Changes in Stroke Volume Induced by Lung Recruitment Maneuver Predict Fluid Responsiveness in Mechanically Ventilated Patients in the Operating Room

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ABSTRACT

Background: Lung recruitment maneuver induces a decrease in stroke volume, which is more pronounced in hypovolemic patients. The authors hypothesized that the magnitude of stroke volume reduction through lung recruitment maneuver could predict preload responsiveness.

Methods: Twenty-eight mechanically ventilated patients with low tidal volume during general anesthesia were included. Heart rate, mean arterial pressure, stroke volume, and pulse pressure variations were recorded before lung recruitment maneuver (application of continuous positive airway pressure of 30 cm H_2O for 30 s), during lung recruitment maneuver when stroke volume reached its minimal value, and before and after volume expansion (250 ml saline, 0.9%, infused during 10 min). Patients were considered as responders to fluid administration if stroke volume increased greater than or equal to 10%.

Results: Sixteen patients were responders. Lung recruitment maneuver induced a significant decrease in mean arterial pressure and stroke volume in both responders and nonresponders. Changes in stroke volume induced by lung recruitment maneuver were correlated with those induced by volume expansion (r^2 = 0.56; P < 0.0001). A 30% decrease in stroke volume during lung recruitment maneuver predicted fluid responsiveness with a sensitivity of 88% (95% CI, 62 to 98) and a specificity of 92% (95% CI, 62 to 99). Pulse pressure variations more than 6% before lung recruitment maneuver discriminated responders with a sensitivity of 69% (95% CI, 41 to 89) and a specificity of 75% (95% CI, 42 to 95). The area under receiver operating curves generated for changes in stroke volume induced by lung recruitment maneuver (0.96; 95% CI, 0.81 to 0.99) was significantly higher than that for pulse pressure variations (0.72; 95% CI, 0.52 to 0.88; P < 0.05).

Conclusions: The authors' study suggests that the magnitude of stroke volume decrease during lung recruitment maneuver could predict preload responsiveness in mechanically ventilated patients in the operating room. **(Anesthesiology 2017; 126:260-7)**

An estimated 230 million surgical procedures per year are performed worldwide, and there is good evidence that hemodynamic optimization in the perioperative period can reduce morbidity and sometimes mortality.[1,2] It is well known that central venous pressure, pulmonary arterial occlusion pressure, and/or physical exam are not accurate to assess fluid responsiveness and to guide fluid therapy.[3,4] On the other hand, dynamic variables that describe the cyclic change in left ventricular stroke volume (SV; SV variation) and pulse pressure (pulse pressure [PP] variation [PPV]) during positive pressure ventilation are robust indicators of preload responsiveness and are currently the best objective measures of fluid responsiveness.[3,5] However, to be accurate, these dynamic

What We Already Know about This Topic

- Previous studies have demonstrated that the lung recruitment maneuver induces a decrease in stroke volume, which is more pronounced in hypovolemic patients
- This study determined the magnitude of stroke volume reduction through the lung recruitment maneuver and whether it could predict preload responsiveness

What This Article Tells Us That Is New

- This study suggests that the magnitude of stroke volume decrease during lung recruitment maneuver may predict preload responsiveness in mechanically ventilated patients in the operating room

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variables should be used under strict conditions.[6] SV variation and PPV are generated by the pressure transmitted from the airways to the pleural and pericardial spaces. Thus, their reliability is limited in patients receiving low tidal volume (V_T) ventilation (V_T less than 8 ml/kg predicted body weight) and in those with a driving pressure lower than 20 cm H_2O.[7–9] Lung-protective ventilation using low V_T is a standard of care in mechanically ventilated patients with acute respiratory distress syndrome.[10,11] It has also recently been demonstrated to significantly improve postoperative outcome in surgical patients.[12–15] Hence, the usefulness of these dynamic variables at the bedside is disputable. Preload responsiveness could be detected in patients receiving low V_T by using an end-expiratory occlusion test. However, few anesthesia ventilators offer the possibility to perform an end-expiratory occlusion, precluding its use in the operating room.

Lung recruitment maneuvers (LRMs), used to reopen collapsed lung, and positive end-expiratory pressure (PEEP) have been proposed as the key components of lung-protective ventilation strategy.[13,16,17] LRM, which refers to a transient increase in transpulmonary pressure induced by an intentional increase in airway pressures, results in an increase in intrathoracic pressure and a decrease in venous return, leading to a decrease in left ventricular end-diastolic areas and in SV.[18,19] The degree of PEEP-induced decrease in SV is related to preexisting preload responsiveness.[20,21] We hypothesized that the degree of SV reduction induced by an LRM could represent a functional test to suggest preload responsiveness and, therefore, predict fluid responsiveness. The aims of the current study were (1) to assess the ability of LRM-induced decrease in SV (ΔSV-LRM) to predict fluid responsiveness in mechanically ventilated patients in the operating room, (2) to compare the ability of ΔSV-LRM and PPV to predict fluid responsiveness, and (3) to assess the relationship between ΔSV-LRM and changes in SV induced by volume expansion (ΔSV-VE).

Materials and Methods

Study Design

This single-center study was approved by the Institutional Review Board (Comité de Protection des Personnes Sud-Ouest et Outre Mer III, Bordeaux, France; number, DC2014/48) and was registered at the French National Commission for Data Protection and Liberties, Paris, France (number, 1765877). Between December 2014 and December 2015, 28 nonconsecutive patients were included after verbal informed consent (written informed consent was waived by the Institutional Review Board). Inclusion criteria were patients older than 18 yr, scheduled for neurosurgery, without intracranial hypertension, and equipped with a radial arterial catheter and cardiac output monitor. LRM and volume expansion were done at the discretion of the attending anesthesiologist. Study patients did not possess comorbidities commonly affecting dynamic waveform indices, including arrhythmia, preoperative lung disease, left ventricular ejection fraction less than 50%, possible right ventricular dysfunction due to sleep apnea/severe chronic obstructive pulmonary disease/pulmonary hypertension, or extremes in body habitus (body mass index more than 40 or less than 15 kg/m^2).

Standard monitoring included continuous electrocardiography, heart rate (HR), peripheral oxygen saturation, and noninvasive blood pressure measurement. Induction and maintenance of general anesthesia were performed using a target-controlled infusion of propofol and remifentanil.[22–24] After tracheal intubation, patients were mechanically ventilated in the volume-control mode, with a V_T of 6 to 8 ml/kg ideal body weight and a PEEP of 5 cm H_2O. The respiratory rate and the inspiratory oxygen fraction were adjusted to maintain an end-tidal carbon dioxide concentration of 30 to 35 mmHg and peripheral oxygen saturation above 96%, respectively, with an inspiratory to expiratory ratio of 1/2.

After induction of anesthesia, an arterial catheter (Vygon, France) was inserted into a radial artery. The catheter was connected to a specific transducer (ProAQT; Pulsion Medical System, Germany) for SV and PPV monitoring.

The study design is shown in Supplemental Digital Content 1, http://links.lww.com/ALN/B347, which is a figure detailing the various steps of the protocol. After induction of anesthesia and after hemodynamic stability was obtained (defined as changes in mean arterial pressure [MAP] less than 10% during 5 min), an LRM was performed followed by volume expansion. To maintain controlled hemodynamics during the study protocol, study patients were not exposed to vasopressors or inotropes before and during anesthesia; similarly, patients were excluded if the target-controlled infusion of propofol and/or remifentanil was modified. Each recruitment maneuver consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s. Volume expansion was obtained by infusing 250 ml saline, 0.9%, more than 10 min. Four sets of measurements including HR, MAP, SV, and PPV were performed immediately before LRM, at the end of LRM when SV reached its minimal value, immediately after MAP, HR, and PPV returned to their baseline values (variations less than 10%), and finally, after volume expansion. All of these measurements were performed in the supine position.

Statistical Analysis

Data are expressed as mean ± SD or median (interquartile range, 25 to 75%), according to the type of variable distribution. Considering previously published results,[25] power analysis showed that at least 28 patients were necessary to detect a difference of 0.25 between ΔSV-LRM and PPV areas under the receiver operating characteristic (ROC) curves (5% type I error rate; 80% power; two-tailed test). Response to volume expansion was defined as an increase in SV greater than or equal to 10% after an infusion of 250 ml saline, 0.9%, more than 10 min.[26,27] The effects of LRM and volume expansion on hemodynamic parameters were analyzed using Student's paired *t* test. The assumptions of

Student's paired *t* test were studied as follows: the normality was analyzed using Shapiro–Wilk test and the homoscedasticity using Fisher–Snedecor test. The relationship between ΔSV-LRM and changes in SV induced by volume expansion was tested using linear correlation, according to data distribution. The intraclass correlation between SV measurements at the two baseline steps (t1 and t3) was measured using random-effects models.[28]

ROC curves were generated for LRM-induced changes in SV LRM (ΔSV-LRM), in pulse pressure (ΔPP-LRM), and in systolic arterial pressure (ΔSAP-LRM), and for PPV, by varying the discriminating threshold of each parameter, and areas under the ROC curves (95% CI) were calculated and compared using the approach described by DeLong *et al.*[29]. The best cutoff value was chosen so as to maximize the Youden index. A $P < 0.05$ was considered to be statistically significant.

The gray zone was constructed using a two-step procedure. First, a bootstrap resampling method was applied on PPV, ΔSV-LRM, ΔPP-LRM, and ΔSAP-LRM data. The best threshold of 1,000 bootstrapped populations and its 95% CI were chosen for each variable.[30] Secondly, we determined the values for which no conclusive information on fluid responsiveness (*i.e.*, cutoff values with a sensitivity less than 90% or a specificity less than 90% [diagnostic tolerance of 10%]) could be provided. The gray zone was defined as the values that did not allow a 10% diagnostic tolerance. Nevertheless, if the characteristics of the study population produced a 95% CI of the best thresholds larger than the inconclusive zone, the values obtained during the first step were retained as the gray zone.

The study protocol (sample size calculation, inclusion, noninclusion and exclusion criteria, ventilator settings, definition of hemodynamic stability, type of LRM, and definition of fluid responder) was determined *a priori*.

Statistical analysis was performed using Medcalc, version 11.6 (MedCalc Software, Belgium) and NCSS 8 (NCSS, LLC., USA).

Results

Patient Characteristics

Twenty-eight nonconsecutive patients were included. Sixteen (57%) patients were responders to volume expansion and 12 were not. Table 1 shows the main characteristics of the patients. The mean effect-site concentration was 4.2 ± 1.2 μg/ml for propofol and 4.7 ± 1.1 ng/ml for remifentanil. Hemodynamic variables in both responders and nonresponders are shown in table 2. The intraclass correlation between SV measurements at the two baseline steps (t1 and t3) was 0.99 (95% CI, 0.99 to 1.00).

Hemodynamic Changes during LRM and Volume Expansion

Hemodynamic parameters in responders and nonresponders during the four-step study period are shown in table 2. LRM induced a significant SV and MAP decrease in both responders and nonresponders. Volume expansion induced a significant PPV decrease in responders only. Figure 1 depicts the evolution of SV in responders and nonresponders during the four-step study period.

Table 1. Main Characteristics of Patients (n = 28)

Characteristics	
Age, yr	61 ± 11
Sex, male/female, n	13/15
Height, cm	167 ± 1
Weight, kg	76 (60–87)
Ideal body weight, kg	60 (52–72)
Tidal volume, ml	427 ± 56
Tidal volume, ml/kg ideal body weight	7.0 ± 0.5
Respiratory rate, cycles/min	14 ± 2
Positive end-expiratory pressure, cm H_2O	5 (5–5)
F_{IO_2}, %	40 (40–50)
Driving pressure, cm H_2O	10 ± 3
ASA physical status I/II/III, n	1/9/18
Comorbidities	
Arterial hypertension	11
Dyslipidemia	5
Diabetes	3
Coronary artery disease	2
Surgery, n	
Cerebral tumor	18
Metastasis	8
Other	4

Values are mean ± SD or median (percentile, 25–75) or number (n).
ASA = American Society of Anesthesiologist; F_{IO_2} = inspired oxygen fraction.

Relationship between Changes in SV Induced by LRM and Changes in SV Induced by Volume Expansion

The relationship between ΔSV-LRM and ΔSV-VE is shown in figure 2 ($r^2 = 0.56$; $P < 0.0001$).

Prediction of Fluid Responsiveness

Individual values of ΔSV-LRM and PPV in responder and nonresponder patients are shown in figure 3. Abilities of ΔSV-LRM, PPV, ΔPP-LRM, and ΔSAP-LRM to predict fluid responsiveness are shown in figure 4. A 30% decrease in SV-LRM predicted fluid responsiveness with a sensitivity of 88% (95% CI, 62 to 98) and a specificity of 92% (95% CI, 62 to 99). A PPV more than 6% before LRM discriminated responders with a sensitivity of 69% (95% CI, 41 to 89) and a specificity of 75% (95% CI, 42 to 95). Using a bootstrap analysis, the median values of the area under the ROC curve (AUC) of ΔSV-LRM and PPV were 0.96 (95% CI, 0.81 to 0.99) and 0.72 (95% CI, 0.52 to 0.88), respectively ($P < 0.001$; fig. 3). ΔPP-LRM and ΔSAP-LRM were not able to predict fluid responsiveness (AUC = 0.50; 95% CI, 0.25 to 0.75 and AUC = 0.52; 95% CI, 0.26 to 0.77, respectively, not different from AUC = 0.50; $P > 0.05$). Using the gray zone approach, inconclusive values ranged from −37 to −22% for ΔSV-LRM (including 36% of the patients) and from 4 to 7% for PPV (including 61% of the patients; fig. 5).

Table 2. Hemodynamic Variables at Baseline, during Lung Recruitment Maneuver, before Volume Expansion, and after Volume Expansion in Responders (n = 16) and Nonresponders (n = 12)

	t1	t2		t3	t4	
	Baseline 1	LRM	*P*1 Value	Baseline 2	After VE	*P*2 Value
HR, beats/min						
Responders	63 ± 10	65 ± 14	0.47	64 ± 11	62 ± 11	0.037
Nonresponders	66 ± 13	62 ± 12	0.053	66 ± 15	62 ± 12	0.0093
Mean arterial pressure, mmHg						
Responders	71 ± 11	51 ± 12	< 0.0001	65 ± 12	67 ± 8	0.32
Nonresponders	71 ± 9	55 ± 11	0.0001	68 ± 11	67 ± 11	0.21
Stroke volume, ml						
Responders	58 ± 23	33 ± 12	< 0.0001	58 ± 23	67 ± 27	< 0.0001
Nonresponders	55 ± 23	44 ± 17	0.0002	54 ± 23	57 ± 24	0.001
PPV, %						
Responders	8 ± 3	—	—	8 ± 3	5 ± 2	< 0.0001
Nonresponders	6 ± 1	—	—	6 ± 2	6 ± 1	0.79

Values are mean ± SD. Patients were considered responders if stroke volume index increased by greater than or equal to 10% after 250 ml intravascular volume expansion.

HR = heart rate; LRM = lung recruitment maneuver; NS = not significant; P1 = comparison between t1 and t2; P2 = comparison between t3 and t4; PPV = pulse pressure variations; t1 = baseline, before LRM; t2 = during LRM; t3 = baseline 2, before volume expansion; t4 = after 250 ml saline infusion; VE = volume expansion.

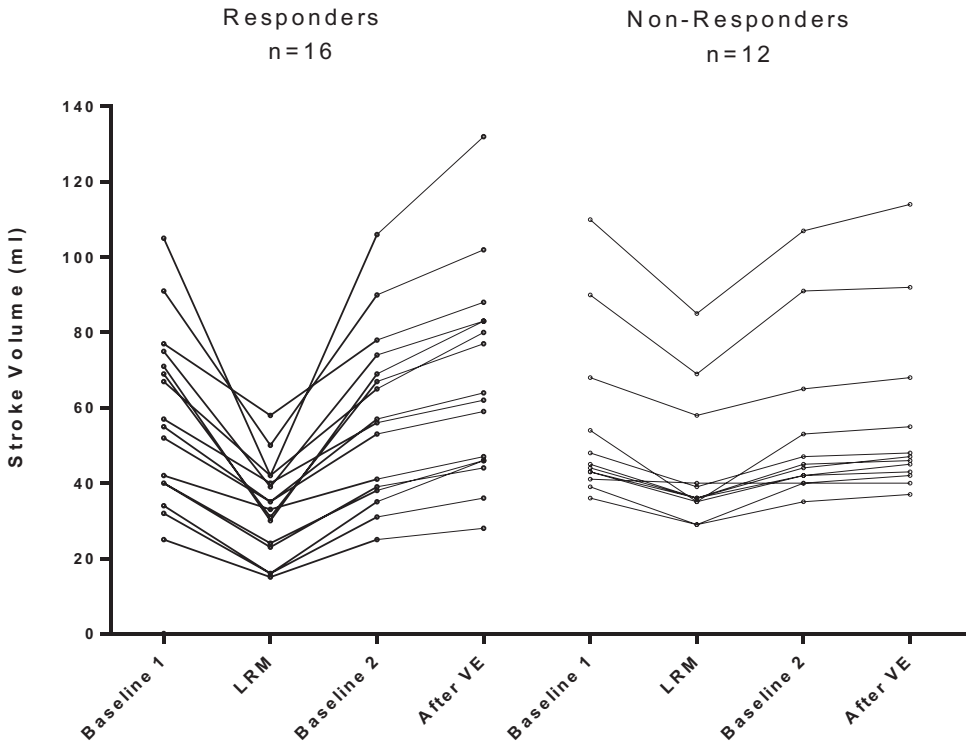

Fig. 1. Individual values of stroke volume (ml) in responders (n = 16) and nonresponders (n = 12) before lung recruitment maneuver (LRM; baseline 1) at the end of lung recruitment maneuver when stroke volume reached its minimal value (LRM), before volume expansion (VE: baseline 2) and after volume expansion (after VE). LRM = consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s) and VE = done using 250 ml saline, 0.9%, more than 10 min.

Discussion

In our study performed in mechanically ventilated patients with low V_T in the operating room, we demonstrated that (1) a 30% decrease in SV during an LRM could predict the effect of infusing 250 ml saline, 0.9%, (2) the ability of ΔSV-LRM was higher than that of PPV to predict fluid responsiveness, and (3) ΔSV-LRM and ΔSV-VE were strongly correlated.

LRM decreases intrapulmonary shunt, reduces lung collapse, and improves arterial oxygenation.[31–33] LRM induces an increase in intrathoracic pressure, leading to an increase in transpulmonary pressure. Previous experimental studies

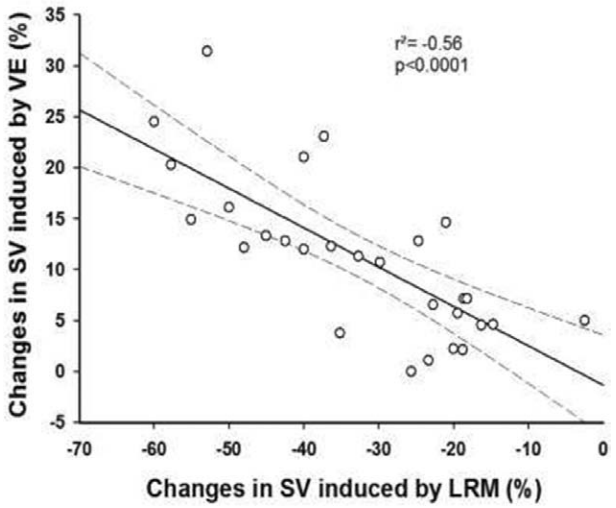

Fig. 2. Relationship between changes in stroke volume (SV; %) induced by lung recruitment maneuver (LRM) and those induced by volume expansion (VE). LRM = consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s and VE = done using saline, 0.9%, more than 10 min.

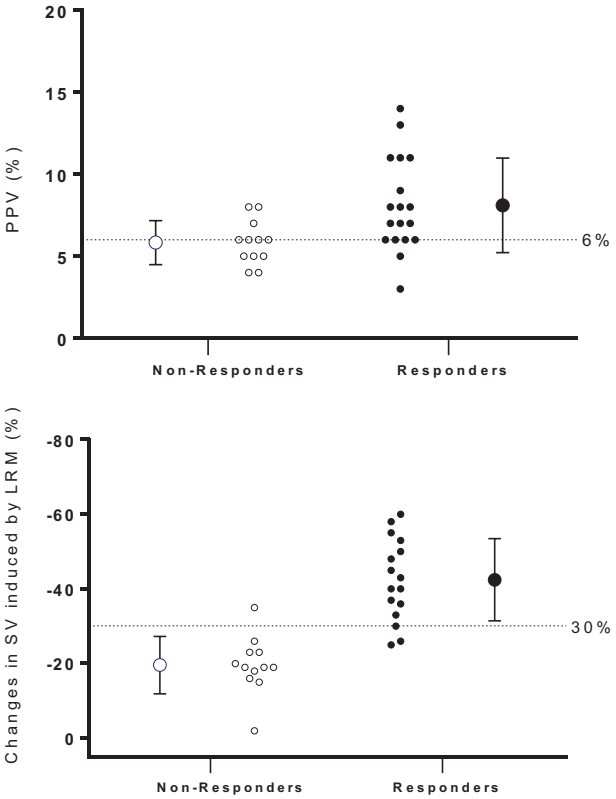

Fig. 3. Mean, SD, and individual values of changes in stroke volume (SV; %) induced by lung recruitment maneuver (LRM) and of pulse pressure variation (PPV; %) in responder and nonresponder patients. LRM = consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s.

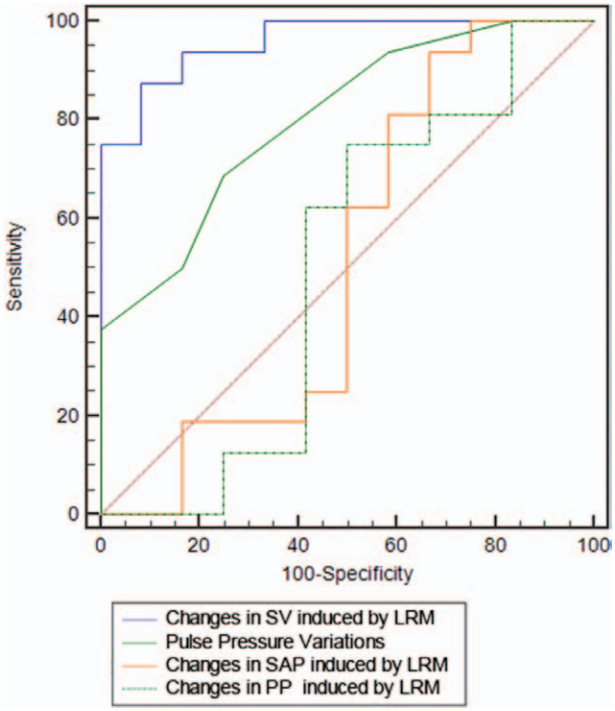

Fig. 4. Receiver operating curves generated for changes in stroke volume (SV) induced by lung recruitment maneuver (LRM), changes in pulse pressure (PP) induced by LRM, changes in systolic arterial pressure (SAP) induced by LRM, and pulse pressure variations showing the ability to predict the effect of a 250 ml volume expansion given more than 10 min. LRM = consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s.

have shown that LRM is associated with a transient decrease in cardiac output.[34] Increased intrathoracic pressure impedes venous return and increases pulmonary vascular resistance, leading to a decrease in right heart preload, an increase in right heart afterload, and thus a decrease in right ventricular SV.[35] Because of ventricular interdependence, LRM induced right heart's alteration, leading to a leftward intraventricular septal shift and to a decrease in left ventricular SV. There is a general acceptance that LRM promotes a decrease in cardiac output and arterial pressure with an increase in the need for fluid and vasopressors. The hemodynamic effects of LRM are, however, widely influenced by the method of recruitment, the applied level of alveolar pressure, the properties of the underlying cardiovascular system, and the lung and chest wall mechanics.[36] In an experimental study in mechanically ventilated pigs with injured lungs, Lim *et al.*[36] found that LRM depressed cardiac output only transiently and that the post-LRM PEEP level, not the LRM itself, determined the lasting effect of the LRM intervention on cardiac output. The volemic status is the cornerstone of hemodynamic tolerance of LRM. Nielsen *et al.*[37] demonstrated in an experimental study that cardiac output and left ventricular end-diastolic volume decrease dramatically in hypovolemic

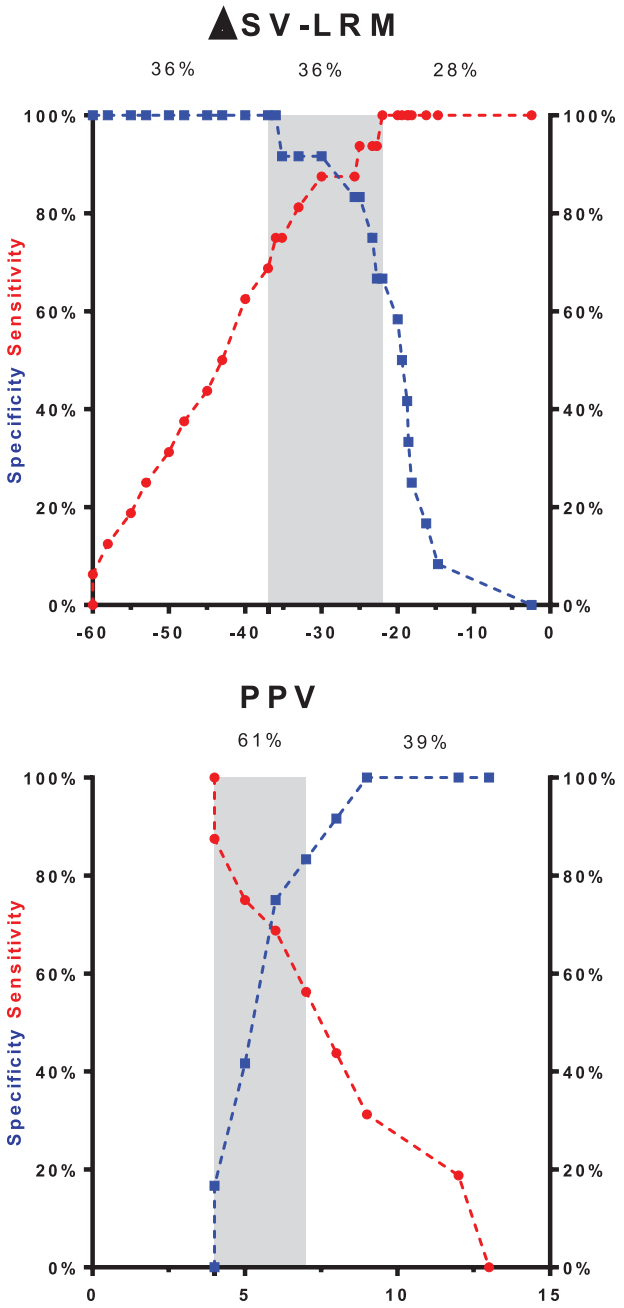

Fig. 5. Gray zone of pulse pressure variations (PPV) and ΔSV-LRM. The *blue curve* indicates sensitivity, and the *red curve* indicates specificity. ΔSV-LRM = changes in stroke volume induced by lung recruitment maneuver (consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s).

animals when compared to normovolemic or hypervolemic states. Our study demonstrated that hemodynamic effects of LRM are more pronounced in preload responsive patients and thus allow the prediction of fluid responsiveness.

Intraoperative management of volume administration remains challenging in daily practice. Neither clinical signs such as tachycardia, low arterial pressure, or low urine output nor cardiac filling pressure as central venous pressure or pulmonary artery occlusion pressure are good indicators of preload responsiveness.[3,4] Increasing focus has been put on dynamic parameters relying on cardiopulmonary interactions, which can be continuously monitored using dedicated devices. Although effective,[5] the use of dynamic variables in the operating room has been made more difficult today because of the evolution of medical practices, especially the use of low V_T in mechanically ventilated surgical patients.[9,12–14,38] In line with previous studies, our study confirmed that the respiratory variation of hemodynamic parameters such as PPV is not accurate for predicting fluid responsiveness in cases with low cutoff values (6%). Figure 3 shows that low PPV values are equally distributed in responder and nonresponder patients but that high PPV values (more than 8%) are present only in responder patients. This underlines once again that low PPV values are not informative in patients ventilated with low V_T but that higher PPV values may still indicate fluid responsiveness. Our study found a PPV gray zone ranging between 4 and 7%, including 61% of patients. Limits of this gray zone (4 to 7%) differ from those described by Cannesson *et al.*[39] in 413 surgical patients (9 to 13%) or by Biais *et al.*[40] in 556 intensive care unit patients (4 to 17%). We can explain the lower limit of the gray zone by the fact that we used low V_T, leading to low PPV values. The higher limit of the gray zone was also relatively low because of the use of low V_T and also because we did not include patients with right ventricular dysfunction and/or intraabdominal hypertension. These situations which may lead to high PPV values and false positive were included in the study by Biais *et al.*[40]

Our study found that LRM-induced changes in SV (but not in SAP and PP) could predict fluid responsiveness. These results are in accordance with previous published studies demonstrating that changes in SV and changes in SAP or PP are neither equivalent nor interchangeable.[41–43]

There is compelling evidence that even short-term mechanical ventilation can damage the lung and that, from a theoretical perspective, all patients receiving respiratory support should benefit from lung-protective mechanical ventilation to minimize ventilator-induced lung injury.[44] An advantage of testing fluid responsiveness by using LRM is that this functional test can be used instead of respiratory variation of hemodynamic parameters in cases of low V_T ventilation, which may have obvious significant clinical implications. A significant decrease in SV during LRM could show fluid responsiveness and thus may indicate volume expansion.

Our study contains several limitations. First, LRM was performed in the supine position during the steady-state period and before skin incision. Our results cannot be extrapolated to positions other than the supine and to other clinical situations such as patients suffering from arrhythmia, right and/or left heart failure, lung disease, obesity or receiving vasopressors, and/or inotropes. Other studies are necessary to confirm the potential interest of our finding in different situations. Second, LRM was performed shortly after the induction of anesthesia.

Hemodynamic effects of LRM may have been impacted by some degree of vasoplegia due to anesthetic drugs. However, fluid management in patients with varying degrees of vasoplegia during general anesthesia is the setting within which this clinical decision is commonly encountered. Third, LRM consisted of applying a continuous positive airway pressure of 30 cm H_2O for 30 s. Our results cannot be extrapolated to other LRMs using different airway pressures and different durations. Fourth, changes in SV induced by LRM and volume expansion were estimated using pulse contour analysis technology. Even though the accuracy of these types of devices, to estimate the absolute values of SV, may be disputable, this technology can track changes in SV induced by rapid changes in ventilator setting (PEEP or end-expiratory occlusion test) and by volume expansion.[21,45,46] SV measurements using ProAQT are an average during the last 12 s and are updated every second. The change in SV induced by LRM may be underestimated using this technology. Finally, sample size is relatively low.

Despite these limitations, our study furthers the current knowledge of fluid responsiveness among intraoperative mechanically ventilated patients. Our study suggests that a decrease in SV of at least 30% during an LRM detects preload responsiveness in this patient population and offers a predictive capability far exceeding current dynamic waveform indices performed without LRM. These findings may serve as a foundation for further studies evaluating goal-directed fluid-management therapies.

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Competing Interests

Dr. Biais received honoraria from Edwards Lifesciences, Irvine, California, and Pulsion Medical System, Munich, Germany, for lecturers. Dr. Futier received honoraria from Dräger, AG, Lübeck, Germany, and GE Healthcare, Chicago, Illinois, for lecturers. The other authors declare no competing interests.

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References

1. Bellamy MC: Wet, dry or something else? Br J Anaesth 2006; 97:755–7
2. Thacker JK, Mountford WK, Ernst FR, Krukas MR, Mythen MM: Perioperative fluid utilization variability and association with outcomes: Considerations for Enhanced recovery efforts in sample US surgical populations. Ann Surg 2016; 263:502–10
3. Marik PE, Cavallazzi R, Vasu T, Hirani A: Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. Crit Care Med 2009; 37:2642–7
4. Osman D, Ridel C, Ray P, Monnet X, Anguel N, Richard C, Teboul JL: Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. Crit Care Med 2007; 35:64–8
5. Benes J, Giglio M, Brienza N, Michard F: The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: A meta-analysis of randomized controlled trials. Crit Care 2014; 18:584
6. Biais M, Ouattara A, Janvier G, Sztark F: Case scenario: Respiratory variations in arterial pressure for guiding fluid management in mechanically ventilated patients. Anesthesiology 2012; 116:1354–61
7. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL: Pulse pressure variations to predict fluid responsiveness: Influence of tidal volume. Intensive Care Med 2005; 31:517–23
8. Muller L, Louart G, Bousquet PJ, Candela D, Zoric L, de La Coussaye JE, Jaber S, Lefrant JY: The influence of the airway driving pressure on pulsed pressure variation as a predictor of fluid responsiveness. Intensive Care Med 2010; 36:496–503
9. Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A: Hemodynamic monitoring and management in patients undergoing high risk surgery: A survey among North American and European anesthesiologists. Crit Care 2011; 15:R197
10. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CR: Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338:347–54
11. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301–8
12. Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ; Prove Network Investigators for the Clinical Trial Network of the European Society of Anesthesiology: High *versus* low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): A multicentre randomised controlled trial. Lancet 2014; 384:495–503
13. Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, Marret E, Beaussier M, Gutton C, Lefrant JY, Allaouchiche B, Verzilli D, Leone M, De Jong A, Bazin JE, Pereira B, Jaber S; IMPROVE Study Group: A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013; 369:428–37
14. Serpa Neto A, Hemmes SN, Barbas CS, Beiderlinden M, Biehl M, Binnekade JM, Canet J, Fernandez-Bustamante A, Futier E, Gajic O, Hedenstierna G, Hollmann MW, Jaber S, Kozian A, Licker M, Lin WQ, Maslow AD, Memtsoudis SG, Reis Miranda D, Moine P, Ng T, Paparella D, Putensen C, Ranieri M, Scavonetto F, Schilling T, Schmid W, Selmo G, Severgnini P, Sprung J, Sundar S, Talmor D, Treschan T, Unzueta C, Weingarten TN, Wolthuis EK, Wrigge H, Gama de Abreu M, Pelosi P, Schultz MJ; PROVE Network Investigators: Protective *versus* conventional ventilation for surgery: A systematic review and individual patient data meta-analysis. Anesthesiology 2015; 123:66–78
15. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, Gajic O, El-Tahan MR, Ghamdi AA, Günay E, Jaber S, Kokulu S, Kozian A, Licker M, Lin WQ, Maslow AD, Memtsoudis SG, Reis Miranda D, Moine P, Ng T, Paparella D, Ranieri VM, Scavonetto F, Schilling T, Selmo G, Severgnini P, Sprung J, Sundar S, Talmor D,

Treschan T, Unzueta C, Weingarten TN, Wolthuis EK, Wrigge H, Amato MB, Costa EL, de Abreu MG, Pelosi P, Schultz MJ; PROVE Network Investigators: Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: A meta-analysis of individual patient data. Lancet Respir Med 2016; 4:272–80

16. Futier E, Marret E, Jaber S: Perioperative positive pressure ventilation: An integrated approach to improve pulmonary care. Anesthesiology 2014; 121:400–8
17. Hedenstierna G: Small tidal volumes, positive end-expiratory pressure, and lung recruitment maneuvers during anesthesia: Good or bad? Anesthesiology 2015; 123:501–3
18. Nielsen J, Østergaard M, Kjaergaard J, Tingleff J, Berthelsen PG, Nygård E, Larsson A: Lung recruitment maneuver depresses central hemodynamics in patients following cardiac surgery. Intensive Care Med 2005; 31:1189–94
19. Luecke T, Pelosi P: Clinical review: Positive end-expiratory pressure and cardiac output. Crit Care 2005; 9:607–21
20. Michard F, Chemla D, Richard C, Wysocki M, Pinsky MR, Lecarpentier Y, Teboul JL: Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP. Am J Respir Crit Care Med 1999; 159:935–9
21. Biais M, Nouette-Gaulain K, Quinart A, Roullet S, Revel P, Sztark F: Uncalibrated stroke volume variations are able to predict the hemodynamic effects of positive end-expiratory pressure in patients with acute lung injury or acute respiratory distress syndrome after liver transplantation. Anesthesiology 2009; 111:855–62
22. Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Gambus PL, Billard V, Hoke JF, Moore KH, Hermann DJ, Muir KT, Mandema JW, Shafer SL: Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. Anesthesiology 1997; 86:10–23
23. Minto CF, Schnider TW, Shafer SL: Pharmacokinetics and pharmacodynamics of remifentanil. II. Model application. Anesthesiology 1997; 86:24–33
24. Schnider TW, Minto CF, Shafer SL, Gambus PL, Andresen C, Goodale DB, Youngs EJ: The influence of age on propofol pharmacodynamics. Anesthesiology 1999; 90:1502–16
25. Lansdorp B, Lemson J, van Putten MJ, de Keijzer A, van der Hoeven JG, Pickkers P: Dynamic indices do not predict volume responsiveness in routine clinical practice. Br J Anaesth 2012; 108:395–401
26. Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, Grocott MP, Ahern A, Griggs K, Scott R, Hinds C, Rowan K; OPTIMISE Study Group: Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: A randomized clinical trial and systematic review. JAMA 2014; 311:2181–90
27. Vallet B, Blanloeil Y, Cholley B, Orliaguet G, Pierre S, Tavernier B; Socie´te´ franc¸aise d'anesthe´sie et de re´animation: Guidelines for perioperative haemodynamic optimization. Ann Fr Anesth Reanim 2013; 32:e151–8
28. Shrout PE, Fleiss JL: Intraclass correlations: Uses in assessing rater reliability. Psychol Bull 1979; 86:420–8
29. DeLong ER, DeLong DM, Clarke-Pearson DL: Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. Biometrics 1988; 44:837–45
30. Carpenter J, Bithell J: Bootstrap confidence intervals: When, which, what? A practical guide for medical statisticians. Stat Med 2000; 19:1141–64
31. Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G: Re-expansion of atelectasis during general anaesthesia: A computed tomography study. Br J Anaesth 1993; 71:788–95
32. Magnusson L, Wicky S, Tydén H, Hedenstierna G: Repeated vital capacity manoeuvres after cardiopulmonary bypass: Effects on lung function in a pig model. Br J Anaesth 1998; 80:682–4
33. Claxton BA, Morgan P, McKeague H, Mulpur A, Berridge J: Alveolar recruitment strategy improves arterial oxygenation after cardiopulmonary bypass. Anaesthesia 2003; 58:111–6
34. Lovas A, Szakmány T: Haemodynamic effects of lung recruitment manoeuvres. Biomed Res Int 2015; 2015:478970
35. Celebi S, Köner O, Menda F, Korkut K, Suzer K, Cakar N: The pulmonary and hemodynamic effects of two different recruitment maneuvers after cardiac surgery. Anesth Analg 2007; 104:384–90
36. Lim SC, Adams AB, Simonson DA, Dries DJ, Broccard AF, Hotchkiss JR, Marini JJ: Transient hemodynamic effects of recruitment maneuvers in three experimental models of acute lung injury. Crit Care Med 2004; 32:2378–84
37. Nielsen J, Nilsson M, Fredén F, Hultman J, Alström U, Kjaergaard J, Hedenstierna G, Larsson A: Central hemodynamics during lung recruitment maneuvers at hypovolemia, normovolemia and hypervolemia. A study by echocardiography and continuous pulmonary artery flow measurements in lung-injured pigs. Intensive Care Med 2006; 32:585–94
38. Mahjoub Y, Lejeune V, Muller L, Perbet S, Zieleskiewicz L, Bart F, Veber B, Paugam-Burtz C, Jaber S, Ayham A, Zogheib E, Lasocki S, Vieillard-Baron A, Quintard H, Joannes-Boyau O, Plantefève G, Montravers P, Duperret S, Lakhdari M, Ammenouche N, Lorne E, Slama M, Dupont H: Evaluation of pulse pressure variation validity criteria in critically ill patients: A prospective observational multicentre point-prevalence study. Br J Anaesth 2014; 112:681–5
39. Cannesson M, Le Manach Y, Hofer CK, Goarin JP, Lehot JJ, Vallet B, Tavernier B: Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: A "gray zone" approach. Anesthesiology 2011; 115:231–41
40. Biais M, Ehrmann S, Mari A, Conte B, Mahjoub Y, Desebbe O, Pottecher J, Lakhal K, Benzekri-Lefevre D, Molinari N, Boulain T, Lefrant JY, Muller L; AzuRea Group: Clinical relevance of pulse pressure variations for predicting fluid responsiveness in mechanically ventilated intensive care unit patients: The grey zone approach. Crit Care 2014; 18:587
41. Monnet X, Letierce A, Hamzaoui O, Chemla D, Anguel N, Osman D, Richard C, Teboul JL: Arterial pressure allows monitoring the changes in cardiac output induced by volume expansion but not by norepinephrine. Crit Care Med 2011; 39:1394–9
42. Le Manach Y, Hofer CK, Lehot JJ, Vallet B, Goarin JP, Tavernier B, Cannesson M: Can changes in arterial pressure be used to detect changes in cardiac output during volume expansion in the perioperative period? Anesthesiology 2012; 117:1165–74
43. Pierrakos C, Velissaris D, Scolletta S, Heenen S, De Backer D, Vincent JL: Can changes in arterial pressure be used to detect changes in cardiac index during fluid challenge in patients with septic shock? Intensive Care Med 2012; 38:422–8
44. Slutsky AS, Ranieri VM: Ventilator-induced lung injury. N Engl J Med 2013; 369:2126–36
45. Monnet X, Vaquer S, Anguel N, Jozwiak M, Cipriani F, Richard C, Teboul JL: Comparison of pulse contour analysis by Pulsioflex and Vigileo to measure and track changes of cardiac output in critically ill patients. Br J Anaesth 2015; 114:235–43
46. Monnet X, Osman D, Ridel C, Lamia B, Richard C, Teboul JL: Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. Crit Care Med 2009; 37:951–6