

CARDIOVASCULAR

# Ability of stroke volume variation measured by oesophageal Doppler monitoring to predict fluid responsiveness during surgery

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## Editor's key points

- Changes in cardiovascular variables during respiration can be used to predict the response of the circulation to infused fluids.
- Most previous studies using oesophageal Doppler have used flow time to guide fluid therapy.
- In this study, changes in stroke volume with respiration predicted fluid responsiveness accurately during surgery.
- In contrast, changes in peak velocity and flow time assessed using oesophageal Doppler were not predictive.

**Background.** The objective of this study was to test whether non-invasive assessment of respiratory stroke volume variation ( $\Delta\text{respSV}$ ) by oesophageal Doppler monitoring (ODM) can predict fluid responsiveness during surgery in a mixed population. The predictive value of  $\Delta\text{respSV}$  was evaluated using a grey zone approach.

**Methods.** Ninety patients monitored using ODM who required i.v. fluids to expand their circulating volume during surgery under general anaesthesia were studied. Patients with a preoperative arrhythmia, right ventricular failure, frequent ectopic beats, or breathing spontaneously were excluded. Haemodynamic variables and oesophageal Doppler indices [peak velocity (PV), stroke volume (SV), corrected flow time (FTc), cardiac output (CO),  $\Delta\text{respSV}$ , and respiratory variation of PV ( $\Delta\text{respPV}$ )] were measured before and after fluid expansion. Responders were defined by a  $>15\%$  increase in SV after infusion of 500 ml crystalloid solution.

**Results.** SV was increased by  $\geq 15\%$  after 500 ml crystalloid infusion in 53 (59%) of the 90 patients.  $\Delta\text{respSV}$  predicted fluid responsiveness with an area under the receiver-operating characteristic (AUC) curve of 0.91 [95% confidence interval (95% CI): 0.85–0.97,  $P < 0.0001$ ]. The optimal  $\Delta\text{respSV}$  cut-off was 14.4% (95% CI: 14.3–14.5%). The grey zone approach identified 12 patients (14%) with a range of  $\Delta\text{respSV}$  values between 14% and 15%. FTc was not predictive of fluid responsiveness (AUC 0.49, 95% CI: 0.37–0.62,  $P = 0.84$ ).

**Conclusions.**  $\Delta\text{respSV}$  predicted fluid responsiveness accurately during surgery over a  $\Delta\text{respSV}$  range between 14% and 15%. In contrast, FTc did not predict fluid responsiveness.

**Keywords:** anaesthesia; cardiac output measurement; Doppler ultrasonography; intraoperative monitoring; stroke volume

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Oesophageal Doppler monitoring (ODM) allows non-invasive continuous monitoring of cardiac output (CO) during surgery.<sup>1–3</sup> Several studies have demonstrated that ODM-guided intraoperative fluid optimization can have a significant impact on outcome in high-risk surgical patients.<sup>4–7</sup> Most of these studies have incorporated corrected flow time (FTc) as a target for fluid optimization. However, FTc is a complex variable affected by left ventricular preload, systemic vascular resistance, and the inotropic state of the heart.<sup>8–10</sup> Many studies over recent years have emphasized the superiority of respiratory variation of pulse pressure ( $\Delta\text{respPP}$ ) and aortic blood flow ( $\Delta\text{respABF}$ ) to predict fluid

responsiveness in a wide range of clinical situations.<sup>11–15</sup>  $\Delta\text{respABF}$  can be evaluated by echocardiography or ODM.<sup>16</sup> Only one ODM study conducted in critically ill patients with acute circulatory failure has demonstrated the accuracy of  $\Delta\text{respABF}$  to predict fluid responsiveness.<sup>17</sup> No data are therefore available concerning ODM respiratory variation indices during surgical anaesthesia.

The primary objective of this study was to demonstrate that respiratory variation of SV ( $\Delta\text{respSV}$ ) measured by ODM can predict fluid responsiveness more accurately than FTc.  $\Delta\text{respSV}$  was evaluated by using a grey zone approach and a risk–benefit assessment model of fluid administration.<sup>15 18</sup>

## Methods

This study was approved by the Institutional Review Board (IRB) for human subjects. Informed consent was waived, as the IRB considered the protocol to be part of routine clinical practice.

We conducted a prospective observational study over a 5 month period (June–October 2011) in Amiens University Hospital. Inclusion criteria were: patients aged >18 yr and monitored by oesophageal Doppler (ODM), in whom the anaesthetist decided to infuse i.v. fluids to expand circulating volume. Exclusion criteria were: patients with a preoperative arrhythmia, right ventricular failure, frequent ectopic beats, patients breathing spontaneously during surgery, and contraindications to ODM probe insertion. Indications for ODM were visceral and gynaecological cancer surgery ( $n=49$ ), peritonitis ( $n=12$ ), radical prostatectomy ( $n=6$ ), nephrectomy ( $n=9$ ), renal transplantation ( $n=2$ ), multiple trauma ( $n=4$ ), haemostatic surgery ( $n=3$ ), and vascular surgery ( $n=5$ ).

Routine monitoring consisted of a three-lead electrocardiogram, pulse oximetry, and non-invasive arterial pressure. All patients underwent balanced general anaesthesia with tracheal intubation and mechanical ventilation in volume-controlled mode. General anaesthesia was induced with propofol or etomidate and either remifentanyl or sufentanyl according to the anaesthetist's preference, and maintained with either propofol or an inhaled hypnotic (desflurane or sevoflurane) and the same opioid used at induction. All patients received neuromuscular block with i.v. cisatracurium ( $0.15 \text{ mg kg}^{-1}$ ) or rocuronium ( $0.6 \text{ mg kg}^{-1}$ ). Tidal volume was set to  $7\text{--}9 \text{ ml kg}^{-1}$  of ideal body weight with a ventilatory frequency adjusted to maintain end-tidal  $\text{CO}_2$  at  $3.99\text{--}4.7 \text{ kPa}$ ; PEEP of  $0.74\text{--}1.24 \text{ kPa}$  was applied.

The ventilator settings (tidal volume, plateau pressure, and end-expiratory pressure) were recorded at the baseline.

### Oesophageal Doppler monitoring

The position of the oesophageal Doppler probe (CardioQ™, Deltex Medical, Gamida, France) was adjusted to obtain the best signal for descending aorta blood velocity.<sup>9</sup> To avoid artifacts concerning precise distinction of the beginning and end of aortic flow with each ventricular beat that may be distorted by wall thump and run-off, respectively, laminar flow was ensured with a narrow frequency range (blunt velocity profile). The reproducibility of SV measurement was tested before the study; the intraobserver and interobserver variability for SV measurements was  $0.3 (0.1)\%$  and  $1.1 (3)\%$ , respectively. Stroke volume (SV), FTc, and peak velocity (PV) were recorded continuously by the ODM software (beat by beat) from aortic blood flow velocity, and their mean values were calculated over 10 s. Respiratory variations ( $\Delta\text{resp}$ ) of ODM values were calculated as described by Monet and colleagues, regardless of the respiratory cycle.<sup>17</sup> The respiratory variation of SV ( $\Delta\text{respSV}$ ) was calculated as  $\Delta\text{respSV} = [(SV_{\text{max}} - SV_{\text{min}}) / (SV_{\text{max}} + SV_{\text{min}}) / 2] \times 100$ , where  $SV_{\text{max}}$  and  $SV_{\text{min}}$  are the maximal and minimal SV values over one respiratory cycle, respectively. Respiratory variation of PV

( $\Delta\text{respPV}$ ) was calculated using a similar formula. All values represented the mean of three measurements. All measurements were analysed off-line using a video sequence of the monitor.

### Study protocol

Only the first fluid challenge infused during surgery was recorded for the study. All patients were studied after 5 min of stable haemodynamic variables with constant ventilator settings and drugs. A first set of measurements [heart rate (HR), systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP), SV, FTc, PV,  $\Delta\text{respSV}$ , and  $\Delta\text{respPV}$ ] was recorded at the baseline. Volume expansion (VE) comprised the infusion of 500 ml crystalloid solution (Ringer or Ringer lactate) over 10 min. A second set of measurements (HR, SAP, MAP, DAP, SV, FTc, PV,  $\Delta\text{respSV}$ , and  $\Delta\text{respPV}$ ) was recorded immediately after, at the end of VE.

### Data analysis

Data are expressed as mean (sd), or proportion (percentage), as appropriate. SV measured before and after VE was used to define responders and non-responders. A positive response was defined as a  $\geq 15\%$  increase in SV. The Pearson rank method was used to test linear correlations between variables in responders and non-responders. The associations between cardiovascular variables (HR, SAP, MAP, DAP, SV, FTc, PV, CO,  $\Delta\text{respSV}$ , and  $\Delta\text{respPV}$ ) and fluid responsiveness were assessed using a univariate logistic model. Variables with a  $P$ -value of  $< 0.10$  were then included in a multivariate logistic model with a backward selection procedure. A receiver-operating characteristic (ROC) curve was generated for  $\Delta\text{respSV}$ ,  $\Delta\text{respPV}$ , and FTc. The ROC curves were obtained by averaging 1000 bootstrapped samples (sampling with replacement) from the original study population. The areas under the ROC curve (AUC) for each variable were compared using the test described by DeLong and colleagues. For clinical practice, it is preferable to avoid a single cut-off that dichotomizes the population (i.e. black or white distinction).<sup>18</sup> The predictive value of  $\Delta\text{respSV}$  was evaluated by using a grey zone approach. The grey zone approach indicated two cut-offs between which the diagnosis of fluid responsiveness remains uncertain; the physician must confirm the diagnosis by additional information.<sup>18</sup> The grey zone was calculated using two approaches previously described by Cannesson and colleagues.<sup>15</sup> The optimal cut-off was defined as the cut-point that maximized Youden's index ( $J = \text{sensitivity} + \text{specificity} - 1 = \text{sensitivity} - \text{false-positive rate}$ ). The optimal cut-point was then determined for each bootstrapped sample, resulting in a set of 1000 values. The median value of the cut-points across 1000 bootstrap replications and its 95% confidence interval (CI) were then estimated. The grey zone was defined as the 95% CI of Youden's index. A second approach defined three classes of response: negative, inconclusive, and positive. Inconclusive responses were cut-off values with a sensitivity of  $< 90\%$  and a specificity of  $< 90\%$  (diagnostic

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