

# Using Dynamic Variables to Guide Perioperative Fluid Management

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Intravenous fluid administration is an integral part of patient management during anesthesia. This practice has a strong clinical rationale since a decrease in blood volume, either present before or developing during surgery, is a major cause of morbidity and mortality. In order to preempt the risk of such hypovolemia large amounts of intravenous fluids are frequently administered, especially during major surgery. However, accumulating evidence in recent years has suggested that a too “liberal” approach to perioperative fluid management may lead to increased complications and worse patient outcome.<sup>1</sup> On the other hand, a “restrictive” strategy designed to achieve zero fluid balance following major abdominal surgery may result in a higher rate of acute kidney injury.<sup>2</sup> Both the “liberal” and the “restrictive” approaches to intraoperative fluid management seem to be equally associated with acute kidney injury, increased morbidity, 30-day mortality, cost, and postoperative length of stay.<sup>3</sup> These recent studies led to the recommendation, repeated in a clinically focused review on perioperative fluid therapy published recently in *ANESTHESIOLOGY*,<sup>4</sup> that perioperative fluid regimen should be kept “moderately liberal.”

While recommendations regarding the general principles of perioperative fluid management do provide useful overall guidance, they may not necessarily be helpful in determining individual patient needs at any specific moment. This may partially explain the observed marked variability in the intraoperative fluid administration across individual anesthesia providers.<sup>3,5</sup> The fact that this marked variability is driven more by the individual provider’s preferences than by patient and procedural characteristics<sup>3,5</sup> seems to highlight the need for more physiologically based variables that may individualize perioperative fluid administration and make it more precise.

## Concept of Fluid Responsiveness

Fluid administration is indicated in the presence of the two following conditions: (a) the patient requires augmentation of his perfusion; and (b) the patient is going to increase his cardiac output (CO) in response to fluid administration (“fluid responsive”).<sup>6</sup> However, the sobering reality, demonstrated repeatedly and consistently, is that fluid

administration is associated with an increase in CO in only about 50% of high-risk surgical and critically ill patients.<sup>7</sup> It seems, therefore, that we routinely administer unnecessary and potentially detrimental fluids to about half of the patients in our care. It also means that the traditional tools that we have been using as conceptual surrogates of the elusive left ventricular preload to guide fluid management, cannot accurately identify individual fluids needs. These needs may be better assessed by the determination of the patient’s “fluid responsiveness” status. Fluid responsiveness is the degree by which a modification of preload affects the stroke volume (SV) and is best described by the slope of the individual left ventricular function curve (fig. 1). Fluid administration is expected to increase SV when the patient is on the steep portion of the curve (“responder”). However, when the patient is on the flat portion of that curve (“nonresponder”), fluids are not going to be effective and other forms of cardiovascular support should be applied in order to improve hemodynamic stability.

Fluid responsiveness is best determined by measuring the change in CO after the administration of a fluid challenge. A fluid challenge may include varying fluid types (colloids or crystalloids) and volumes (500, 250, and 100 ml), with either 10 or 15% change in CO or SV being considered as a positive test. These marked variabilities may affect the definition of a “responder” or a “nonresponder.” Furthermore, using a fluid challenge to determine fluid responsiveness has some other shortcomings: (a) it requires the use of a (preferably continuous) CO monitor; (b) in 50% of the cases the test will be negative and, when frequently repeated, may lead to unintended fluid overload; (c) when administered to a “nonresponder” it may result in an unidentified decrease in oxygen delivery due to hemodilution<sup>8</sup>; and (d) it has to be proactively initiated and offers only intermittent information. Having other variables that can accurately predict fluid responsiveness by modifying preload without the actual administration of fluids is obviously of great clinical value.

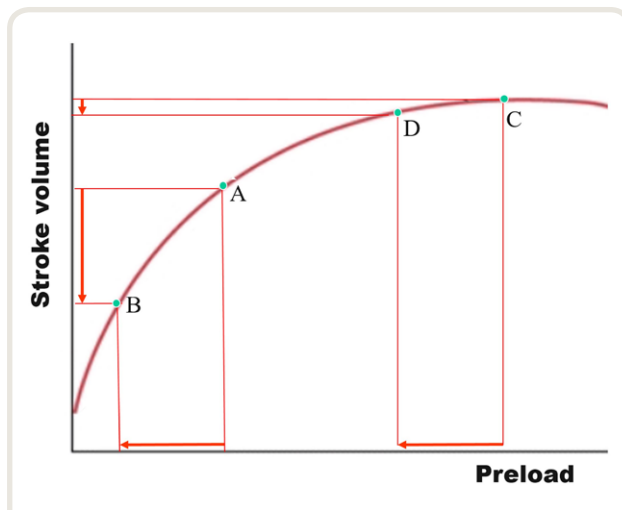
## Dynamic Variables of Fluid Responsiveness

Variables that describe fluid responsiveness are termed “dynamic” since they result from a combination of a

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**Fig. 1.** The left ventricular function curve describes the effect of a change in preload on the stroke volume. The decrease in venous return during the mechanical breath will cause a significant change in stroke volume (A to B) when the patient is on the steep portion of the curve (“responder”), and a small change (C to D) in a “nonresponder.”

preload-modifying maneuver (e.g., mechanical breath) and the measurement of its immediate hemodynamic response (e.g., change in SV).

### Dynamic Variables Induced by Mechanical Ventilation

The increase in intrathoracic pressure during a mechanical breath has direct effects on all heart chambers (for more information, see Michard,<sup>9</sup> Perel *et al.*,<sup>10</sup> and Teboul *et al.*<sup>11</sup>). Prominent among these effects is the transient decrease in venous return that may be regarded as a preload-modifying test of fluid responsiveness. In a patient who is on the steep portion of the left ventricular function curve (“responder”), a mechanical breath will be associated with a transient reduction in venous return and an eventual decrease in left ventricular SV (fig. 1). However, in a patient who is on the flat portion of the left ventricular function curve (“non-responder”) the mechanical breath will not produce any significant reduction in the left ventricular SV (fig. 1). The magnitude of the respiratory-induced changes in the SV is reflected by the respective variations in the arterial blood pressure and the plethysmographic waveforms, which have become the source of the most widely used dynamic variables.<sup>9,10,12,13</sup> The graphic depiction of these variables and the way they are calculated are shown in figure 2. Before describing these variables in more detail, it is important to bear in mind that all have been repeatedly demonstrated to be better predictors of fluid responsiveness compared with any of the commonly used static preload variables like central venous pressure, pulmonary artery occlusion, and left ventricular end-diastolic area.<sup>9,10,12,14</sup>

### Pulse Pressure Variation

The pulse pressure variation (PPV) reflects the changes that occur in the pulse pressure (systolic minus diastolic pressure) during one mechanical breath (fig. 2). Among the dynamic variables that are induced by mechanical ventilation, the pulse pressure variation is considered to be the most accurate and frequently serves as a gold standard in the evaluation of new dynamic variables.<sup>9,11–13</sup> A pulse pressure variation threshold value of about 12% has been shown by numerous studies to accurately predict fluid responsiveness in surgical and in critically ill patients.<sup>12</sup> These threshold values are valid only for patients who have sinus rhythm and are ventilated with tidal volumes of 8 to 10 ml/kg with no spontaneous breathing activity. A significant (greater than or equal to 3%) decrease in the pulse pressure variation value following fluid loading is highly indicative of an associated significant increase in the CO.<sup>15</sup> However, a pulse pressure variation value in the range of 9 to 13%, termed the “gray zone,” was found to be inconclusive in approximately 25% of patients during general anesthesia.<sup>16</sup>

### Stroke Volume Variation

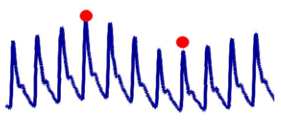
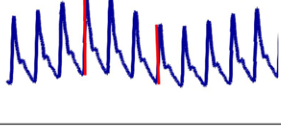
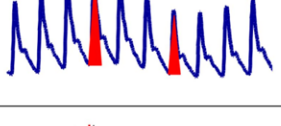
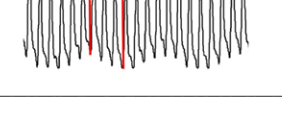
The SV variation (SVV) reflects the respiratory-induced changes in the left ventricular SV during one mechanical breath (fig. 2). The automatic measurement of the SV variation has become available with the introduction of pulse contour analysis for the continuous measurement of CO. An SV variation threshold value of 10% has been originally described in neurosurgical patients,<sup>17</sup> but more recently reported threshold values for the SV variation included 9 to 12%<sup>18</sup> and 14%.<sup>19</sup> The SV variation is somewhat less accurate than the pulse pressure variation<sup>12</sup> due, most probably, to the computational limitations of the pulse contour method in measuring individual SVs in real time.

### Systolic Pressure Variation

The systolic pressure variation (SPV) which is the difference between the maximal and minimal values of the systolic arterial pressure during one mechanical breath (fig. 2), was the first dynamic parameter to undergo extensive experimental and clinical validation.<sup>10,20,21</sup> The systolic pressure variation is normally about 8 to 10 mmHg in normotensive anesthetized patients who are ventilated with tidal volume of 8 ml/kg.<sup>22</sup> The systolic pressure variation is somewhat less accurate than the pulse pressure variation, but equally accurate to the SV variation.<sup>9,11,12</sup> When the automatic measurement of dynamic variables is unavailable, the detection of increased respiratory variations in the arterial pressure waveform may be the first sign of developing hypovolemia. These variations are easier to quantify by visually assessing the systolic pressure variation than the pulse pressure variation.<sup>23,24</sup>

### Plethysmographic Variability Index

The respiratory variations in the plethysmographic waveform that is displayed by most pulse oximeters present the

<b>Systolic Pressure Variation</b>		$\frac{SP_{max} - SP_{min}}$
<b>Pulse Pressure Variation</b>		$\frac{(PP_{max} - PP_{min})}{[(PP_{max} + PP_{min})/2]}$
<b>Stroke Volume Variation</b>		$\frac{(SV_{max} - SV_{min})}{SV_{mean}}$
<b>Plethysmographic Variability Index</b>		$\left[ \frac{(PI_{max} - PI_{min})}{PI_{max}} \right] \times 100$

**Fig. 2.** Graphic display and formulas of the main dynamic variables that are derived from the respiratory changes in the arterial pressure and plethysmographic waveform during mechanical ventilation.  $PI_{max}$ , maximal perfusion index;  $PI_{min}$ , minimal perfusion index;  $PP_{max}$ , maximal pulse pressure;  $PP_{min}$ , minimal pulse pressure;  $SP_{max}$ , maximal arterial systolic pressure;  $SP_{min}$ , minimal arterial systolic pressure;  $SV_{max}$ , maximal stroke volume;  $SV_{mean}$ , mean stroke volume;  $SV_{min}$ , minimal stroke volume.

most available dynamic parameter in mechanically ventilated anesthetized patients.<sup>25</sup> The plethysmographic variability index (PVI) is calculated as the difference between the maximal and minimal values of the perfusion index (the ratio between pulsatile and nonpulsatile infrared light absorption) during one mechanical breath divided by the maximal perfusion index (fig. 2).<sup>26</sup> The plethysmographic variability index has been shown to be a good predictor of fluid responsiveness, with an originally reported cut-off value of 14%,<sup>27</sup> although other cut-off values have been reported as well. The plethysmographic variability index may be significantly affected by a changing vasomotor tone (e.g., hypothermia, vasoconstriction). However, it is able to reflect even mild decreases in circulating blood volume intraoperatively,<sup>21</sup> and may be the only source of information on fluid responsiveness during low and medium risk surgery.

**Limitations of Ventilation-induced Dynamic Variables.** The limitations and confounding factors of ventilation-induced dynamic variables have been extensively described and should be well recognized.<sup>9,11,13,28</sup>

**Spontaneous Ventilation.** The hemodynamic effects of a spontaneous breath are very different than those that occur during mechanical ventilation, include an increase rather than a decrease in venous return, and may vary from one breath to another.<sup>29</sup> As a result, dynamic variables poorly predict fluid responsiveness during spontaneous breathing. Many small studies that examined the utility of dynamic

variables during spontaneous breathing had either negative or inconclusive results, and in many of them attempts were made to intentionally augment spontaneous respiratory efforts.<sup>29</sup> Of note, when blood volume is severely reduced, a deep spontaneous breath may collapse the very compliant venae cavae, cause a sudden significant decrease in the venous return and CO, and produce large variations in the systolic blood pressure (pulsus paradoxus).<sup>30</sup>

Dynamic variables during spontaneous breathing do, however, reflect true hemodynamic events and therefore should not be automatically discarded as meaningless or artefactual.<sup>29</sup> During spontaneous breathing these variables may be used to monitor respiratory rate, respiratory effort, pulsus paradoxus (e.g. asthma, cardiac tamponade), and, most importantly, upper airway obstruction.<sup>29,31</sup> Spontaneous breathing efforts during patient-ventilator asynchronies may exaggerate dynamic variables and decrease their predictive accuracy.<sup>32</sup> The potential ability of these variables to serve as an alert to the appearance of such asynchronies and to estimate their severity is obvious yet unexplored.

**Size of Tidal Volume/Inflation Pressures during Mechanical Ventilation.** Dynamic variables predict fluid responsiveness best when the tidal volume is at least 8 ml/kg.<sup>28,33</sup> Lower tidal volumes (e.g., 6 ml/kg) used during protective lung ventilation, may produce inadequate changes in the CO and reduce the accuracy of dynamic variables. However, hypovolemia may produce high values of dynamic variables even under such circumstances.<sup>11</sup> Excessively high tidal volumes,

inflation pressures and positive end-expiratory pressure levels, air-trapping, reduced lung and chest wall compliance, prone position, and increased intraabdominal pressure may all increase the numerical value of dynamic variables in the absence of fluid responsiveness (false positive), while open-chest conditions (e.g., cardiac surgery) decrease the predictive ability of dynamic variables.<sup>9,11,28</sup>

**Nonsinus rhythm.** Arrhythmias cause increased variability of the SV and therefore decrease the usability and accuracy of respiratory-induced dynamic variables.

**Right heart failure.** The output of the failing right heart may be further decreased by the increase in its afterload during the mechanical breath. The resulting increased respiratory variations may be erroneously attributed to increased fluid responsiveness.

**Early inspiratory SV augmentation.** During early inspiration, the mechanical breath squeezes the pulmonary blood volume into the left side of the heart, which, in turn, leads to an early augmentation of left ventricular ejection.<sup>9,10</sup> This augmentation, also termed delta Up, is further facilitated by the simultaneous decrease in left ventricular afterload, is more prominent during hypovolemia or congestive heart failure, and may decrease the accuracy of dynamic variables.

**Other Dynamic (Intermittent) Variables.** When ventilation-induced dynamic variables are unavailable or deemed inaccurate, and when clinical circumstances demand a more precise fluid administration, other dynamic variables may be helpful in the assessment of fluid responsiveness. It is important to realize, however, that nearly all of these other variables are measured *intermittently*, as opposed to the pulse pressure, SV and systolic pressure variations, and the plethysmographic variability index, which are all measured *continuously*. Obviously, *continuous* dynamic variables may identify hemodynamic changes much earlier than *intermittent* ones. Studies that compare various dynamic variables focus mostly on their performance as predictors of fluid responsiveness but disregard this major difference in their clinical utility.

**Passive Leg Raising.** The response to the passive leg raising maneuver has gained growing recognition as a reliable dynamic parameter that can be used even in the presence of spontaneous breathing.<sup>4,34</sup> The effect of passive leg raising has to be immediately assessed by a continuous measurement of CO, since relying on the changes in blood pressure alone may be misleading.<sup>34</sup> Since it is recommended that passive leg raising should start from the semi-recumbent and not from the supine position,<sup>34</sup> the execution of such a major positional change makes passive leg raising less practical intraoperatively.

**Echocardiographic Dynamic Variables.** Respiratory variations of the superior and inferior vena cava diameter and of Doppler velocity in the left ventricular outflow tract are examples of dynamic variables that can be intermittently measured by echocardiography in mechanically ventilated

patients.<sup>35</sup> Of note, the collapsibility index of the inferior vena cava that has been claimed to reflect fluid responsiveness in spontaneously breathing patients is greatly affected by the magnitude of the inspiratory effort.<sup>36</sup>

**New Dynamic Variables.** The end-expiratory occlusion test is performed by interrupting the ventilator at end-expiration for 15 to 30 s and assessing the resulting changes in CO.<sup>37</sup> The physiologic rationale of this test is that as ventilation is stopped in expiration, the cyclic impediment to venous return is interrupted leading to an eventual increase in left ventricular preload and increase CO in “responders.” Another new test, designed especially for the determination of fluid responsiveness during mechanical ventilation with low tidal volumes, is the “tidal volume challenge” which introduces a transient 1-min increase in tidal volume from 6 to 8 ml/kg predicted body weight.<sup>33</sup>

**Dynamic Variables and Perioperative Goal-directed Therapy.** There seems to be a growing consensus that perioperative goal-directed therapy is associated with decreased mortality and morbidity especially in high-risk surgical patients undergoing noncardiac surgery.<sup>4,38,39</sup> However, this consensus embraces a variety of strategies,<sup>39</sup> some of which may have opposing impact on fluid balance.<sup>40</sup> The “classic” strategy, which advocates the administration of fluid challenges as long as the SV increases by more than 10%, or when the SV decreases by more than 10%,<sup>39</sup> frequently leads to many ineffective fluid challenges and to more fluids being administered compared with standard care.<sup>39,40</sup> The administration of consecutive fluid challenges during goal-directed therapy may also result in iatrogenic hemodilution and a paradoxical decrease in oxygen delivery.<sup>8</sup> In contrast, protocols that use SV variation greater than 12% or plethysmographic variability index greater than 13% as triggers for fluid administration have been repeatedly shown to result in *less* fluids being administered and in better outcome compared with standard care.<sup>41–43</sup> This under-recognized, yet most important, value of dynamic variables stems from their ability to identify “nonresponders” and to prevent the administration of ineffective fluid challenges.<sup>40</sup> This advantage has been recognized by the investigators of the large contemporary trial that is aimed at reexamining the effectiveness CO-guided goal-directed therapy.<sup>44</sup> According to the trial’s amended protocol, a fluid challenge is to be repeated only if the SV increased by more than 10% in response to the previous challenge *and* only if the SV variation is at least 5%.<sup>44</sup> This significant addition to the protocol may improve the results of the original study and decrease the number of ineffective fluid challenges.<sup>39</sup>

Although goal-directed therapy that is based on dynamic variables has been reported to decrease postsurgical morbidity and intensive care unit length of stay,<sup>45</sup> its impact on patient outcome may be significantly affected by the specific values that are applied in the protocol. Using inconclusive values that are well within the “gray zone” (e.g., SV

variation greater than 10%) may in fact lead to the administration of more fluids compared with standard care.<sup>46</sup> New “closed-loop” systems provide the ability to preset the level of pulse pressure variation that will trigger a fluid challenge, and thus may be helpful in achieving the optimal net overall fluid balance.<sup>47</sup>

**Clinical Context and Application.** Appropriate conditions for the determination of fluid responsiveness from the respiratory variations of the plethysmographic and arterial pressure waveforms are present in many surgical patients.<sup>25</sup> Anesthesia providers should regularly inspect these analog waveforms and assess the magnitude of their respiratory variations, as these may precede any change in vital signs. However, the correct interpretation and clinical application of dynamic variables require some preliminary important considerations. The first is familiarity with the basic principles of heart–lung interaction during mechanical ventilation and the physiologic significance of these variables. The second is the ability to identify the various confounding factors that may limit the accuracy and usefulness of dynamic variables. The interpretation of dynamic variables should then take into account the actual clinical situation. High values of dynamic variables may indeed be a sign of developing hypovolemia that needs to be corrected by fluid administration. However, a high SV variation value that accompanies hypotension soon after the induction of anesthesia may be due to vasodilation and may be best addressed by the administration of a vasoconstrictor rather than bolus fluid therapy.<sup>48</sup> Of note, a recently published study demonstrated that when preload dependence (pulse pressure variation greater than 13%) is accompanied by hypotension during abdominal surgery, it may also be associated with a low SV and reduced sublingual microcirculation, both of which can improve after fluid administration.<sup>49</sup>

The correct interpretation of dynamic variables may benefit from their integration with information provided by other available sources, such as physical examination, echocardiography, filling pressures, the amplitude of the plethysmographic perfusion index, and changes in the partial pressure of end-tidal carbon dioxide that may reflect changes in CO.<sup>50</sup> Such a multiparametric approach may complement dynamic variables in determining context-specific fluid needs (e.g., vasodilation, increased risk of fluid administration) or when their values seem inconclusive.

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Dr. Perel has received speaker fees and served as a consultant for Masimo Inc., Irvine, California and for Pulsion Medical Systems (GETINGE), Munich, Germany.

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### References

- Chappell D, Jacob M, Hofmann–Kiefer K, Conzen P, Rehm M: A rational approach to perioperative fluid management. *ANESTHESIOLOGY* 2008; 109:723–40
- Myles PS, Bellomo R, Corcoran T, Forbes A, Peyton P, Story D, Christophi C, Leslie K, McGuinness S, Parke R, Serpell J, Chan MTV, Painter T, McCluskey S, Minto G, Wallace S; Australian and New Zealand College of Anaesthetists Clinical Trials Network and the Australian and New Zealand Intensive Care Society Clinical Trials Group: Restrictive *versus* liberal fluid therapy for major abdominal surgery. *N Engl J Med* 2018; 378:2263–74
- Shin CH, Long DR, McLean D, Grabitz SD, Ladha K, Timm FP, Thevathasan T, Pieretti A, Ferrone C, Hoeft A, Scheeren TWL, Thompson BT, Kurth T, Eikermann M: Effects of intraoperative fluid management on postoperative outcomes: A hospital registry study. *Ann Surg* 2018; 267:1084–92
- Miller TE, Myles PS: Perioperative fluid therapy for major surgery. *ANESTHESIOLOGY* 2019; 130:825–32
- Lilot M, Ehrenfeld JM, Lee C, Harrington B, Cannesson M, Rinehart J: Variability in practice and factors predictive of total crystalloid administration during abdominal surgery: Retrospective two-centre analysis. *Br J Anaesth* 2015; 114:767–76
- Navarro LH, Bloomstone JA, Auler JO Jr, Cannesson M, Rocca GD, Gan TJ, Kinsky M, Magder S, Miller TE, Mythen M, Perel A, Reuter DA, Pinsky MR, Kramer GC: Perioperative fluid therapy: A statement from the international Fluid Optimization Group. *Perioper Med (Lond)* 2015; 4:3
- Bentzer P, Griesdale DE, Boyd J, MacLean K, Sirounis D, Ayas NT: Will this hemodynamically unstable patient respond to a bolus of intravenous fluids? *JAMA* 2016; 316:1298–309
- Bubenek–Turconi ȘI, Văleanu L, Popescu M, Panaitescu E, Tomescu D, Cacoveanu MC, Perel A: Continuous noninvasive hemoglobin monitoring reflects the development of acute hemodilution after consecutive fluid challenges. *Anesth Analg* 2020; 130:696–703
- Michard F: Changes in arterial pressure during mechanical ventilation. *ANESTHESIOLOGY* 2005; 103:419–28; quiz 449–5
- Perel A, Pizov R, Cotev S: Respiratory variations in the arterial pressure during mechanical ventilation

- reflect volume status and fluid responsiveness. *Intensive Care Med* 2014; 40:798–807
11. Teboul JL, Monnet X, Chemla D, Michard F: Arterial pulse pressure variation with mechanical ventilation. *Am J Respir Crit Care Med* 2019; 199:22–31
  12. 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
  13. Cannesson M, Aboy M, Hofer CK, Rehman M: Pulse pressure variation: Where are we today? *J Clin Monit Comput* 2011; 25:45–56
  14. Preisman S, Kogan S, Berkenstadt H, Perel A: Predicting fluid responsiveness in patients undergoing cardiac surgery: Functional haemodynamic parameters including the respiratory systolic variation test and static preload indicators. *Br J Anaesth* 2005; 95:746–55
  15. 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
  16. 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
  17. Berkenstadt H, Margalit N, Hadani M, Friedman Z, Segal E, Villa Y, Perel A: Stroke volume variation as a predictor of fluid responsiveness in patients undergoing brain surgery. *Anesth Analg* 2001; 92:984–9
  18. Zhang Z, Lu B, Sheng X, Jin N: Accuracy of stroke volume variation in predicting fluid responsiveness: A systematic review and meta-analysis. *J Anesth* 2011; 25:904–16
  19. Guinot PG, de Broca B, Abou Arab O, Diouf M, Badoux L, Bernard E, Lorne E, Dupont H: Ability of stroke volume variation measured by oesophageal Doppler monitoring to predict fluid responsiveness during surgery. *Br J Anaesth* 2013; 110:28–33
  20. Perel A, Pizov R, Cotev S: Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to graded hemorrhage. *ANESTHESIOLOGY* 1987; 67:498–502
  21. Pizov R, Eden A, Bystritski D, Kalina E, Tamir A, Gelman S: Arterial and plethysmographic waveform analysis in anesthetized patients with hypovolemia. *ANESTHESIOLOGY* 2010; 113:83–91
  22. Perel A: Assessing fluid responsiveness by the systolic pressure variation in mechanically ventilated patients. Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. *ANESTHESIOLOGY* 1998; 89:1309–10
  23. Thiele RH, Colquhoun DA, Blum FE, Durieux ME: The ability of anesthesia providers to visually estimate systolic pressure variability using the “eyeball” technique. *Anesth Analg* 2012; 115:176–81
  24. Rinehart J, Islam T, Boud R, Nguyen A, Alexander B, Canales C, Cannesson M: Visual estimation of pulse pressure variation is not reliable: A randomized simulation study. *J Clin Monit Comput* 2012; 26:191–6
  25. Maguire S, Rinehart J, Vakharia S, Cannesson M: Technical communication: respiratory variation in pulse pressure and plethysmographic waveforms: Intraoperative applicability in a North American academic center. *Anesth Analg* 2011; 112:94–6
  26. Sandroni C, Cavallaro F, Marano C, Falcone C, De Santis P, Antonelli M: Accuracy of plethysmographic indices as predictors of fluid responsiveness in mechanically ventilated adults: A systematic review and meta-analysis. *Intensive Care Med* 2012; 38:1429–37
  27. Cannesson M, Desebbe O, Rosamel P, Delannoy B, Robin J, Bastien O, Lehot JJ: Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. *Br J Anaesth* 2008; 101:200–6
  28. Perel A, Habicher M, Sander M: Bench-to-bedside review: Functional hemodynamics during surgery – should it be used for all high-risk cases? *Crit Care* 2013; 17:203
  29. Perel A: The value of dynamic preload variables during spontaneous ventilation. *Curr Opin Crit Care* 2017; 23:310–7
  30. Cohn JN, Pinkerson AL, Tristani FE: Mechanism of pulsus paradoxus in clinical shock. *J Clin Invest* 1967; 46:1744–55
  31. Perel A: Excessive variations in the plethysmographic waveform during spontaneous ventilation: An important sign of upper airway obstruction. *Anesth Analg* 2014; 119:1288–92
  32. de Haro C, Ochagavia A, López-Aguilar J, Fernandez-Gonzalo S, Navarra-Ventura G, Magrans R, Montanyà J, Blanch L: Asynchronies in the Intensive Care Unit (ASYNICU) Group: Patient-ventilator asynchronies during mechanical ventilation: Current knowledge and research priorities. *Intensive Care Med Exp* 2019; 7(Suppl 1):43
  33. Myatra SN, Prabu NR, Divatia JV, Monnet X, Kulkarni AP, Teboul JL: The changes in pulse pressure variation or stroke volume variation after a “tidal volume challenge” reliably predict fluid responsiveness during low tidal volume ventilation. *Crit Care Med* 2017; 45:415–21
  34. Monnet X, Teboul JL: Passive leg raising: Five rules, not a drop of fluid! *Crit Care* 2015; 19:18
  35. Vignon P, Repessé X, Bégot E, Léger J, Jacob C, Bouferrache K, Slama M, Prat G, Vieillard-Baron A: Comparison of echocardiographic indices used to

- predict fluid responsiveness in ventilated patients. *Am J Respir Crit Care Med* 2017; 195:1022–32
36. Gignon L, Roger C, Bastide S, Alonso S, Zieleskiewicz L, Quintard H, Zoric L, Bobbia X, Raux M, Leone M, Lefrant JY, Muller L: Influence of diaphragmatic motion on inferior vena cava diameter respiratory variations in healthy volunteers. *ANESTHESIOLOGY* 2016; 124:1338–46
  37. Gavelli F, Teboul JL, Monnet X: The end-expiratory occlusion test: Please, let me hold your breath! *Crit Care* 2019; 23:274
  38. Hamilton MA, Cecconi M, Rhodes A: A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg* 2011; 112:1392–402
  39. 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
  40. Perel A: Perioperative goal-directed therapy with uncalibrated pulse contour methods: Impact on fluid management and postoperative outcome. *Br J Anaesth* 2017; 119:541–3
  41. Forget P, Lois F, de Kock M: Goal-directed fluid management based on the pulse oximeter-derived pleth variability index reduces lactate levels and improves fluid management. *Anesth Analg* 2010; 111:910–4
  42. Thiele RH, Rea KM, Turrentine FE, Friel CM, Hassinger TE, McMurry TL, Goudreau BJ, Umapathi BA, Kron IL, Sawyer RG, Hedrick TL: Standardization of care: Impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. *J Am Coll Surg* 2015; 220:430–43
  43. Cannesson M, Ramsingh D, Rinehart J, Demirjian A, Vu T, Vakharia S, Imagawa D, Yu Z, Greenfield S, Kain Z: Perioperative goal-directed therapy and postoperative outcomes in patients undergoing high-risk abdominal surgery: A historical-prospective, comparative effectiveness study. *Crit Care* 2015; 19:261
  44. Edwards MR, Forbes G, MacDonald N, Berdunov V, Mihaylova B, Dias P, Thomson A, Grocott MP, Mythen MG, Gillies MA, Sander M, Phan TD, Evered L, Wijesundera DN, McCluskey SA, Aldecoa C, Ripollés-Melchor J, Hofer CK, Abukhudair H, Szczeklik W, Grigoras I, Hajjar LA, Kahan BC, Pearse RM; OPTIMISE II investigators: Optimisation of Perioperative Cardiovascular Management to Improve Surgical Outcome II (OPTIMISE II) trial: Study protocol for a multicentre international trial of cardiac output-guided fluid therapy with low-dose inotrope infusion compared with usual care in patients undergoing major elective gastrointestinal surgery. *BMJ Open* 2019; 9:e023455
  45. 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
  46. Lai CW, Starkie T, Creanor S, Struthers RA, Portch D, Erasmus PD, Mellor N, Hosie KB, Sneyd JR, Minto G: Randomized controlled trial of stroke volume optimization during elective major abdominal surgery in patients stratified by aerobic fitness. *Br J Anaesth* 2015; 115:578–89
  47. Coeckelenbergh S, Zaouter C, Alexander B, Cannesson M, Rinehart J, Duranteau J, Van der Linden P, Joosten A: Automated systems for perioperative goal-directed hemodynamic therapy. *J Anesth* 2020; 34:104–14
  48. Thiele RH, Raghunathan K, Brudney CS, Lobo DN, Martin D, Senagore A, Cannesson M, Gan TJ, Mythen MM, Shaw AD, Miller TE: American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on perioperative fluid management within an enhanced recovery pathway for colorectal surgery. *Perioper Med (London)* 2016; 5:24
  49. Bouattour K, Teboul JL, Varin L, Vicaut E, Duranteau J: Preload dependence is associated with reduced sublingual microcirculation during major abdominal surgery. *ANESTHESIOLOGY* 2019; 130:541–9
  50. Vincent JL, Pelosi P, Pearse R, Payen D, Perel A, Hoefft A, Romagnoli S, Ranieri VM, Ichai C, Forget P, Della Rocca G, Rhodes A: Perioperative cardiovascular monitoring of high-risk patients: A consensus of 12. *Crit Care* 2015; 19:224