CRITICAL CARE

Hypotension during gradual blood loss: waveform variables response and absence of tachycardia

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Editor’s key points

- Changes in plethysmographic waveform may be a useful way to predict hypovolaemia.
- This study used controlled hypovolaemia as a model to study waveform changes in anaesthetized patients.
- Elderly treated hypertensive patients were relatively intolerant of hypovolaemia displaying early hypotension.
- In general, baseline arterial and plethysmographic waveforms were not predictive of hypotension with controlled blood loss.

Background. Variation in arterial pressure and plethysmographic waveforms has been shown to be predictors of cardiac output response to fluid challenge. The objective of this study was to evaluate the ability of arterial and plethysmographic waveform variables to predict hypotension during blood loss.

Methods. Patients undergoing autologous haemodilution were studied. After anaesthesia induction, blood was withdrawn in steps of 2% of estimated circulating blood volume (ECBV). Arterial and plethysmographic waveforms were recorded and analysed offline at each step of blood withdrawal.

Results. Thirty-four (29%) out of 118 studied patients tolerated 20% ECBV withdrawal without hypotension. Patients who tolerated 20% ECBV withdrawal were younger than those who did not [mean (SD): 53.8 (11.1) vs 62.7 (10.7); P<0.0001]. Patients with hypertension developed hypotension earlier than healthier patients did. There were no differences at the baseline in arterial and plethysmographic waveform variables between those who did and those who did not tolerate 20% of ECBV withdrawal. All values of variables increased significantly from the baseline after the withdrawal of 4% of ECBV (P<0.005). There were no changes in heart rate (HR), 73 (12) at the baseline and 76 (13) after 20% of ECBV withdrawal (P=0.4).

Conclusions. Arterial and plethysmographic waveform variables were augmented with increasing blood loss in all patients. Older patients, patients who received anti-hypertensive drugs, or both developed hypotension earlier than others. Baseline values were weak predictors of hypotension during stepwise blood withdrawal. No clinically significant increase in HR was observed, regardless of tolerance of arterial pressure to blood withdrawal.

Keywords: arterial pressure; hypotension; hypovolaemia; pulse oximetry waveform

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Patients undergoing anaesthesia for elective surgery, even without bowel preparation, can have different blood volumes at the baseline due to chronic medications, stress, and fasting. In addition, changing from spontaneous breathing to positive pressure ventilation may decrease cardiac preload and predispose the cardiovascular system to hypotension. This led us to the hypothesis of the current study: baseline values of arterial and plethysmographic respiratory-induced waveform variables can predict arterial hypotension during gradual blood withdrawal. To test our hypothesis, we evaluated selected respiratory-induced arterial and pulse oximetry plethysmographic waveform variables during gradual hypovolaemia.

Methods

Patients undergoing elective hip arthroplasty, suprapubic prostatectomy, or nephrectomy, who were planned to undergo autologous haemodilution, were eligible for the study. Excluded were patients who had a haemoglobin (Hb) concentration of <13.0 g dl\(^{-1}\), a creatinine concentration of >1.5 mg dl\(^{-1}\), those who had experienced a coronary or cerebrovascular event during the last 6 months, and those who did not have a normal sinus rhythm. The study was approved by the institutional IRB (920040086) and all participants gave their written informed consent. Patients who were treated chronically with \(\beta\)-adrenergic antagonists received regular doses of their medication and diazepam 10 mg p.o. on the morning of surgery. Angiotensin-converting enzyme (ACE)-inhibitors and diuretics were withheld on the day of surgery. Each patient received 7 ml kg\(^{-1}\) lactated Ringer solution during the induction of general anaesthesia by fentanyl 1.5 g kg\(^{-1}\) and propofol 2.0–2.5 mg kg\(^{-1}\). Tracheal intubation was facilitated with rocuronium 0.6 mg kg\(^{-1}\), positive pressure ventilation was applied (\(V\(_I\): 8 ml kg\(^{-1}\) of ideal body weight), and anaesthesia was maintained with \(N_2O/O_2\) (1:1) + isoflurane (\(F\(_I\): 0.4%) throughout the period of blood auto-donation. The frequency of mechanical ventilation was adjusted to remain between 8 and 12 bpm in order to keep \(F\(_{\text{CO}_2}\) at 4.4–5 kPa.

Blood was withdrawn in steps of 2% of ECBV up to 20% of ECBV (10 steps), which was calculated by the following formula: \([((1486 \times \text{BSA}) - 825) + (1578 \times \text{BSA})]\) for males and \([((1.06 \times \text{age}) + (822 \times \text{BSA})] + (1395 \times \text{BSA})]\) for females.\(^{18}\) Blood was collected into a citrate phosphate dextrose adenine bag.

The primary outcome of the study was hypotension. Blood withdrawal was stopped when systolic AP decreased by 20% from the values observed immediately before the start of the withdrawal, or below 80 mm Hg, or if dysrhythmia occurred. Each step of blood withdrawal with concomitant recording of the waveforms took about 3 min, with no pauses between steps. The study was completed at the point of 20% of ECBV withdrawal without the occurrence of hypotension or at the stage of blood withdrawal when systolic AP decreased at least by 20% or to less than 80 mm Hg. After the completion of blood withdrawal, the blood volume was replaced with an equal volume of colloid solution (6% HES 200/0.5, Fresenius Kabi, Deutchland GmbH, Germany).

The systolic pressure variations (SPVs), delta up (dUp), delta down (dDown), and pulse pressure variations (PPVs) were analysed using standard methods.\(^{5,10}\) SPV\(_%\) = SPV/systolic AP during apnoea \(\times 100\). The plethysmographic waveform variations (PWVs) of the pulse oximetry signal were calculated as follows: the difference between the maximal and minimal plethysmographic signals divided by the amplitude of the plethysmographic signal during apnoea.\(^{8}\) The delta pulse oximetry plethysmographic waveform amplitude (dPOP) was calculated as follows: \((\text{POP}_{\text{max}} - \text{POP}_{\text{min}})/(\text{POP}_{\text{max}} + \text{POP}_{\text{min}})/2\).\(^{13}\) Waveforms were recorded with a Datex-Ohmeda AS-3 (Datex, Helsinki, Finland) recorder and analysed offline at the baseline and after each step of blood withdrawal.\(^6\)

Statistical analysis

The primary variables of interest were waveform variables; the SPV value was used to calculate power analysis. Values are presented as mean (so), unless otherwise stated. Comparisons of continuous variables between patients who tolerated 20% blood withdrawal and those who did not were performed using the \(t\)-test or the Mann–Whitney test as appropriate. Comparisons of dichotomous variables between patients who tolerated 20% blood withdrawal and those who did not were performed using the \(\chi^2\) test. Correlation between variables at the baseline and the number of steps tolerated were evaluated with the Spearman correlation coefficient, as was the effect of changes between baseline values and values after 4% ECBV withdrawal on AP tolerance.

Comparisons of variables before and after blood withdrawal were performed using paired \(t\)-tests. The Bonferroni correction was applied when multiple comparisons were used. A value of \(P<0.005\) was considered significant for each comparison to have a total \(P\)-value of 0.05.

Changes in haemodynamic variables between the values at the baseline and those after 10% blood withdrawal and between 10% and 20% blood withdrawal were analysed with the paired \(t\)-test. Age 60 was the mean age of the studied patients in our population. Thus, dividing patients according to this age gave us two almost equal subgroups. A value of \(P<0.05\) was considered significant.

The sample includes 118 patients, thus enabling the detection of a difference (SPV variable) of \(\sim 0.6\) so with an \(\alpha\) of 0.05 and power of 80%. Statistical calculations were performed with the SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 118 patients were recruited into this study [80 males, 38 females, mean age 60.1 (11.5) yr, range 23–85]. Thirty-four of them (29%) tolerated gradual 20% ECBV withdrawal without significant hypotension, and the haemodynamics of this group of patients are reported elsewhere.\(^6\) The ability of the patients to maintain systolic AP during blood withdrawal was highly variable (Fig. 1). As a result of blood withdrawal, the Hb concentration decreased from
13.7 (1.1) to 13.0 (1.1) g dl⁻¹ (P<0.00001) before replacement with colloids in all 118 patients. The initial peak airway pressure of 20.5 (3.5) cm H₂O did not change at any point during the study period. Patients with chronic obstructive pulmonary disease (COPD) had similar values of peak airway pressure, and these did not change during blood withdrawal.

### Patient characteristics and co-morbidities as predictors of hypotension

Younger patients tolerated blood withdrawal significantly better than older ones: this finding held true when patients who tolerated 20% of blood withdrawal were compared with those who did not, and for analysis of the correlations between age and the number of blood withdrawal stages the patients tolerated (Table 1). Weight, height, and body mass index were not significant predictors of AP tolerance during blood withdrawal (Tables 1 and 2). There was no gender-based difference in AP tolerance during blood withdrawal (Table 1).

Hypertension and chronic therapy with calcium channel antagonists, ACE-inhibitors, and/or diuretics were associated with early development of hypotension during blood withdrawal (Tables 1 and 2). None of the 14 patients chronically treated with calcium channel antagonists tolerated 20% of ECBV withdrawal without hypotension (Table 1; 95% confidence interval 0–19.3%). Patients who had stable ischaemic heart disease or diabetes mellitus tolerated blood withdrawal similarly to those patients without these co-morbidities. Patients with COPD appeared to tolerate 20% of ECBV withdrawal somewhat better than patients without COPD: although the difference between those who tolerated 20% ECBV and those who did not was not significant (P=0.07; Table 1); however, patients with COPD tolerated more steps of blood withdrawal than did patients without COPD.

### Table 1  Patient characteristics and medical history of patients who did and did not tolerate 20% ECBV reduction and correlation to the number of steps of blood withdrawal. BMI, body mass index; ECBV, estimated circulating blood volume; IHD, ischaemic heart disease; HTN, hypertension; DM, diabetes mellitus; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; NS, non-significant; NA, not available. Data are express as mean (sd)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>20% ECBV reduction</th>
<th>Correlation to number of steps of blood volume reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tolerated</td>
<td>Did not tolerate</td>
</tr>
<tr>
<td>Total, n</td>
<td>34</td>
<td>84</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>53.8 (11.1)</td>
<td>62.7 (10.7)</td>
</tr>
<tr>
<td>Gender, F/M (%)</td>
<td>13/21 (34/26)</td>
<td>25/59 (66/74)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77 (18.3)</td>
<td>79 (13.6)</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>27.5 (6.0)</td>
<td>27.8 (3.8)</td>
</tr>
<tr>
<td>ECBV (ml)</td>
<td>4699 (861)</td>
<td>4862 (727)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IHD</td>
<td>2 (5.9%)</td>
<td>7 (8.3%)</td>
</tr>
<tr>
<td>HTN</td>
<td>8 (23.5%)</td>
<td>50 (59.5%)</td>
</tr>
<tr>
<td>DM</td>
<td>5 (14.7%)</td>
<td>13 (15.5%)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (2.9%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>COPD</td>
<td>8 (23.5%)</td>
<td>8 (9.5%)</td>
</tr>
<tr>
<td>Chronic medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>0 (0%)</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>β-Antagonists</td>
<td>4 (11.8%)</td>
<td>21 (25%)</td>
</tr>
<tr>
<td>Ca-channel antagonists</td>
<td>0 (0%)</td>
<td>14 (16.7%)</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>5 (14.7%)</td>
<td>29 (34.5%)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>0 (0%)</td>
<td>12 (14.3%)</td>
</tr>
<tr>
<td>At least one of the above</td>
<td>5 (14.7%)</td>
<td>38 (45.2%)</td>
</tr>
</tbody>
</table>

![Fig 1](https://example.com/fig1.png) Per cent patients who tolerated and did not tolerate each of the 10 steps of ECBV reduction (each step is 2% of ECBV).
al was chosen because at that stage of blood withdrawal, all evaluated waveform variables became different from the baseline (Fig. 3). The difference in waveform variation; dPOP, delta pulse oximetry plethysmographic waveform amplitude; NS, non-significant. Data are express as mean (SD).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values at the baseline</th>
<th>Correlation to number of steps of blood volume reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (n=118)</td>
<td>Did not tolerate 20% ECBV reduction (n=84)</td>
</tr>
<tr>
<td>Systolic AP (mm Hg)</td>
<td>106.5 (17.6)</td>
<td>106 (19.2)</td>
</tr>
<tr>
<td>Mean AP (mm Hg)</td>
<td>73.8 (12.1)</td>
<td>74.0 (13.2)</td>
</tr>
<tr>
<td>Pulse pressure (mm Hg)</td>
<td>49.0 (11.0)</td>
<td>49.2 (11.9)</td>
</tr>
<tr>
<td>Heart rate (beats min⁻¹)</td>
<td>71.2 (13.2)</td>
<td>70.2 (13.6)</td>
</tr>
<tr>
<td>SPV (mm Hg)</td>
<td>6.4 (2.6)</td>
<td>6.4 (2.7)</td>
</tr>
<tr>
<td>dUp (mm Hg)</td>
<td>2.2 (1.7)</td>
<td>2.3 (1.9)</td>
</tr>
<tr>
<td>dDown (mm Hg)</td>
<td>4.3 (2.8)</td>
<td>4.2 (2.9)</td>
</tr>
<tr>
<td>SPV% (%</td>
<td>6.2 (2.5)</td>
<td>6.2 (2.6)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>9.6 (4.6)</td>
<td>10.0 (4.9)</td>
</tr>
<tr>
<td>PWV (%)</td>
<td>9.1 (4.9)</td>
<td>9.6 (5.1)</td>
</tr>
<tr>
<td>dPOP (%)</td>
<td>5.4 (5.3)</td>
<td>5.3 (4.8)</td>
</tr>
</tbody>
</table>

(P=0.009; Table 1). This difference persisted even when comparing COPD patients with those patients not receiving any chronic medication (P=0.05; Fig. 2). Chronic therapy with β-adrenergic antagonists had no effect on the development of hypotension during blood withdrawal, although patients treated with β-adrenergic antagonists had lower HRs at the baseline.

### Standard haemodynamic and waveform variables during blood withdrawal

Table 2 shows the values of waveform variables at the baseline of all 118 study participants. There was a weak correlation between systemic AP at the baseline and the number of steps of blood withdrawal that patients tolerated. There was no difference in AP and HR or in pulse pressure at the baseline between the patients who tolerated 20% of ECBV withdrawal and those who did not. Even at the stage of hypotension, HR did not change (Table 2 and Fig. 3).

There was also no correlation between pulse pressure values at the baseline and the number of steps tolerated without hypotension. Moreover, there were no differences at the baseline in arterial and plethysmographic waveform variables between those who did and those who did not tolerate 20% of ECBV withdrawal. However, there was a significant but weak correlation between SPV%, PPV, PWV, and dPOP at the baseline and the number of steps of blood withdrawal that patients tolerated without hypotension (Table 2). All measured haemodynamic variables except dUp changed gradually during blood withdrawal and became significantly different from the baseline after 2% or 4% of ECBV withdrawal in all 118 patients (Fig. 3). The effect of co-morbidities and medications on the waveform variables during the study period was not observed.

The ability to predict arterial pressure tolerance to hypovolaemia during the early stages of blood withdrawal was evaluated by comparing the relevant variables between the baseline and 4% ECBV withdrawal. The 4% of ECBV withdrawal was chosen because at that stage of blood withdrawal, all evaluated waveform variables became different from the baseline (Fig. 3). The differences between values at the baseline and values after 4% ECBV withdrawal in all measured waveforms except SPV% were not different in patients who tolerated 20% ECBV withdrawal and those who did not, and there were no correlations between those differences and the number of steps tolerated without hypotension.

Analysis of patients who tolerated 10% (n=70) and 20% (n=34) of ECBV withdrawal without hypotension showed a significant increase in all evaluated waveform variables at both steps (Fig. 4). Although HR decreased at the early steps and increased only slightly (by 3 beats min⁻¹) during more advanced blood withdrawal steps, these changes were physiologically insignificant (Fig. 3). The arterial and plethysmographic waveform variables of older patients tended to undergo more significant changes during blood withdrawal from the baseline to 10% of ECBV compared with the variables of patients younger than 60 yr, and this increase was significantly different in their SPVs (Fig. 4).

### Discussion

To the best of our knowledge, this is the first study to evaluate the clinically important event of gradual blood loss in...
Arterial and plethysmographic waveform variables as predictors of tolerance to blood loss

We hypothesized that baseline values of waveform variables would be able to predict arterial hypotension during gradual blood withdrawal in patients undergoing 20% of ECBV withdrawal. The results of this study do not support the hypothesis; moreover, changes in waveform variables after 4% withdrawal of ECBV did not predict AP intolerance either. The study was adequately powered and showed similar increases in waveform variables in patients who tolerated all 10 steps of blood withdrawal without hypotension and those who developed hypotension early on.

There are several factors that can explain the lack of support for our hypothesis. AP during hypovolaemia depends on many factors including the degree of vasoconstriction and blood volume recruitment from the venous reservoir, located predominantly in the splanchnic venous system; in other words, the transfer of blood from unstressed to stressed volume.10 Waveform variables are a good tool to estimate preload, but not vascular tone or degree of vasoconstriction both of which may lead to different changes in AP.

Age and co-morbidities as predictors of tolerance to blood loss

Older awake patients exhibit impaired blood volume recruitment from the venous reservoirs, which may account for the increases in arterial and plethysmographic waveforms that were seen. In addition, vascular and cardiac adaptation to any haemodynamic and homeostatic changes in the older population is impaired, so it is therefore not surprising that

anaesthetized patients without concomitant volume replacement or pharmacological intervention.

Fig 2 Box plots of the number of steps of blood withdrawal that patients tolerated without hypotension. Three groups of patients were compared: patients treated chronically with one of the three types of medications (calcium channel antagonists, ACE-inhibitors, or diuretics) who suffered from COPD; patients not treated with any medications who did not suffer from COPD; and patients who had COPD but received no chronic medication. The box represents the inter-quartile range which contains 50% of the values. The whiskers are lines that extend from the box to the highest and lowest values. *Significant compared with the patients with COPD (P<0.05). COPD patients tolerated blood withdrawal better than patients who did not have COPD, regardless of whether they had concomitant hypertension and were treated with anti-hypertensive medication or not. One patient with COPD who received chronic anti-hypertensive treatment was not included in this analysis.

Fig 3 Systolic arterial pressure (SAP), pulse pressure (PP), HR, SAP variations (SPVs), dDown, and PPVs of AP, plethysmographic waveform variations (PWVs), and pulse oximetry PWVs (dPOPs) during all 10 steps of blood withdrawal. n represents the number of patients who developed hypotension at that step. The data are presented as mean (sd); *significant compared with the baseline (BL) (P<0.005).
older patients experienced a higher incidence of hypotension after induction of general anaesthesia compared with younger patients.\textsuperscript{21–25} Similar hypovolaemia in non-anaesthetized volunteers resulted in a much weaker effect on AP.\textsuperscript{26–28} Such differences in responses to hypovolaemia between awake and anaesthetized mechanically ventilated patients can be attributed to at least two factors. First, general anaesthesia decreases the sympathetic tone needed for appropriate adjustment of vascular tone to decreased blood volume and mobilization of blood volume from reservoirs.\textsuperscript{29} Secondly, an increase in intrathoracic pressure that results from positive pressure ventilation impedes venous return, further decreasing the ability to compensate for hypovolaemia.\textsuperscript{30}

In addition, decreased ability to constrict vasculature and mobilize blood volume from the reservoirs may explain the poor tolerance of AP to blood withdrawal found in patients on long-term ACE antagonists, Ca-channel antagonists, and/or diuretics.

Patients who had COPD tolerated blood withdrawal better than patients without COPD. A possible explanation for patients with COPD tolerating blood withdrawal better is a probable increased baseline blood volume in these patients.\textsuperscript{31}

**Tachycardia during blood loss**

It has been shown that HR was elevated while AP remained unchanged during mild and moderate hypovolaemia in awake volunteers.\textsuperscript{21, 26–28} Since tachycardia develops before a decrease in AP, it is considered to be one of the earliest signs of hypovolaemia. Our patients did not develop clinically relevant tachycardia, regardless of whether or not they developed hypotension which is in agreement with the few studies that evaluated haemodynamic responses to blood withdrawal in patients anaesthetized with different anaesthetics. They did not observe a clinically significant increase in HR, despite the fact that in the majority of these studies, some degree of arterial hypotension was observed.\textsuperscript{4, 7, 8, 17} Thus, together with the previous reports,\textsuperscript{4, 7, 8, 17} the current study provides more evidence that mild-to-moderate hypovolaemia does not result in tachycardia in anaesthetized patients, even among those who develop hypotension. Since most of the patients referred to in this and previous reports were not treated with \(\beta\)-adrenergic antagonists, the absence of tachycardia could not be explained by the pharmacological blockade of \(\beta\)-adrenergic receptors.

**Possible role of increases in arterial and plethysmographic waveform variables**

During gradual blood loss, the values of waveform variables were already significantly increased after 4% of ECBV withdrawal both in patients who became hypotensive and in those who did not. The increases in the values of the variables and arterial hypotension occurred almost simultaneously in patients who did not tolerate 20% of ECBV withdrawal; therefore, while these increases per se cannot serve as predictors of arterial hypotension in patients who do not tolerate blood withdrawal (older and with co-morbidities),

![Graph showing changes in hemodynamic and waveform variables from baseline to 10% of ECBV reduction and from 10% to 20% of ECBV reduction.](https://academic.oup.com/bja/article-abstract/109/6/911/365451)
they can in patients who do tolerate it (younger and healthier).

The results of our study suggest that the monitoring of both AP and changes in respiratory-induced waveform variables may be particularly useful in the clinical setting: a decrease in AP without changes in waveform variables would suggest vasodilatation rather than hypovolaemia, while a decrease in AP, increases in waveform variables, or both would suggest hypovolaemia. These speculations warrant further studies. All the waveform variables were more sensitive to hypovolaemia than AP, pulse pressure, or HR.

It is important to recognize the limitations of the current study. First, there was no blood volume measurement after blood withdrawal, and so the role of the changes in blood volume was not determined. Secondly, we did not measure cardiac output, and this limits our interpretation of the reason for any hypotension that occurred during hypovolaemia. Thirdly, the threshold of hypotension (i.e. a systolic AP of 80 mm Hg or within 20% of the baseline) was chosen arbitrarily, although it was based on accepted clinical practice. Despite these limitations, the current study presents a reasonable human model of mild, gradual hypovolaemia with important clinical implications.

In summary, fewer than 30% of the studied patients tolerated withdrawal of 20% of ECBV without hypotension. Older patients who had hypertensive disease treated with anti-hypertensive drugs developed arterial hypotension after smaller amounts of blood withdrawal than did younger and healthier patients. All arterial and plethysmographic waveform variables increased after a small amount of blood withdrawal; these increases preceded a decrease in AP in younger and healthier patients but developed simultaneously in older and sicker ones. Respiratory-induced arterial and plethysmographic waveform variables at the baseline were weak predictors of hypotension during stepwise blood withdrawal. Patients who had COPD tolerated blood withdrawal better than others.

There was no clinically significant tachycardia, regardless of whether patients did or did not receive β-blockers, or did or did not tolerate withdrawal of 20% of ECBV.

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Declaration of interest
None declared.

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References
5 Perel A, Pizov R, Cotev S. Systolic blood pressure variation is a sensitive indicator of hypovolaemia in ventilated dogs subjected to graded hemorrhage. Anesthesiology 1987; 67: 498–502
9 Michard F. Changes in arterial pressure during mechanical ventilation. Anesthesiology 2005; 103: 419–28; quiz 49–5
11 Geerts BF, Aerts LPHJ, Groeneveld AB, Jansen JRC. Predicting cardiac output responses to passive leg raising by a PEEP-induced increase in central venous pressure, in cardiac surgery patients. Br J Anaesth 2011; 107: 150–6
14 Perel A. The physiological basis of arterial pressure variation during positive-pressure ventilation. Reanimation 2005; 14: 162–71
19 Cannesson M, Besnard C, Durand PG, Bohe J, Jacques D. Relation between respiratory variations in pulse oximetry plethysmographic