Chapter 8

A Comparison of Stroke Volume Variation measured by the LiDCO-plus and FloTrac-Vigileo system

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Summary

Background The aim of the study was to compare the accuracy of stroke volume variation (SVV) measured by the LiDCOplus system (SVVli) (LiDCO Ltd., Cambridge, UK) (SVVli) and by the FloTrac-Vigileo system (SVVed) (Edwards Lifesciences, Irvine, CA, USA).

Methods In fifteen postoperative cardiac surgical patients SVVli and SVVed was measured after; a 50% increase in tidal volume (VT), an increase of PEEP with 10 cm H₂O, passive legs raising (PLR), a head-up tilt procedure (HUT), and after fluid loading (FL). Between these applied study interventions baseline measurements were performed.

Results 136 data pairs were obtained. SVVli ranged from 1.4 to 26.8%, average 8.7 ± 4.6%, SVVed from 2.0 to 26.0%, average 10.2 ± 4.7%. The bias is significantly different from zero, 1.5 ± 2.5%, p < 0.001, (95% confidence interval 1.1 to 1.9). The upper and lower limits of agreement are 6.4 and -3.5%. The coefficient of variation for the differences between SVVli and SVVed is 26%. This result in a relative large range for the limits of agreement, expressed in percentages, is 52%. Analysis of repeated measurements shows a coefficient of variation of 21 and 22% for SVVli and SVVed, respectively.

Conclusion The LiDCOplus and FloTrac-Vigileo system are not interchangeable. Furthermore, the determination of SVVli and SVVed are too ambiguous, as can be concluded from the high values of the coefficient of variation for repeated measurements. These findings underlines Pinsky’s warning to be careful in the clinical use of SVV by pulse contour techniques.

Introduction

With the introduction of continuous cardiac output measurement by arterial pulse contour analysis, real time measurement of stroke volume (SV) stroke volume variation (SVV) and pulse pressure variation (PPV) during mechanical ventilation was introduced in clinical practice. Most studies showed, SVV and PPV to be a good indicators of fluid responsiveness [1-3]. However, in two separate publications [4, 5] Pinsky advised caution in the clinical use of SVV based on the fact that beat-to-beat SV by the pulse contour technique has not been validated to monitor rapid changes in SV, as occur within a single breath. This is further complicated by the use of different algorithms to calculate SV and SVV by different monitoring systems. In this light, a clinical validation study on SVV seems important.

Aim of our study was to compare SVV estimates by the LiDCOplus system (SVVli) (LiDCO Ltd. Cambridge, UK) with SVV estimates by the FloTrac-Vigileo system (SVVed) (Edwards Lifesciences, Irvine, CA, USA) in post operative cardiac surgery patients. To induce changes in SVV we applied 6 different conditions to these study subjects; measurements in supine or baseline position, after an increase of tidal volume (VT), an increase in level of PEEP, after head up tilt procedure (HUT), during passive leg raising (PLR) and after fluid loading (FL). Effects of these interventions on SVVli and SVVed, were compared with simultaneously measured PPV and bolus thermodilution cardiac output (COtd).

Methods

After approval of the study protocol by the University Medical Ethics committee, fifteen patients were studied after coronary arterial bypass grafting with or without
mitral valve repair. The study was conducted according to the principles of the Helsinki declaration and written informed consent was obtained from all patients the day before surgery. All patients had symptomatic coronary artery disease without previous myocardial infarction and were on β-adrenergic blocking medication. Patients with a history of abnormal ventricular function, aortic aneurysm, extensive peripheral arterial occlusive disease, or postoperative valvular insufficiencies were not considered for this study. Patients with postoperative severe arrhythmia or the necessity for artificial pacing or heart assist devices were also excluded.

All patients were included in the study during their initial post-operative period in the ICU. Anesthesia during surgery and ICU-stay was maintained with propofol (2.5 mg·kg⁻¹·h⁻¹), sufentanil (0.06-0.20 mg·kg⁻¹·h⁻¹) and vasoactive medication according to institutional standards. The lungs were mechanically ventilated (EVITA 4, Dräger AG, Lübeck, Germany) in a volume-control mode with settings aimed to achieve normocapnia with a tidal volume of 8-12 ml·kg⁻¹ and a respiratory frequency of 12-14 breaths·min⁻¹. Fraction of inspired oxygen was 0.4 and PEEP 5 cmH₂O. During the observation period sedation and vasoactive medication, when used, were unchanged.

Measurements
Measurements started in the postoperative period. Prior to ICU admission, all patients were catheterized with a 20G radial artery catheter (RA 04220, Arrow Int., Reading, PA, USA) to monitor arterial pressure (Pa) and a pulmonary artery catheter (139HF75P, Edwards Lifesciences, Irvine, CA, USA) introduced via the right jugular vein to monitor central venous pressure (CVP), pulmonary artery pressure (PAP) and to estimate cardiac output (CO) by the intermittent thermodilution method (COtd).

The radial artery pressure (Pa), derived via the radial artery catheter was measured with a FloTrac pressure transducer (Edwards Lifesciences). Of the bifurcated cable, one limb was connected to the Vigileo system (Edwards Lifesciences, software version v1.07) to measure pulse contour cardiac output and SVVed and the other limb was connected to a bedside monitor pressure module Hewlett Packard model M1006A, (Hewlett Packard Company, Palo Alto, CO, USA) of which the output signal was used as input signal for the LiDCOplus pulse contour system to deliver cardiac output, pulse pressure variation (PPVli) and SVVli. Detailed information about both pulse contour techniques can be found in recent literature [6-9]. Pa, PAP and CVP, were recorded online on computer disk for documentation and offline calculations. Pa, PAP and CVP transducers were referenced to the intersection of the anterior axillar line and 5th intercostal space. After changes in position of the patient the transducers were re-referenced. Airway pressure (Paw) was measured at the proximal end of the endotracheal tube with an air-filled catheter connected to a pressure transducer. Paw was balanced at zero level against ambient air. We calibrated the LiDCOplus system with 3 thermodilution cardiac output measurements at start of the observation period. The FloTrac-Vigileo system used its internal auto-calibration. From the beat-to-beat cardiac output values with the LiDCOplus and FloTrac-Vigileo system, stroke volume (SVli and SVVed), stroke volume variation (SVVli and SVVed) and pulse pressure variation (PPVli) were determined. SVV and PPV were calculated over 20 second periods of Pa data.

Study protocol
To induce changes in CO, SVV and PPV, and evaluating clinical relevance, measurements were performed during baseline in supine position, after increased tidal volume (+50%) (VT), during increased PEEP (+10 cm H₂O), during passive leg
raising (PLR) of both legs with 30 degrees, during 30 degrees head up tilting (HUT) and in supine position after fluid loading (FL) with 500 ml Hydroxyethyl Starch (HES 130/0.4) in 15 minutes. Between study interventions, baseline conditions were re-established. Measurements of MAP, HR, COtd, SVVli, SVVed and PPV, from the Pa signal, were collected during each study period, 2 minutes after the change in study intervention, and between study interventions at baseline. The study protocol lasted about 90 minutes where after sedation was stopped and weaning procedures were started. During the protocol we encountered no adverse events. All patients were discharged from the intensive care unit on the first postoperative day.

Statistical analysis
After confirming a normal distribution of data with the Kolmogorov – Smirnov test, differences between SVVed and SVVli during study interventions and baseline were analyzed using a paired t-test. Values of SVV and changes in SVV based on interventions and devices are analyzed with factorial ANOVA. Calculations of bias and precision and limits of agreement between SVVed and SVVli are performed using Bland-Altman analysis [10]. In which bias is the difference between SVVli and SVVed and precision the standard deviation (SD) of this difference. The upper and lower limits of agreement are calculated as the bias ± 2·SD. The coefficient of variation (CV) is calculated as 100%·SD/mean (SVVli and SVVed). The percentage limits of agreement are calculated as 2·CV. A p-value < 0.05 was considered statistically significant. Unless otherwise stated, data are presented as mean (SD).

Results
In fifteen post operative cardiac surgical patients, gender; male/female 12/3, mean age 66 (range 55 to 82) years, mean BSA 1.98 ± 0.20 m², were included. Only 8 patients received fluid loading. A total of 136 paired data sets were obtained. The data was normally distributed. COtd ranged from 2.6 to 7.7 with an average of 5.0 ± 1.1 L.min⁻¹. HR ranged from 54 to 92, average was 75 ± 8 min⁻¹. SVVli ranged from 1.4 and 26.8%, average 8.7 ± 4.6%, SVVed from 2.0 to 26.0%, average 10.2 ± 4.7% and PPVli from 1.9 to 25.3, average 8.8 ± 4.7%.

Agreement of SVVli and SVVed
Bland-Altman statistics are indicated in the figure by bias and limits of agreement (LOA). The bias is significantly different from zero, 1.5 ± 2.5%, p < 0.001, (95% confidence interval 1.1 to 1.9). The upper and lower limits of agreement are 6.4 and -3.5%.Coefficient of vanriance for the differences between SVVli and SVVed is 26%. This result in a large range for (error-percentage) limits of agreement of 52% (2·CV). The error diagram for difference between SVVli and SVVed is shown in figure 8.1.
Interventions
COtd, HR, PPVli, SVVli and SVVed as well as the differences between SVVli and SVVed for the different experimental conditions are presented in table 8.1. With Factorial ANOVA the main effects on SVV values related to the measurement techniques was \( (F = 14.49, p = 0.02) \), and related to the interventions was \( (F = 8.29, p < 0.001) \). Differences between SVV measurement methods were consistent across all interventions \( (F = 1.54, p = 0.142) \). One-way ANOVA statistics showed no significant difference between the five baseline measurements for COtd \( (F = 0.203, p = 0.936) \), HR \( (F = 0.094, p = 0.984) \), PPVli \( (F = 0.184, p = 0.946) \), SVVli \( (F = 0.254, p = 0.906) \) and SVVed \( (F = 0.390, p = 0.815) \) expressing that there were no significant effects over time. On average VT showed no change in COtd and an increase in PPVli, SVVli and SVVed; PEEP and HUT decreased COtd and increased PPVli, SVVli and SVVed whereas PLR and FL increase COtd and decreased PPVli, SVVli and SVVed. Heart rate did not change during study interventions. When analyzing our observations as repeated measures, analysis showed the following coefficient of variation, for PPVli = 23%, SVVli = 21% and SVVed = 22%.

Discussion
We found SVVli and SVVed to differ significantly. With percentage limits of agreement of 52% we conclude that the LiDCOplus and FloTrac-Vigileo devices are not interchangeable. Furthermore, the determination of SVVli and SVVed appeared to be ambiguously as can be concluded from the high value of coefficient of variation.
(21 and 22%) for repeated measurements. These findings underlines Pinsky’s warning to be careful in the clinical use of SVV by pulse contour techniques [5].

The significant mean difference between SVV measured by the LiDCO and FloTrac-Vigileo device is most probably not caused by the calculation of SVV because both systems use a similar computation i.e. $SVV = 100 \cdot \frac{SV_{\text{max}} - SV_{\text{min}}}{SV_{\text{mean}}}$. Therefore, most likely, it must be explained by the difference in the calculation of $SV_{\text{min}}, SV_{\text{max}}$ and $SV_{\text{mean}}$ by the two systems. The main difference in computation of SV is based on the correction for individual arterial compliance. The LiDCO system uses a pressure dependent correction for compliance based on Remington’s equations [11] whereas the FloTrac-Vigileo uses Langewouter’s equations [12]. There is a large similarity between the computations of SV, figure 8.2. With both systems these equations lead to a diminished SV at higher pressure levels compared to lower pressure levels with the same arterial pressure curve. However, this correction for compliance may differ between the two systems. A difference in calibration between the two systems has no influence on SVV, indeed, assuming a calibration constant $k$ leads to $SVV = 100 \cdot \frac{(k \cdot SV_{\text{max}} - k \cdot SV_{\text{min}})}{k \cdot SV_{\text{mean}}}$. With $k$ in the nominator and denominator the calibration factor is ruled out in the determination of SVV.

In a recent paper Hofer et al. [13] compared the FloTrac-Vigileo and the PiCCOplus system for assessment of SVV to predict fluid responsiveness. The authors concluded for similar performance of the two systems. Although, the SVV threshold level of predicting fluid responsiveness, by the PiCCO system (12.1%) and FloTrac-Vigileo system (9.6%), differ. Not confirmed by the small number of patients in our study, but based on similarity of their study with ours, and our results, we predict different threshold levels for the LiDCO and FloTrac-Vigileo system, as well.

Besides the difference in mean SVV we observed a wide range of the percentage limits of agreement (52%) between the two systems. This wide range for the percentage limits of agreement can be observed also in two recent papers [13, 14].

![Figure 8.2](image)

**Figure 8.2** Similarity of calculation of cardiac output by the LiDCO system and by Edwards FloTrac-Vigileo system. Arterial volume ($V$) changes derived after transformation of the radial artery pressure ($P_{\text{rad}}$) with Remington’s equations. Edward’s corrects cardiac output after SD calculation with Langewouter’s equation.
Table 8.1 Differences in cardiac output, heart rate (HR), pulse pressure variation (PPV) and stroke volume variation (SVV) at interventions.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cardiac Output</th>
<th>Heart rate</th>
<th>PPV</th>
<th>SVVli</th>
<th>SVVed</th>
<th>Difference SVVed-SVVli</th>
<th>Coefficient of variation</th>
<th>SVV difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L.min⁻¹ Mean ± SD</td>
<td>Beats.min⁻¹ Mean ± SD</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
<td>P-value*</td>
</tr>
<tr>
<td>Baseline 1</td>
<td>4.9 ± 1.0</td>
<td>76 ± 7</td>
<td>7.9 ± 4.3</td>
<td>7.8 ± 3.4</td>
<td>9.4 ± 3.9</td>
<td>1.6 ± 1.7</td>
<td>20</td>
<td>0.003</td>
</tr>
<tr>
<td>VT</td>
<td>4.9 ± 1.0</td>
<td>78 ± 9</td>
<td>11.2 ± 5.6</td>
<td>10.6 ± 5.8</td>
<td>12.9 ± 6.5</td>
<td>2.3 ± 2.9</td>
<td>24</td>
<td>0.009</td>
</tr>
<tr>
<td>Baseline 2</td>
<td>5.1 ± 0.9</td>
<td>74 ± 8</td>
<td>7.5 ± 3.6</td>
<td>7.6 ± 3.0</td>
<td>8.5 ± 3.3</td>
<td>1.0 ± 2.4</td>
<td>30</td>
<td>0.134</td>
</tr>
<tr>
<td>PEEP</td>
<td>4.3 ± 1.1</td>
<td>75 ± 8</td>
<td>12.4 ± 5.8</td>
<td>12.4 ± 5.6</td>
<td>13.3 ± 5.0</td>
<td>0.9 ± 2.4</td>
<td>19</td>
<td>0.171</td>
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<tr>
<td>Baseline 3</td>
<td>5.2 ± 0.9</td>
<td>75 ± 7</td>
<td>7.7 ± 3.7</td>
<td>7.6 ± 2.9</td>
<td>8.9 ± 3.4</td>
<td>1.7 ± 1.9</td>
<td>24</td>
<td>0.010</td>
</tr>
<tr>
<td>PLR</td>
<td>5.4 ± 1.0</td>
<td>74 ± 8</td>
<td>6.5 ± 3.3</td>
<td>5.9 ± 2.8</td>
<td>8.7 ± 3.1</td>
<td>2.9 ± 3.2</td>
<td>44</td>
<td>0.004</td>
</tr>
<tr>
<td>Baseline 4</td>
<td>5.2 ± 1.0</td>
<td>75 ± 8</td>
<td>8.5 ± 3.9</td>
<td>8.3 ± 4.2</td>
<td>10.0 ± 4.1</td>
<td>1.7 ± 1.9</td>
<td>21</td>
<td>0.004</td>
</tr>
<tr>
<td>HUT</td>
<td>4.9 ± 1.0</td>
<td>75 ± 9</td>
<td>9.7 ± 5.0</td>
<td>10.8 ± 4.5</td>
<td>11.6 ± 8.3</td>
<td>0.8 ± 2.9</td>
<td>26</td>
<td>0.287</td>
</tr>
<tr>
<td>Baseline 5</td>
<td>4.9 ± 1.3</td>
<td>75 ± 11</td>
<td>8.6 ± 4.0</td>
<td>9.0 ± 6.1</td>
<td>10.1 ± 5.4</td>
<td>1.2 ± 1.9</td>
<td>20</td>
<td>0.009</td>
</tr>
<tr>
<td>FL</td>
<td>5.6 ± 1.2</td>
<td>74 ± 12</td>
<td>6.7 ± 4.0</td>
<td>5.9 ± 2.9</td>
<td>6.5 ± 3.3</td>
<td>0.7 ± 1.0</td>
<td>15</td>
<td>0.095</td>
</tr>
</tbody>
</table>

The interventions are: increase of tidal volume with 50% (VT); increase in PEEP with 10 cm H₂O (PEEP); passive leg raising (PLR); head-up tilt (HUT) and fluid loading (FL). Method of measurement: SVV LiDCO system (SVVli), SVV FloTrac-Vigileo system (SVVed). Statistic analysis paired T-test (*).
From the results of Hofer et al. [13] we calculated percentage limits of agreement of 40% during 30⁰ head up-position and 42% during 30⁰ head-down position. Also in the paper of de Castro et al. [14], comparing SVV measured by the PiCCOplus system with SVV measured by aortic Doppler echocardiography, a wide range for the percentage limits of agreement of approximately 40% can be observed. Given these margins of error, we concluded that none of these systems is interchangeable with one of the others. Furthermore, it seems that the calculation of SVV is prone to propagation of errors in the calculation of SVV [14]. This is supported by the high coefficient of variation for repeated measurements of SVVli of 21% and SVVed of 22% in our study. This fluctuation can also be seen on the display of both monitor systems by the frequent changes in SVV value. The reason for these fluctuations is still unclear. As the errors in the measurements of SVVli and SVVed are not completely independent we cannot estimate the coefficient of variation for the difference from the coefficient of variations of both systems. The coefficient of variation for the difference may vary between 1 and 43%. The coefficient of variation found for the difference of 26%, is in range with these numbers.

Nevertheless the above, the changes in SVV induced by our interventions are in concordance with what was expected (Table 8.1). During the increase in tidal volume we observe, in comparison to baseline, no change in cardiac output but an increase in SVV. A similar increase in SVV to the increase of VT was observed by Kim and Pinsky [15] in a well controlled animal study. During PEEP and head up position CO decreased and SVV increased and during passive leg raising and after fluid loading we observed an increase in CO and decrease in SVV with both systems. However, the difference between SVVli and SVVed fluctuates considerably.

Despite these shortcomings, SVV seems a variable of considerable interest. Several authors have shown that SVV can predict the effects of fluid loading on cardiac output, however with different thresholds ranging from 9.5 to 12.5% to separate responder and non responders [13, 16-18]. Although there is no reason to doubt about the general principle of SVV as predictor of fluid responsiveness, we conclude from our results that some precaution in the use of SVV in an individual patient is justified. Indeed, based on Bland-Altman analysis for repeated measurements for SVV with percentage limits of agreement, the value of SVV may differ up to approximately 40% between measurements. Taking in mind a stable condition with at a certain moment in time we measure a SVV of 10%, a moment later in time this value may be 14% and an at another moment 6%. With SVV = 14% one may conclude for fluid loading to improve cardiac output, whereas with 6% one may conclude for catecholamines.

Conclusions
SVVli and SVVed differ significantly. With a percentage limits of agreement of 52% the two methods do not agree and cannot be used interchangeably. Furthermore, the determination of SVVli and SVVed appeared to be ambiguously as can be concluded from the high value of coefficient of variation (21 and 22%) for repeated measurements. These findings limit clinical use in individual patients and limit the comparability of fluid loading responsiveness results between different studies.
References


