Mini-fluid challenge predicts fluid responsiveness during spontaneous breathing under spinal anaesthesia

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BACKGROUND The ability to predict fluid responsiveness in spontaneously breathing patients under spinal anaesthesia is desirable.

OBJECTIVE The objective of this study was to test whether variations in stroke volume (SV) in response to a fixed mini-fluid challenge (ΔSV₁₀₀) measured by thoracic impedance cardiography (ICG) can predict fluid responsiveness in spontaneously breathing patients under spinal anaesthesia.

DESIGN A prospective observational study.

SETTING Anaesthesiology department in a university hospital.

PARTICIPANTS Seventy-three patients monitored by ICG during surgery under spinal anaesthesia.

INTERVENTIONS Patients received a 100-ml fluid challenge followed by volume expansion with 500 ml of crystalloid.

MAIN OUTCOMES MEASURES Haemodynamic variables and bioimpedance indices [blood pressure, SV, cardiac output (CO)] were measured before and after fluid challenge and before and after volume expansion. Responders were defined by more than 15% increase in SV after volume expansion.

RESULTS SV increased by at least 15% in 27 (37%) of the 73 patients. ΔSV₁₀₀ predicted fluid responsiveness with an area under the receiver-operating characteristic (AUC) curve of 0.93 [95% confidence interval (95% CI) 0.8 to 0.97, \( P < 0.001 \)]. The cut-off was 7% and a grey zone ranging between 3 and 8% was observed in up to 14% of patients. SVBaseline was a poor predictor of fluid responsiveness [AUC of 0.69 (95% CI 0.57 to 0.79, \( P = 0.002 \)].

CONCLUSION ΔSV₁₀₀ greater than 7% accurately predicted fluid responsiveness during surgery with a grey zone ranging between 3 and 8%.

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Introduction

Over the last decade, several studies have shown that guided intraoperative fluid therapy can achieve significant improvement in outcome in high-risk surgical patients.¹² Getting the best from fluid loading may depend on the ability to detect preload responsiveness. Several authors have emphasised the ability of dynamic preload indicators, based on an interaction between respiratory and circulatory functions under positive mechanical ventilation such as respiratory variation of pulse pressure and respiratory variation of stroke volume (SV), to predict fluid responsiveness.³⁴ However, these respiratory-derived indices are reliable predictors only under strict conditions. When breathing is spontaneous and not controlled, respiratory-derived indices are unable to accurately predict fluid responsiveness.⁵⁶ The passive leg-raising (PLR) test has been developed to predict accurately fluid responsiveness, even in spontaneously breathing patients.⁷ But this manoeuvre cannot be easily performed in the operating theatre, especially during orthopaedic surgery under spinal anaesthesia. Another approach consists of testing fluid responsiveness by a ‘mini’ fluid challenge. Two studies in critical care have demonstrated that an increase in cardiac output (CO) (or its surrogate) during limited fluid loading predicted subsequent fluid responsiveness.⁸⁹ In these studies, CO was measured using oesophageal Doppler or transthoracic echocardiography. These two devices cannot be easily used in awake patients under spinal
anaesthesia in the operating theatre. Thoracic impedance cardiography (ICG) is a noninvasive and operator-independent device that can be used to continuously assess CO and SV. No data are currently available concerning a mini-fluid challenge in spontaneously breathing patients under spinal anaesthesia. There are a number of surgical procedures often performed under spinal anaesthesia that may benefit from the improved outcome associated with intraoperative fluid therapy. A noninvasive haemodynamic approach able to predict fluid responsiveness in spontaneously breathing patients under spinal anaesthesia. The predictive value of this variable was assessed by a grey zone approach. We also evaluated the correlation between SV variations and arterial pressure during fluid expansion.

Materials and methods

Ethics

This study was approved by the Institutional Review Board (IRB) of the Amiens University Hospital for humans (CEERNI no. 92 de 2012, Comité de Protection des Personnes Nord-Ouest II CHU - Place V. Pauchet, 80054 AMIENS Cedex 1). Informed consent was waived, as the IRB considered the protocol to be part of routine clinical practice. The manuscript was prepared in accordance with the STROBE Statement checklist for cohort studies.

Patients

A prospective, observational study was conducted over a period of 6 months during 2013. Inclusion criteria were patients over the age of 18 years undergoing spinal anaesthesia monitored by ICG, in whom the anaesthetist decided to infuse intravenous fluids to expand circulating volume. Indications for fluid expansion were suspected hypovolaemia, arterial hypotension or surgical bleeding. Exclusion criteria were patients with chronic obstructive pulmonary disease, prior cardiac or thoracic surgery, valvular heart disease, frequent ectopic beats, arrhythmia, vasoactive or sedative drug administration during the study period.

Anaesthesia

Routine monitoring consisted of a three-lead electrocardiogram, pulse oximetry and noninvasive blood pressure. All patients underwent spinal anaesthesia with spontaneous ventilation through a face mask with oxygen. Spinal anaesthesia was induced with a single intrathecal dose of 15 to 20 mg levobupivacaine (Chirocaine 5 mg ml⁻¹). Levobupivacaine was injected through a 25 or 27-gauge needle into the L3/L4 or L4/L5 interspaces. Prophylactic ephedrine or fluid loading was not given.

Thoracic impedance cardiography monitoring

After cleaning the skin with alcohol, two gel pad sensors were carefully placed on each side of the thorax along the midaxillary line, and two sensors were placed on each side of the neck just above the clavicle. An ear clip was placed on the ear lobe. Bi impedance values were recorded continuously (beat-by-beat) on the ICG monitor (NICCOMO, Imedex, France). An ICG quality indicator, corresponding to the percentage of evaluable heart beats, was determined. Only patients with ICG signal quality higher than 50% were included in the study. Heart rate (HR) was obtained continuously from the three-lead electrocardiogram. The reproducibility of SV measurements was tested before the study; the intraobserver and interobserver variability for SV measurements was 1.8% [95% confidence interval (95% CI) 0.9 to 6.6] and 2.1% (95% CI 0.7 to 6), respectively. All values were analysed offline using dedicated Niccomo software. All values represented the mean of 20 consecutive beat measurements.

Study protocol

Only the first fluid challenge infused during surgery was used for the study. The study was composed of four steps. A first set of measurements [HR, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), SV, CO] was recorded at baseline (T1). A first fluid administration of 100 ml of Ringer’s lactate was infused over 1 min. A second set of measurements was then recorded immediately (T2). A third set of measurements was recorded 5 min after the second set and was called baseline 2 (T3). Volume expansion consisted of the infusion of 500 ml of Ringer’s lactate over 10 min. A final set of measurements was recorded 1 min after the end of volume expansion (T4).

Statistical analysis

The distribution of the variables was assessed using the D’Agostino–Pearson test. Data were expressed as mean (SD) or number (%), as appropriate. SV measured before and after volume expansion was used to define responders and nonresponders. A positive response was defined as an increase greater than 15% in SV in response to volume expansion (between T3 and T4).12,13 A Student’s paired t-test was used for within-group comparisons (between T1 and T2, T3 and T4). Differences between responders and nonresponders were compared by Student’s t-test. The Pearson method was used to test linear correlations. A receiver-operating characteristic curve (ROC) was generated for ΔSV₁₀₀ and baseline SV. The predictive value of ΔSV₁₀₀ was evaluated by using a grey zone approach. Correlations between baseline cardiovascular variables (HR, SAP, MAP, DAP, SV, ΔSV₁₀₀) and responsiveness were assessed using a univariate logistic model. Variables with a P value less than 0.10 were included in a multivariate logistic model with a backward selection procedure. Differences with a P value less than
Fluid responsiveness during spinal anaesthesia

Baseline SV had a poor predictive value for fluid responsiveness, with an AUC of 0.69 (95% CI 0.57 to 0.79, \( P = 0.002 \)). The cut-off was 65 ml with a grey zone ranging between 50 and 78 ml. For this cut-off, the sensitivity was 36% (95% CI 35 to 74) and the specificity was 80% (95% CI 66 to 91). The AUC of \( \Delta SV_{100} \) was a better predictor of fluid responsiveness than the AUC of baseline SV \( (P < 0.05) \).

On multivariate logistic regression, \( \Delta SV_{100} \) was the only factor associated with fluid responsiveness [odds ratio (OR) 1.4; 95% CI 1.19 to 1.637, \( P = 0.001 \)].

**Correlation between changes of stroke volume and arterial pressure**

In the overall population, \( \Delta SV_{100} \) correlated poorly solubylate with a subsequent increase in SAP in response to volume expansion: \( r = 0.25 \) (95% CI 0.02 to 0.45, \( P = 0.037 \)). This correlation was higher in patients with SAP less than 100 mmHg (arterial hypotension): \( r = 0.57 \) (95% CI 0.13 to 0.79, \( P = 0.014 \)).

**Discussion**

This is the first study to evaluate the predictive value of a mini-fluid challenge in spontaneously breathing patients under spinal anaesthesia. A \( \Delta SV_{100} \) greater than 7% measured by ICG accurately predicted subsequent fluid responsiveness with a grey zone ranging between 3 and 8% that contained up to 14% of patients. Moreover, \( \Delta SV_{100} \) was associated with a subsequent increase of SAP in patients with a SAP less than 100 mmHg.

In the operating theatre, fluid administration is frequently used to treat hypovolaemia, increase SV and consequently CO. The Frank–Starling law of the heart describes the relationship in which SV increases in response to an increase in preload.\(^8,9\) In spontaneously breathing patients when mechanical ventilation cannot be controlled, preload dependency can be tested by a fixed fluid challenge.\(^8,9\) If SV increases in response to limited fluid loading, it should also increase in response to volume expansion.\(^8,9\) We confirmed these results in spontaneously breathing patients under spinal anaesthesia. A greater than 7% increase in SV\(_{100} \) had a good predictive value for a subsequent increase in SV in response to fluid loading. According to the Frank–Starling law, the correlation between \( \Delta SV_{100} \) and \( \Delta SV_{500} \) indicates that a more marked increase of \( \Delta SV_{100} \) would be associated with a more marked increase of \( \Delta SV_{500} \). The \( \Delta SV_{100} \) cut-off in our study was higher than that reported by Muller \textit{et al}.\(^9\) These differences could be due to the cardiac effects of the fluids used in our study and in the study by Muller \textit{et al}.\(^9\) We used a saline solution that has a lower effect on volume expansion than colloid solutions.\(^14\) Furthermore, the good intra-individual and inter-individual reproducibility of ICG justify maintenance of this cut-off value for \( \Delta SV_{100} \).\(^9,10\)

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### Results

Seventy-seven patients were included during the study period. Four of these patients were excluded: two because of drug administration and two because of recording failure, leaving 73 men and women undergoing hip or knee surgery, in whom the anaesthetist had decided to administer intravenous fluids to expand the circulating volume, for analysis. They had a mean age of 73 (10) years and 30 (41%) were men (Table 1).

**Haemodynamic and NICCOMO changes with volume expansion**

Twenty-seven (37%) of the 73 patients were defined as responders, as SV increased by more than 15% in response to volume expansion. At baseline, SV and CO were lower and HR was higher in responders than in nonresponders (Table 2). The mean increase in SV in response to mini-fluid challenge was 6% (95% CI 0.5 to 12). It differed between patients who were fluid responsive and those in whom SV did not increase in response to volume expansion [12% (95% CI 10 to 16) vs. 1.3% (95% CI –2 to 6), \( P < 0.001 \)]. Volume expansion increased SAP, SV and CO only in responders (Table 2). A significant correlation was demonstrated between \( \Delta SV_{100} \) and \( \Delta SV_{500} \) \( (r = 0.72; 95\% \text{ CI } 0.59 \text{ to } 0.82, P < 0.001) \) (Fig. 1).

**Predictive value of \( \Delta SV_{100} \) and baseline stroke volume**

\( \Delta SV_{100} \) demonstrated an excellent predictive value for fluid responsiveness, with an AUC of 0.93 (95% CI 0.84 to 0.97, \( P < 0.001 \)). The cut-off was 7% with a grey zone ranging between 3 and 8%. For this cut-off, the sensitivity was 89% (95% CI 71 to 98), the specificity was 89% (95% CI 76 to 96), the positive likelihood ratio was 8.18 (95% CI 3.5 to 18.9), the negative likelihood ratio was 0.12 (95% CI 0.01 to 0.4), the positive predictive value was 83% (95% CI 64 to 94) and the negative predictive value was 93% (95% CI 81 to 99). Ten patients (14%) were situated in the grey zone.

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**Table 1** Patients’ characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>( n ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73 (10)</td>
</tr>
<tr>
<td>Sex, F/M (n)</td>
<td>43/30</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165 (14)</td>
</tr>
<tr>
<td>ASA, n (%)</td>
<td>8 (13)</td>
</tr>
<tr>
<td>1</td>
<td>3 (4)</td>
</tr>
<tr>
<td>2</td>
<td>30 (41)</td>
</tr>
<tr>
<td>3</td>
<td>35 (48)</td>
</tr>
<tr>
<td>4</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Type of surgery, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hip replacement</td>
<td>44 (60)</td>
</tr>
<tr>
<td>Knee replacement</td>
<td>29 (40)</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD) or number (\%). ASA, American Society of Anesthesiologists.
Bedside evaluation of haemodynamic changes during spinal anaesthesia remains an everyday challenge. Hypovolaemia and decreased CO during spinal anaesthesia may be due to various mechanisms. Spinal anaesthesia induces sympathetic block that decreases arterial resistance and increases venous capacitance resulting in decreased CO and arterial pressure, resulting in relative hypovolaemia. These effects are difficult to predict and may depend on several factors: the dose and rostral extension of the intrathecal anaesthetic, baseline vascular tone, the patient’s age and other factors. In addition to these haemodynamic changes, patient position, anaesthetic drugs and blood loss during surgery can further alter blood pressure, blood volume and CO. In view of the above, haemodynamic evaluation based exclusively on HR and blood pressure measurement may not be sufficient to identify the mechanism involved in the haemodynamic changes observed during spinal anaesthesia. Studies evaluating the effect of fluid loading on prevention of arterial hypotension provide a good illustration of this problem.

Assessing preload dependency by a limited fluid challenge may help physicians in the event of arterial hypotension during surgery. Arterial hypotension due to hypovolaemia should be treated by fluid expansion. In our study, the correlation between ∆SV_{100} and a subsequent increase in blood pressure may corroborate the link between arterial hypotension and decreased CO due to low preload. Moreover, a better correlation between these two variables was observed in hypotensive patients. A marked increase in ∆SV_{100} may be associated with a subsequent increase in blood pressure. Evaluation of haemodynamic changes during spinal anaesthesia by monitoring CO, preload and postload by ICG may therefore help the physician in the everyday management of surgery with spinal anaesthesia.

This study has a number of limitations. Failure to determine the level of spinal anaesthesia, which may reflect the level of sympathetic block, must be considered to be a flaw, as the level of sympathetic block can cause different haemodynamic effects. The accuracy of thoracic ICG to evaluate CO and CO trends may be subject to criticism. After several years of improvement, ICG is now an operator-independent device and appears to be a reliable method for noninvasive monitoring of CO and CO trends. We used an improved version of ICG that incorporates new hardware and software designs for measurement of ICG signals. The Niccomo device used for our study incorporates a technology described as arterial compliance modulation technology that is able to derive an arterial pulse curve from the ear lobe using infrared light and provide additional useful information, allowing much more accurate detection of aortic valve closing, further increasing the accuracy of SV.

**Table 2 Cardiovascular variables in responders and nonresponders expressed as mean (SD)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline 1</th>
<th>100 ml</th>
<th>Baseline 2</th>
<th>Volume expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR (beats min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>65 (15)*</td>
<td>63 (15)</td>
<td>62 (15)</td>
<td>59 (12)**</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>60 (13)</td>
<td>60 (12)</td>
<td>62 (12)</td>
<td>59 (13)</td>
</tr>
<tr>
<td><strong>SAP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>116 (28)</td>
<td>118 (29)</td>
<td>115 (29)</td>
<td>124 (21)**</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>119 (25)</td>
<td>118 (24)</td>
<td>117 (22)</td>
<td>122 (24)</td>
</tr>
<tr>
<td><strong>DAP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>61 (16)</td>
<td>63 (17)</td>
<td>60 (17)</td>
<td>64 (14)</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>64 (14)</td>
<td>64 (13)</td>
<td>62 (13)</td>
<td>64 (13)</td>
</tr>
<tr>
<td><strong>SV (ml)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>66 (21)*</td>
<td>75 (23)**</td>
<td>70 (23)*</td>
<td>91 (29)**</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>82 (24)</td>
<td>82 (28)</td>
<td>82 (25)</td>
<td>83 (27)</td>
</tr>
<tr>
<td><strong>CO (l min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>4.1 (1.2)*</td>
<td>4.6 (1.4)**</td>
<td>4.3 (1.3)*</td>
<td>5.3 (1.5)**</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>4.9 (1.5)</td>
<td>4.9 (1.6)</td>
<td>5.1 (1.5)</td>
<td>4.8 (1.6)</td>
</tr>
</tbody>
</table>

CO, cardiac output; DAP, diastolic arterial pressure; HR, heart rate; SAP, systolic arterial pressure; SV, stroke volume. *P < 0.05 between responders and nonresponders. **P < 0.05 between baseline 1 and 100 ml. ***P < 0.05 between baseline 2 and volume expansion.
determination. ICG may represent a more appropriate device to evaluate haemodynamic variables in patients under spinal anaesthesia than thermodilution or oesophageal Doppler, which are more invasive procedures. This study was not designed to evaluate the ability of $\Delta SV_{100}$ to predict correction of arterial hypotension. Further prospective and interventional studies are needed to confirm the ability of $\Delta SV_{100}$ to predict an increase of arterial pressure in a specific population of hypotensive patients. In conclusion, we found that a mini-fluid challenge with 100 ml of saline solution in spontaneously breathing patients under spinal anaesthesia accurately predicted fluid responsiveness, with a grey zone ranging between 3 and 8%. A greater than 7% increase in $SV_{100}$ was associated with a subsequent increase of SV in response to volume expansion. In addition, in hypotensive patients, $SV_{100}$ was associated with an increase in arterial pressure. $SV_{100}$ may be useful to physicians to guide fluid or vasopressor therapy. Further studies are needed to confirm these results.

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Presentation: none

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