100)	91 (57–98)	0.84
Global end-diastolic volume index at baseline	0.69 ± 0.11[a]	.090	—	—	—	—	—	—
Compliance of respiratory system ≤30 cmH_2O/mL (n = 28)								
Pulse pressure variation at baseline	0.69 ± 0.10	.04	4%	100 (79–100)	31 (9–61)	64 (42–82)	100 (39–61)	0.31
Passive leg-raising–induced changes in CI	0.94 ± 0.05[a]	<.0001	10%	94 (70–100)	100 (75–100)	100 (78–100)	93 (66–100)	0.94
End-expiratory occlusion-induced changes in CI	0.93 ± 0.05[a]	<.0001	5%	93 (68–99)	92 (64–100)	93 (67–100)	92 (62–99)	0.85
Global end-diastolic volume index at baseline	0.48 ± 0.11[a]	.980	—	—	—	—	—	—

CI, cardiac index.

[a]$p < .05$ vs. positive predictive value at baseline. Mean ± SD or value (95% confidence interval).

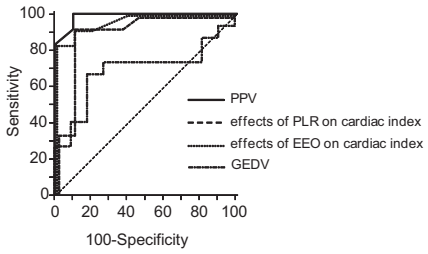

Figure 2. Receiver-operating characteristic curves comparing the ability of the passive leg-raising (*PLR*) test, of the end-expiratory occlusion (*EEO*) test, of pulse pressure variation (*PPV*), and of the global end-diastolic volume (*GEDV*) to predict an increase in cardiac index ≥15% induced by the fluid challenge in patients ventilated with a compliance of the respiratory system >30 mL/cmH_2O.

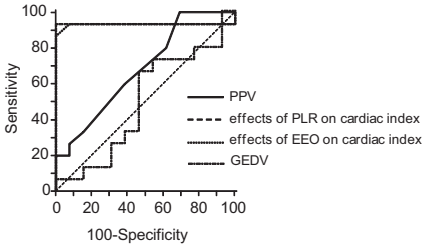

Figure 3. Receiver-operating characteristic curves comparing the ability of the passive leg-raising (*PLR*) test, of the end-expiratory occlusion (*EEO*) test, of pulse pressure variation (*PPV*), and of the global end-diastolic volume (*GEDV*) to predict an increase in cardiac index ≥15% induced by the fluid challenge in patients ventilated with a compliance of the respiratory system ≤30 mL/cmH_2O.

study, we addressed another condition in which PPV might be invalid, i.e., ARDS, as suggested by some previous studies (6, 8, 9) and confirmed in the present one.

However, the reason why PPV loses part of its predictive value in ARDS is a matter of debate. In several previous publications, this was related to the low Vt used in these patients (5, 6, 9); a low Vt would be insufficient to generate significant changes in alveolar pressure and, in turn, in intrathoracic pressure and PP, even in the case of fluid responsiveness. However, in addition to Vt, Crs might be another key factor in explaining the magnitude of PPV (23), especially in cases of ARDS. Because of the reduced compliance of ARDS lungs, the changes in alveolar pressure might still be high even if Vt is low (24). However, airway pressure transmission is reduced in cases of low lung compliance (24), such that the cyclic changes in intrathoracic pressure could be attenuated even in cases of marked changes in alveolar pressure. The present study shows that the predictive value of PPV is clearly related to Crs. In addition, although Crs and Vt are mathematically linked, we observed that the value of PPV was significantly correlated with Crs but not with Vt in volume responders. We also could identify a small but illustrative subgroup of patients with a low Vt, a relatively high Crs, and a high PPV, and another subgroup with a relatively high Vt, a low Crs, and a low PPV. Besides lung compliance, chest wall compliance might also influence the magnitude of PPV. Reuter et al (23) previously demonstrated that PPV is abruptly decreased if chest wall compliance is increased by thoracotomy. Nevertheless, in this study (23) the decrease in PPV was clearly explained by the thoracotomy-induced increase in cardiac preload and not by the reduction in chest wall compliance itself. In accordance with the latter hypothesis, the same authors (22) later showed that PPV remains a good predictor of fluid responsiveness in open chest conditions. In line with the present results, these previous studies (22, 23) provide evidence that lung compliance rather than chest wall compliance is the decisive factor explaining why PPV loses its diagnostic ability in cases of ARDS.

An important practical message from our study is that when PPV was >12%–13% (the cut-off value that is generally used in patients without ARDS) (3), it predicted fluid responsiveness with a 100% positive predictive value, whatever the value of Crs. In other words, a low Crs is mainly responsible for false-negative cases. Nevertheless, in the context of ARDS, in which the main issue of fluid resuscitation is to avoid fluid overload (2), one may prefer an indicator with a 100% negative predictive value. One should also bear in mind that it is likely that there is no precise cut-off of Crs below which PPV becomes an invalid predictor of fluid responsiveness. Our results suggest that the diagnostic ability of PPV continuously increases with Crs. In patients with a Crs <30 mL/cmH_2O, a PPV ≥4% could predict fluid responsiveness. Nevertheless, the specificity was relatively low with this cut-off (64%) and, more importantly, such a low value of PPV is likely not far from the precision of the variable.

The present study might define valuable methods for replacing PPV in cases of low Crs. In contrast to PPV, the PLR and EEO tests were not influenced by the

value of Vt or of Crs. Concerning PLR, the present study adds to the evidence from a number of previous studies (12, 17, 25–30) that were included in a recent positive meta-analysis (31). PLR was recently shown to be of less diagnostic accuracy in the case of abdominal hypertension (32). We did not encounter this condition in our patients. Some flaws have been described (33) in the aforementioned study (32), such that the issue of PLR reliability in cases of abdominal hypertension deserves further investigation. As an original result, the present study shows that because the hemodynamic effects of the postural changes do not depend on ventilatory conditions, a low Crs might be another condition in which PLR is better than PPV, as already demonstrated for spontaneous breathing activity (12, 25–29) and cardiac arrhythmias (17, 30).

The EEO test is based on the principle that during tidal ventilation, the venous return is cyclically impeded by mechanical insufflations (12). By interrupting cyclic ventilation at end-expiration for a few seconds, one allows the venous return to be completed and the cardiac preload to increase. This preload challenge was found to increase cardiac output during the last seconds of the EEO in patients with preload dependency (12). In the present study, we found that, unlike with PPV, the reliability of the EEO test in predicting fluid responsiveness was not affected by the value of Crs. At first glance, this may appear quite surprising because the amplitude of change in alveolar pressure that accounts for the hemodynamic effect of EEO (i.e., the driving pressure) is the same as that for PPV. However, even though the amplitude of the change in alveolar pressure is similar, the duration of the change in alveolar pressure is more prolonged during EEO (15 secs) than during normal tidal ventilation. During tidal ventilation, the exsufflation is short and the next insufflation might occur before the venous return has increased to its maximal level. By contrast, during the EEO the more prolonged end-expiratory time might allow the venous return to increase to its maximal level. According to this hypothesis, we previously reported that EEO produces its maximal effects during its last seconds (12). In turn, the changes in CI induced by EEO are more pronounced than those occurring during tidal ventilation. For instance, in patients with a Crs $\leq$30 mL/cmH_2O, the effects of EEO on CI were lower than in patients with a higher Crs, but these effects were still able to predict fluid responsiveness.

As a first limitation of our study, we could not investigate another potential limitation of PPV in ARDS, i.e., some false-positive cases attributable to acute cor pulmonale (34). Despite the fact that acute cor pulmonale occurs in 14% of ARDS patients with protective ventilation (35), we did not observe any cases in our population. Second, we were only able to assess the total Crs without differentiating the effects of lung and chest wall compliance. In particular, this precluded testing the effects of paralysis on the chest wall compliance and its influence on the relationship between Vt and PPV. Nevertheless, we could not identify any patient with potential decrease in chest wall compliance (absence of obvious intra-abdominal hypertension), such that one could reasonably suppose that the differences we observed between patients with relatively low and high Crs were related to differences in lung compliance. Finally, we did not measure the central venous pressure in the study population and did not investigate whether the dynamic changes in central venous pressure could predict fluid responsiveness in cases of low Crs.

To conclude, this study suggests that PPV is clearly influenced by the value of Crs. The lower the Crs, the lower the sensitivity of PPV as a test for predicting fluid responsiveness. By contrast, the PLR and the EEO tests were not influenced by Crs and should be used instead of PPV under these conditions in this group of patients with ARDS.

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