Non-invasive cerebral oxygenation reflects mixed venous oxygen saturation during the varying haemodynamic conditions in patients undergoing transapical transcatheter aortic valve implantation

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INTRODUCTION

Aortic valve stenosis remains the most common indication for heart valve surgery [1]. Aortic valve replacement with cardiopulmonary bypass is still the treatment of choice for symptomatic aortic stenosis but carries a significant risk of morbidity and mortality, particularly in patients with comorbidities [2]. Transapical transcatheter aortic valve implantation (TA-TAVI) is a less-invasive technique used to treat aortic stenosis in high-risk cardiac surgery patients [3]. Cerebral oximetry by near-infrared spectroscopy offers the possibility to non-invasively determine the cerebral oxygen balance. Recent data suggest that cerebral oxygenation might reflect not only regional but also the systemic oxygen balance [4]. Several groups have investigated the relationship between regional cerebral oxygen saturation (rScO2) and mixed venous oxygen saturation (SvO2) in adult cardiac patients [5–7] coming to conflicting results. Due to heterogeneity of design and patient populations in the published data, the reliability of the rScO2 as a surrogate parameter of global haemodynamic state is still unclear.

Recently, we reported, in this journal, on the excellent agreement between rScO2 and SvO2 in a cardiac surgery patient undergoing TA-TAVI who required temporary cardiopulmonary resuscitation [8].

The present prospective observational study was designed to further explore the relationship between rScO2 and SvO2 during varying haemodynamic conditions in patients undergoing TA-TAVI.

METHODS

All patients included in the analysis had given written informed consent in an observational study determining the impact of preoperative cerebral oxygenation on postoperative organ dysfunction (unpublished). Following approval of an amendment (amendment 5) to the primary request by the local ethical committee, n = 20 patients with severe symptomatic aortic stenosis scheduled for TA-TAVI were enrolled. All patients had undergone preoperative duplex sonography of supraaortic vessels and no patient with symptomatic carotid artery disease or internal carotid artery stenosis of 75% or more was included. Two patients had an incidence of ischaemic stroke within 24 months before cardiac surgery, without residue. Following oral premedication, sensors for the determination of rScO2 with an...
INVOS® 5100 monitor (Somanetics, Troy, MI, USA) were applied bihemispirally. Anaesthesia was induced with sufentanil and etomidate and maintained with sevoflurane and remifentanil with the goal of early postoperative extubation. Muscle relaxation was achieved with rocuronium bromide. All patients were ventilated in volume-controlled mode with a tidal volume of 6 ml/kg body weight and adjusted to achieve normocapnia. Depth of anaesthesia was guided by bispectral index (BIS) and anaesthetics were modified individually to achieve a BIS between 40 and 50. All patients were warmed by heating blankets to maintain a body temperature between 35.5 and 37.0°C.

After induction all patients were equipped with a pulmonary artery catheter (PAC) (CCombo; Edwards Lifesciences, Irvine, CA, USA) for semi-continuous determination of cardiac output and measurement of SvO2 connected to a Vigilance II® monitor (Edwards Lifesciences).

**Data collection**

Haemodynamic data as well as SvO2 and rScO2 were recorded continuously throughout the surgical procedure. Stored electronic data were processed after cessation of the study period. Comparative measurements of SvO2 and bilateral rScO2 were determined from the recorded data file at predefined time points during the surgical period. rScO2 levels of both hemispheres were averaged for analysis. The first data set (t1) was taken ~20 min after induction of anaesthesia and accurate placement of the PAC. The second set (t2) was taken at the beginning of the first period of rapid pacing for valvuloplasty. The third data pair (t3) was set at the end of the first period of rapid pacing. The fourth data pair (t4) was taken at the beginning of the second period of rapid pacing for aortic valve implantation during the phase of free aortic insufficiency. The fifth set (t5) was taken at the end of the second period of rapid pacing and the last (t6) at the end of surgical procedure. The duration of the each phase of rapid ventricular pacing did not exceed 10 s but has not been documented in particular.

**Statistical analysis**

Data entry and analysis were conducted using MedCalc 10 for Windows. The relationship between values was determined by Pearson’s correlation coefficient and Bland–Altman analysis for method comparison. A mean percentage error not exceeding 30% was defined to indicate clinically acceptable interchangeability of the methods [9]. After verification of normal distribution by Kolmogorov–Smirnov test relative values of rScO2 and SvO2 were compared with Student’s t-test. A \( P < 0.05 \) was considered statistically significant.

**RESULTS**

Twenty patients (11 females and 9 males) undergoing TA-TAVI were enrolled. Mean age, height and weight were 82 (range 73–91) years, 167 (153–180) cm and 68 (52–90) kg, respectively. Specific patient characteristics are given in Table 1.

Mean rScO2 levels at baseline (mean of both hemispheres) before induction of anaesthesia were 57.7% (range 42–76). Stable rScO2 and SvO2 signals could be obtained in all patients during the intraoperative course and no interhemispheric differences in rScO2 of >10% were observed. In all patients an aortic prosthesis Edwards-Sapien valve (Edwards Lifesciences) was successfully implanted.

**Analysis of all data pairs**

Correlation analysis of all collected data pairs showed a correlation coefficient of \( r = 0.76 \) (95% confidence interval 0.67–0.82) between rScO2 and SvO2 \( (P < 0.0001) \) (see Fig. 1). Bland–Altman analysis showed a mean percentage error not exceeding 15.7% (see Table 1).

**Table 1: Risk-related characteristics of patients, and size of implanted prosthesis**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Log. EuroSCORE (%)</th>
<th>EuroSCORE add. (%)</th>
<th>STS score (%)</th>
<th>LVEF (%)</th>
<th>Prosthesis size (mm)</th>
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</thead>
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<tr>
<td>1</td>
<td>23.30</td>
<td>11</td>
<td>14.30</td>
<td>75</td>
<td>26</td>
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<tr>
<td>2</td>
<td>54.86</td>
<td>11</td>
<td>18.70</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
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<td>24.00</td>
<td>45</td>
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<td>15</td>
<td>9.10</td>
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<td>26</td>
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<td>10</td>
<td>6.00</td>
<td>35</td>
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</tr>
<tr>
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<td>8.98</td>
<td>8</td>
<td>2.70</td>
<td>70</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>15.83</td>
<td>10</td>
<td>3.50</td>
<td>57</td>
<td>26</td>
</tr>
<tr>
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<td>36.24</td>
<td>13</td>
<td>3.90</td>
<td>61</td>
<td>26</td>
</tr>
<tr>
<td>9</td>
<td>45.78</td>
<td>14</td>
<td>15.50</td>
<td>61</td>
<td>26</td>
</tr>
<tr>
<td>10</td>
<td>9.84</td>
<td>8</td>
<td>21.00</td>
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<tr>
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</tr>
<tr>
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<td>12</td>
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<td>11</td>
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<td>53.74</td>
<td>15</td>
<td>4.00</td>
<td>40</td>
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</tbody>
</table>

analysis of the complete data set revealed acceptable agreement between the methods with a mean difference (bias) of 5.8% and limits of agreement (1.96 SD) of −6.8 to 18.3%, the percentage error was 17.5%.

### DISCUSSION

The present prospective observational study was designed to evaluate the agreement between rsCO2 and SvO2 during a procedure with rapidly changing haemodynamic states. With the exception of a recent case report from our group [8], no further data are available about the course of rsCO2 during TA-TAVI and about its relation to SvO2. The study revealed moderate-to-close correlations between rsCO2 and SvO2 and percentage errors in a clinically acceptable range [9]. However, the measurements

### Analysis at particular time points

Table 2 shows the results of the analysis of the predefined time points, and Fig. 2 illustrates the course of SvO2 versus rsCO2 throughout the procedure. The agreement between both variables was best after induction of anaesthesia (t1) and before the first rapid pacing (t2). Thereafter, the percentage error between the parameters increased until the end of the procedure (t6). Comparably, the degree of correlation varied from close (t1, t2, t3, t5) to moderate (t4, t6).

### Analysis of changes after rapid pacing

To compare the changes of rsCO2 and SvO2 from before to after rapid pacing the value before rapid pacing was set as 100% and the value after rapid pacing determined as relative proportion of this ‘baseline value’. The relative value of rsCO2 and SvO2 was comparable for the first and second rapid pacing (see Figs 3 and 4).

### Table 2: Comparative statistic between rsCO2 and SvO2 at different time points throughout the transapical transcatheter aortic valve implantation.

<table>
<thead>
<tr>
<th>Time</th>
<th>Bias</th>
<th>Limits of agreement</th>
<th>Percentage error</th>
<th>Correlation r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>t1</td>
<td>5.3</td>
<td>−4.9 to 15.5</td>
<td>13.8</td>
<td>0.81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>t2</td>
<td>5.7</td>
<td>−3.5 to 14.9</td>
<td>12.3</td>
<td>0.84</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>t3</td>
<td>3.4</td>
<td>−9.0 to 15.7</td>
<td>18.9</td>
<td>0.78</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>t4</td>
<td>6.2</td>
<td>−7.1 to 19.1</td>
<td>17.7</td>
<td>0.50</td>
<td>0.026</td>
</tr>
<tr>
<td>t5</td>
<td>4.2</td>
<td>−10.8 to 19.2</td>
<td>23.1</td>
<td>0.76</td>
<td>0.0002</td>
</tr>
<tr>
<td>t6</td>
<td>10.0</td>
<td>−2.0 to 28.0</td>
<td>15.5</td>
<td>0.59</td>
<td>0.006</td>
</tr>
</tbody>
</table>

- **t1**: after induction of anaesthesia and accurate placement of the PAC.
- **t2**: at the beginning of the first period of rapid pacing.
- **t3**: at the end of the first period of rapid pacing.
- **t4**: at the beginning of the second period of rapid pacing.
- **t5**: at the end of the second period of rapid pacing.
- **t6**: at the end of the surgical procedure.

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Figure 2: SvO2 and rsCO2 at different time points throughout the transapical transcatheter aortic valve implantation. Data are presented as mean and standard deviation. rsCO2: regional cerebral oxygen saturation; SvO2: mixed venous oxygen saturation; RP: rapid ventricular pacing.

Figure 3: Relative regional cerebral oxygenation and relative SvO2 after the first rapid ventricular pacing. Data are given in means and error bars are given in standard deviation. rsCO2: regional cerebral oxygen saturation; SvO2: mixed venous oxygen saturation; RP: rapid ventricular pacing.

Figure 4: Relative rsCO2 and relative SvO2 after the second rapid ventricular pacing. Data are given in means and error bars are given in standard deviation. rsCO2: regional cerebral oxygen saturation; SvO2: mixed venous oxygen saturation; RP: rapid ventricular pacing.
before the rapid pacing phase showed a better agreement between SvO₂ and rScO₂ than during the periods with haemodynamic instability. One possible explanation may be the retention of carbon dioxide during the rapid pacing period, leading to a discrete increase in arterial carbon dioxide tension and a subsequent increase in rScO₂. In this study we did not take blood gas analyses at all time points and therefore this speculation needs to be verified by a prospective trial. However, the relative changes from before to after both rapid pacing periods were comparable for rScO₂ and SvO₂. During these short haemodynamic low-flow periods, the drop in regional cerebral oxygenation reflects the drop in the surrogate parameter for global oxygen balance, the SvO₂.

GOAL-DIRECTED HAEMODYNAMIC OPTIMIZATION TARGETING AT SVO₂ >70% HAS BEEN SHOWN TO REDUCE POSTOPERATIVE ORGAN DYSFUNCTION AND LENGTH OF HOSPITAL STAY IN CARDIAC SURGERY PATIENTS [10]. THEREFORE, SVO₂-GUIDED THERAPY HAS RECEIVED A ‘GRADE A RECOMMENDATION’ IN THE GERMAN S3 GUIDELINE [11]. THE USE OF A PAC FOR DETERMINATION OF SVO₂ MAY THEREFORE BE CONSIDERED AS A ‘GOOD PRACTICE’ IN THIS CLINICAL SITUATION. However, the insertion of a PAC is not without risk. Based on the guidelines and due to pertinent experience [8] in our centre, we monitor the haemodynamic state during TA-TAVI procedure with PAC.

Near-infrared spectroscopy is increasingly used for monitoring of the adequacy of cerebral oxygen delivery [12]. Interestingly, intraoperative cerebral desaturation has not only been linked to postoperative cerebral complications after cardiac surgery but also to worse general clinical outcome [13]. A recently published observational trial of our own group showed that preoperative rScO₂ levels are closely related to relevant measures of cardiopulmonary function, postoperative morbidity and short- and long-term mortality [4].

Several studies have evaluated the relationship between rScO₂ and SvO₂ as a measure for global oxygen delivery-to-demand ratio with conflicting results [5, 6]. Baraka et al. [5] reported a strong agreement between rScO₂ and SvO₂ during tepid hypothermia during coronary artery bypass grafting surgery, but interestingly only a poor agreement during moderate hypothermia. One possible explanation may be changes in cerebral perfusion following temperature changes during the cardiopulmonary bypass period, i.e. cooling, rewarming. In line with these assumptions, we have recently shown a clinically acceptable correlation between rScO₂ and SvO₂ in spontaneously breathing patients after cardiac surgery [7]. Comparably, we observed a good agreement between rScO₂ and SvO₂ in patients requiring temporary circulatory support by extracorporeal membrane oxygenation due to refractory cardiogenic shock [14]. These results are in contrast to the findings of Dullenkopf et al. [5] who observed only a poor correlation (r = 0.3) between SvO₂ and rScO₂ after cardiac surgery, but an acceptable sensitivity to detect changes in SvO₂.

The discrepancies between the results may be caused by variations in clinical management. Cerebral perfusion in relation to global perfusion might be altered by changes in carbon dioxide tension. This can be influenced by ventilation or, in patients awake, by sedation. Sedation itself as well as temperature changes might influence cerebral activity and hereby cerebral metabolism, which has important impact on cerebral blood flow and cerebral oxygen delivery-to-demand ratio [15]. Due to the observational nature of the present study we did not define specific goals for PCO₂ levels and body temperature. However, all patients were treated according institutional standards aiming for normocapnia, normothermia and depth of anaesthesia. Thus, these potentially confounding variables influencing rScO₂ were controlled as far as possible.

Another point is the statistical interpretation of the results. We interpreted a percentage error of smaller 30% as clinically acceptable as recommended by Critchley and Critchley [9]. Actually, at most measured time points the percentage error between the methods did not exceed 20%, and the correlations between the methods were moderate to close.

Of note, at all measured time points the rScO₂ was lower than the SvO₂. If the rScO₂ would have been used to estimate SvO₂, SvO₂ would have been rather underestimated, so the patient would have been rather over-treated. This might, in many cases, avoid hypoperfusion, but certainly the risks of unnecessary isotropic treatment should not be disregarded.

**Limitations**

This study has several limitations:

(1) The small sample size is a clear limitation of the study. Larger observations and prospective interventional trials are needed to determine factors influencing the relationship between rScO₂ and SvO₂.

(2) Since the rapid pacing periods were rather short, and the sampling rates of the Vigilance II-Monitor and the INVOS-Monitor differ, the measurements during the rapid pacing periods may be incongruent. This may, at least in part, explain the less optimal correlations during these periods. However, the haemodynamic deterioration was evident in both methods and was reflected readily.

(3) Comparable to other studies investigating the agreement between rScO₂ and SvO₂, we used the mean of the bihemispheric measurements for calculation of rScO₂. In case of large interhemispheric differences this may introduce a systematic error. However, since in the present study the differences between both hemispheres were small, the potential error is rather low.

In conclusion, the results of the present study show that rScO₂ determined by near-infrared spectroscopy correlates well with SvO₂ during the rapidly changing haemodynamic conditions in patients undergoing TA-TAVI. Whether this non-invasive technology may be used as an alternative for SvO₂ measurements or is giving additional information to SvO₂ monitoring warrant further investigation.

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**Conflict of interest:** Julika Schöns and Matthias Heringlake receive lecture fees from Covidien, Germany, and Edwards Lifesciences, Germany.

**REFERENCES**


