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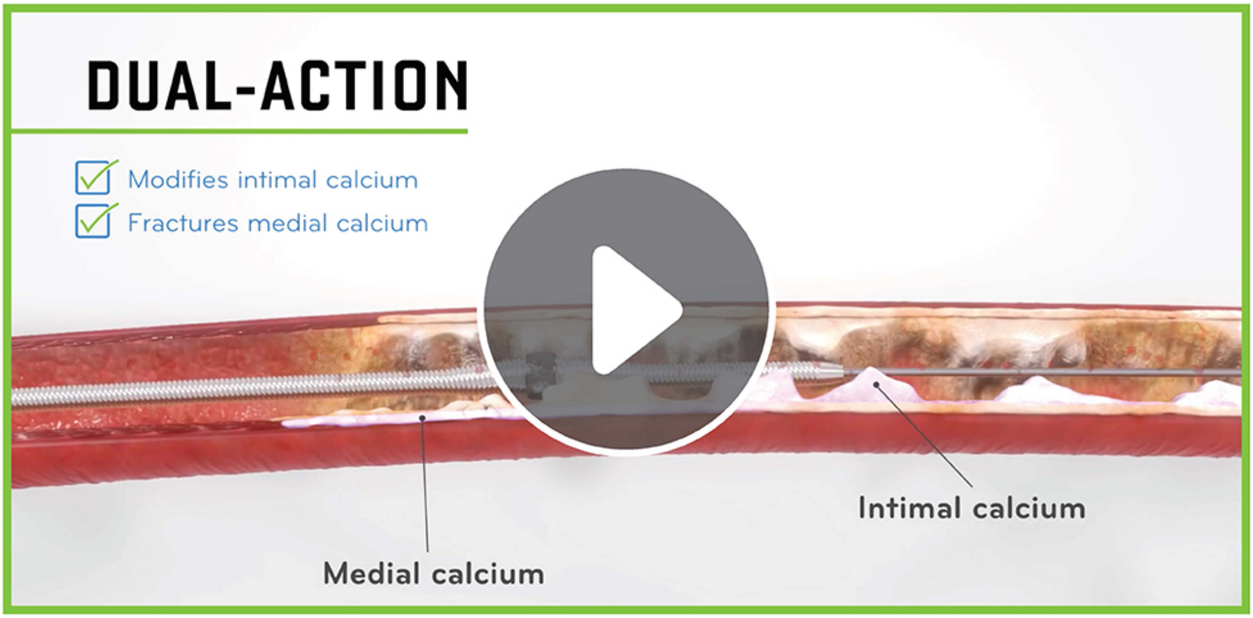

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ORIGINAL STUDIES

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Dynamics of cerebral oxygenation during rapid ventricular pacing and its impact on outcome in transfemoral transcatheter aortic valve implantation

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Abstract

Background: Cerebral O_2 saturation (ScO_2) reflects cerebral perfusion and can be measured noninvasively by near-infrared spectroscopy (NIRS).

Objectives: In this pilot study, we describe the dynamics of ScO_2 during TAVI in non-ventilated patients and its impact on procedural outcome.

Methods and Results: We measured ScO_2 of both frontal lobes continuously by NIRS in 50 consecutive analgo-sedated patients undergoing transfemoral TAVI (female 58%, mean age 80.8 years). Compared to baseline ScO_2 dropped significantly during RVP (59.3% vs. 53.9%, $p < .01$). Five minutes after RVP ScO_2 values normalized (post RVP 62.6% vs. 53.9% during RVP, $p < .01$; pre 61.6% vs. post RVP 62.6%, $p = .53$). Patients with an intraprocedural pathological ScO_2 decline of >20% ($n = 13$) had higher EuroSCORE II (3.42% vs. 5.7%, $p = .020$) and experienced more often delirium (24% vs. 62%, $p = .015$) and stroke (0% vs. 23%, $p < .01$) after TAVI. Multivariable logistic regression revealed higher age and large ScO_2 drops as independent risk factors for delirium.

Conclusions: During RVP ScO_2 significantly declined compared to baseline. A ScO_2 decline of >20% is associated with a higher incidence of delirium and stroke and a valid cut-off value to screen for these complications. NIRS measurement during TAVI procedure may be an easy to implement diagnostic tool to detect patients at high risks for cerebrovascular complications and delirium.

KEYWORDS
aortic stenosis, delirium, NIRS, stroke, TAVI

Abbreviations: CAM-ICU, confusion assessment method for the ICU; EuroSCORE II, European System for Cardiac Operative Risk Evaluation score II; LVEF, left ventricular ejection fraction; MMSE, mini mental state examination; NIRS, near-infrared spectroscopy; RASS, Richmond Agitation Sedation Scale; RVP, rapid ventricular pacing; ScO_2, cerebral O_2 oxygenation; SpO_2, peripheral oxygen saturation; STS-PROM, Society of Thoracic Surgeons' risk model score for mortality; STS-PROMM, Society of Thoracic Surgeons' risk model score for mortality and morbidity; TAVI, transcatheter aortic valve implantation; TIA, transient ischemic attack; VI, valve implantation.

1 | INTRODUCTION

Aortic valve stenosis is the leading heart valve disease in developing countries with an estimated prevalence of up to 3% in patients over 70 years.[1] Today, transcatheter aortic valve replacement (TAVI) is becoming the treatment of choice for patients with aortic valve stenosis and high to intermediate operative risk. Recent studies demonstrated similar and superior results of the transfemoral TAVI approach compared to surgical replacement in patents with low operative risk.[2] However, TAVI related complications such as cerebrovascular adverse events, periprocedural stroke, postoperative delirium and neurocognitive dysfunction, may affect the patient's quality of life and procedural outcome and generate higher overall costs.[3,4]

Recent data suggest, that cerebral O_2 saturation is an indicator not only for cerebral perfusion but may mirrors the mixed venous oxygen saturation, one important determinate of the systemic oxygen balance.[5,6] Furthermore, cerebral oxygenation was reported as predictor for 30-day mortality and postoperative delirium in on-pump cardiac surgery patients.[7,8] The cerebral oxygenation of both frontal hemispheres can be measured noninvasively and continuously by near-infrared spectroscopy (NIRS). Like pulse oximetry, NIRS detects the different light absorption spectra of oxygenated and deoxygenated hemoglobin of the cerebral blood in a ratio of 84% venous to 16% arterial blood. Therefore, oxygen saturation measured by NIRS is mainly a venous saturation.[9] Methodically, NIRS does not measure absolute hemoglobin concentration but only relative changes of the chromophores. Moreover, extracerebral tissue (calvarium and scalp) contributes to the light absorption (extracerebral contamination) and may mask low cerebral oxygen saturations, as observed during cerebral ischemia.[10] Important to note, focal ischemic lesions or hypoperfusion outside of the frontal lobes remain undetected by NIRS configurations used in clinical practice.[11]

The measurement of cerebral oxygenation saturation has been reported in a cohort undergoing transapical TAVI in general anesthesia.[5] However, the dynamics of cerebral oxygenation during transfemoral TAVI procedure performed in spontaneously breathing patients with analgo-sedation and its impact on outcome and postoperative delirium has not been described yet. In our pilot study, we prospectively analyzed the dynamics of cerebral oxygenation and its impact on clinical outcome, continuously measured by NIRS, in a consecutive patient cohort with aortic valve stenosis undergoing TAVI.

2 | METHODS

2.1 | Study design

Between July 2018 and April 2019, we measured ScO_2 in 50 consecutive patients undergoing transfemoral TAVI in analgo-sedation. All patients underwent preoperative duplex sonography to rule out hemodynamic relevant stenosis of the supraaortic vessels (defined as >75% lumen stenosis). Mini-Mental State Examination (MMSE) was performed 1 day prior intervention to screen for neurocognitive impairment. A test result below 24 was interpreted as abnormal indicating a cognitive impairment.[12] Postoperative delirium was assessed by CAM-ICU (Confusion Assessment Method for the ICU) on the first three consecutive postinterventional days or during the intensive care unit stay. CAM-ICU was defined as positive (patient had delirium) if RASS (Richmond Agitation Sedation Scale) was ≥ −3 and patients showed acute onset change in mental status or fluctuating course in mental status occurred and patients demonstrated two or more errors in letters attention test.[13]

Decision for valve intervention was made by an interdisciplinary heart team consisting of anesthesiologists, cardiologists and cardiac surgeons. Patients with symptomatic carotid artery disease, patients in cardiogenic shock or patients requiring inotropic support prior to the procedure were excluded.

The study was conducted as approved by the ethics committee of the University Hospital of Frankfurt (296/16) and all patients gave signed and informed consent prior to intervention. Short-Term follow-up information was obtained via contact with General Practitioner, other hospitals or with the patient or family directly (completeness of follow-up 100%).

2.2 | Transcatheter aortic valve implantation

TAVI procedures were performed in our hybrid operating room by an interventional cardiologist, an anesthesiologist and a cardiac surgeon. Procedures were performed exclusively under analgo-sedation using fentanyl (1–2 μg/kg body weight), and in four patients with additional midazolam (1 mg). Local anesthesia was applied at the puncture sites (usually 10–20 ml Mepicavain 10 mg/ml). Briefly, femoral access was obtained with re-closure devices (Perclose ProGlide, Abbott Vascular, Abbott Park, IL or Manta closure device, Teleflex, Wayne, PA). A temporary pacing wire was placed via the femoral vessels in the right ventricular apex for rapid ventricular pacing (RVP). Retrograde passing of the aortic stenosis was performed as per interventionist standards, a preshaped wire (SAFARI[2] Boston Scientific, Marlborough, MA) was placed in the left ventricle and the delivery sheath for each valve was then placed in the femoral vessel. RVP was performed as per interventionist standard either for predilatation, for deployment of balloon-expandable valves and for prosthesis postdilatation if required. In all cases at least one RVP was performed. At the end of the procedure, patients were transferred to an intermediate care unit and were monitored for at least 48 hr post intervention.

2.3 | Measurements of cerebral oxygenation

Cerebral oxygenation (ScO_2) of both frontal lobes was monitored by placing two NIRS-sensor pads on the hair free forehead of the patients. For all measurements, the same NIRS measurement device was used (Root®, Masimo, Irvine) and mean of both hemispheres was used for analysis. Before induction of sedation baseline values of cerebral oxygenation were determined (Figure 1). If the peripheral oxygen saturation (SpO_2), measured by standard peripheral oximetry, was below 95% patients received supplementary oxygen (aim SpO_2 > 94%). The ScO_2-values were documented prior, during and 5 min after RVP. If two or more RVPs were performed mean values were used for analysis. Additionally, lowest and highest ScO_2 were documented. As previously described, pathological ScO_2 values were defined as decrease of >20%, unihemispheric decrease of 10% compared to the contralateral sensor and an absolute value <50% (one or both frontal lobes).[14]

2.4 | Statistics

Continuous variables are shown as mean ± *SD* and categorical data are shown as number + percentage. Society of Thoracic Surgeons' risk model score for mortality (STS PROM) and mortality and morbidity (STS PROMM), European System for Cardiac Operative Risk Evaluation score II (EuroSCORE II) and Mini Mental State Examination (MMSE) are presented as median ± interquartile range.[15-17] Unadjusted differences were compared with $\chi 2$ tests for categorical variables and 2-tailed unpaired *t* tests for continuous variables. Wilcoxon-Mann–Whitney-Test was used to analyze STS, EuroSCORE II and MMSE, Risk factors for postoperative delirium were assessed by logistic regression. For adjusting the logistic model, the variables age, sex and EuroSCORE II were included into the model. First, possible relevant risk factors were tested with this adjusted model by backward LR stepwise selection (LR, Likelihood Ratio, selection and significance criteria $p < .1$ and $p < .05$, respectively). Final model was calculated by entering all selected variables en bloc in a single step (Enter mode). The a priori level of statistical significance was set at $p < .05$ for all analyses, which were always two-tailed and performed with SPSS, version 25 (IBM SPSS, Chicago, IL).

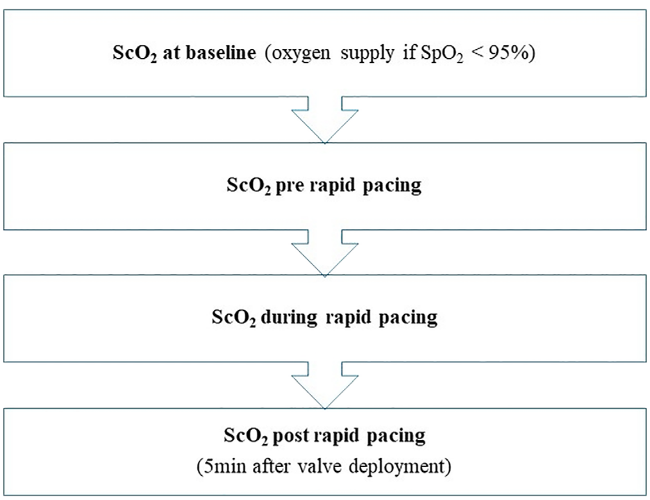

FIGURE 1 Protocol for cerebral oxygen saturation (ScO_2) measurement during transfemoral TAVI procedure. ScO_2, cerebral oxygen saturation; SpO_2, peripheral oxygen saturation; TAVI, transcatheter aortic valve implantation

3 | RESULTS

3.1 | Baseline characterization of the study cohort

Mean age was 80.8 (±6.5) years with a cohort of 58% female patients (*n* = 29, Table 1). MMSE score below 24 (median 27 points) was found in 7 patients (14%), identifying a relevant neurocognitive dysfunction prior to intervention. The prevalence of common cardiovascular risk factors was high (STS-PROM 3.9%, EuroSCORE II 4.2%). In 19 patients (*n* = 38%) a nonsignificant cerebral artery disease was diagnosed, verified by preoperative duplex sonography, and 10 patients (*n* = 20%) had either a minor or major stroke in their medical history.

3.2 | Intraprocedural course and dynamics of ScO_2

In 28 patients a self-expandable prothesis (Boston Scientific Symetis ACUATE Neo *n* = 21, Portico Abbott Medical *n* = 4, and Medtronic EvoluteR *n* = 3) and in 22 patients a balloon-expandable prothesis (Sapien3 Edwards) was implanted (Table 2). In all procedures at least

TABLE 1 Patients characteristic

Patients characteristic (*n* = 50)	
Female (*n*)	29 (58%)
Age (years)	80.8 ± 6.5
Body mass index (kg/m^2)	28.3 ± 6.4
EuroSCORE II (%)	4.2 (2.5–6.6)
STS PROM	3.9 (2.4–5.6)
STS PROMM	20.1 (13.5–25.6)
MMSE (pts)	27 (25.5–28)
Hypertension (*n*)	47 (94%)
Chronic kidney disease (*n*)	22 (44%)
Diabetes mellitus (*n*)	15 (30%)
Atrial fibrillation (*n*)	16 (32%)
Coronary heart disease (*n*)	34 (68%)
Previous PCI (*n*)	23 (46%)
Previous myocardial infarction	5 (10%)
Cerebral arterial disease	19 (38%)
Previous stroke (*n*)	10 (20%)
Peripheral artery disease (*n*)	23 (46%)
LVEF (%)	52.9 ± 11.4
Aortic valve area (cm^2)	0.69 ± 0.19
Creatinine (mg/dl)	1.2 ± 0.5
NT-proBNP (ng/l)	4,098 ± 6,099
Hemoglobin (g/dl)	11.9 ± 2.0

Note: Data shown as *n* (percentage) or mean ± *SD*. EuroSCORE II, MMSE and STS Scores are presented as median (interquartile range). LVEF, left ventricular ejection function; MMSE, mini mental state examination; PCI, percutaneous coronary intervention; STS PROM/PROMM, Society of Thoracic Surgeons risk model score for mortality/mortality and morbidity.

one RVP was conducted (overall mean 1.34). We could measure a valid and evaluable NIRS signal in all conducted cases (feasibility 100%). Mean baseline ScO_2 without oxygen supply was 59.3% without significant interhemispheric differences (mean left 59.8%, right 58.7%, $p = .499$). In patients receiving oxygen supply (aim SpO_2 > 95%, in total 39 patients [78%], mean supply 4.7 L ± 2.6 L/min) ScO_2 increased non-significantly after oxygen application (58.4% vs. 61.2%, $p = .107$). During RVP we observed a significant decrease of mean ScO_2 compared to pre RVP values (mean Δ, 7.7%, 61.6% vs. 53.9%, $p < .001$; Figure 2). Five minutes after RVP ScO_2 increased again to values comparable to pre RVP (61.6% vs. 62.6%, $p = .530$). Immediately prior RVP and with oxygen supply we observed higher ScO_2 compared to baseline values, although not statistically significant (59.3% vs. 61.6%, $p = .124$). Mean delta of the highest-to-lowest ScO_2 during the procedure was 15.7% (±6.5%), whereas 37 patients (74%) demonstrated a pathological decrease of either 20% (n = 13, 26%), 10% difference between the hemispheres (n = 16, 32%) or an absolute ScO_2 value below 50% (n = 21, 42%). Baseline hemoglobin (11.9 g/dl) and pre RVP ScO_2 values did not correlate significantly ($r^2 = .229$, $p = .110$, Spearman-Rho correlation). The number of RVP per patient itself had a moderate correlation with ScO_2 drop (RVP [n] – delta highest-to-lowest ScO_2, $r^2 = .312$, $p = .027$, Spearman-Rho correlation).

TABLE 2 Procedural outcome

Procedural outcome (*n* = 50)	
Aortic valve protheses: Edwards S3 (*n*)	22 (44%)
Boston Scientific Symetis ACUATE Neo (*n*)	21 (42%)
St. Jude Portico (*n*)	4 (8%)
Medtronic CoreValve EcvoluteR (*n*)	3 (6%)
Valve size (mm)	26.2 ± 3.1
RVP	
n = 1	34 (68%)
n = 2	15 (30%)
n = 3	1 (2%)
Contrast medium (ml)	78.0 ± 29.7
Postoperative delirium (*n*)	17 (34%)
Bleeding (*n*)	4 (8%)
Access site vascular complication (*n*)	4 (8%)
Need for renal replacement therapy (*n*)	1 (2%)
Paravalvular leak	
I-II	30 (60%)
III-IV	0 (0%)
Stroke (*n*)	2 (4%)
TIA (*n*)	1 (2%)
Reoperation (*n*)	0 (0%)
Need for new pacemaker (*n*)	8 (16%)
New left bundle branch block (*n*)	12 (24%)
Complete A-V block	5 (10%)
30-day mortality (*n*)	1 (2%)
Days on intensive care unit (days)	5.7 ± 5.2
Days in hospital (days)	12.0 ± 6.4

Note: Data shown as *n* (percentage) or mean ± *SD*. A-V block, atrio-ventricular block; TIA, transient ischemic attack.

3.3 | Postprocedural course, outcome, and early mortality

Overall 30-day mortality was 2% (n = 1) and three patients suffered a new neurological event (2 thromboembolic strokes, three and six points according to the modified Rankin scale, one transient ischemic attack, TIA, Rankin scale 0).[18] In two cases, we observed an acute and pathological unilateral rapid ScO_2 decrease mirroring a new neurological symptom occurring during the procedure. One patient developed post RVP a transient tremor of the left arm (TIA, new hemorrhagic or ischemic event was later ruled out by cerebral CT scan). The second patient presented post RVP a left-sided hemiplegia later verified by cerebral CT scan as thromboembolic stroke of the right cerebri media artery (Figure 3).

3.4 | Correlation of postintervention delirium and cerebral oxygen saturation

In total 17 patients (34%) developed postoperative delirium, validated by CAM-ICU test. Patients experiencing postoperative delirium had significant lower pre RVP ScO_2 values (53.7% vs. 57.4%, $p = .006$) as well as higher deltas highest-to-lowest ScO_2 values (intraprocedural ScO_2 drop, 19.2% vs. 13.9%, $p = .005$) compared to nondelirious counterparts. One out of four patients receiving sedation with fentanyl and additional midazolam developed postoperative delirium (25%). Patients with an intraprocedural ScO_2 drop of >20% had a higher EuroSCORE II, lower baseline LVEF and a higher incidence for post-interventional delirium and a new neurological complication such as stroke or TIA (Table 3). Multivariable logistic regression adjusted for age, sex and EuroSCORE II revealed a large intraprocedural drop of ScO_2 as an independent risk factor for the development of postoperative delirium (Table 4).

4 | DISCUSSION

Cerebrovascular complications and delirium are important peri-procedural complications of transcatheter aortic valve implantation. We investigated whether continuous, non-invasive measurements of cerebral oxygen saturation by NIRS are useful for the diagnostic and prediction of delirium and cerebrovascular complications following TAVI.

We observed a significant decrease of cerebral oxygenation during RVP in patients undergoing transfemoral TAVI with spontaneous breathing and analgo-sedation. Any significant impairment in cerebral oxygenation predicted the occurrence of neurological complications that is, TIA/stroke and post-intervention delirium. Moreover, patients who developed a post interventional delirium had significant lower

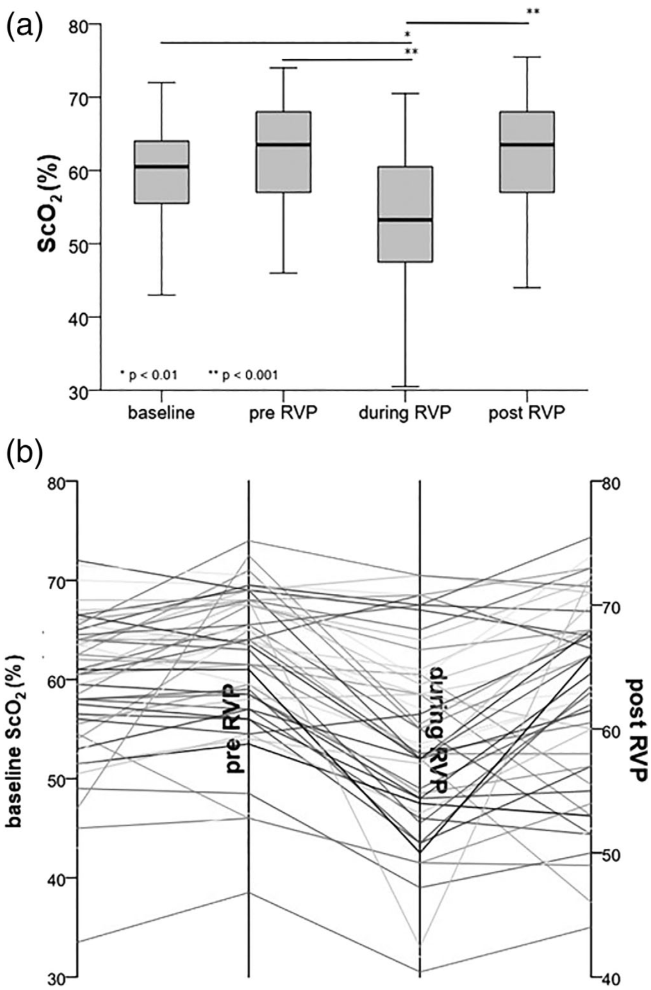

FIGURE 2 Course of cerebral oxygen saturations during transfemoral TAVI. (a) Mean ScO_2 values at the different time points. (b) Individual course of ScO_2 at the different time points. ScO_2, cerebral oxygen saturation; RVP, rapid ventricular pacing; TAVI, transcatheter aortic valve implantation

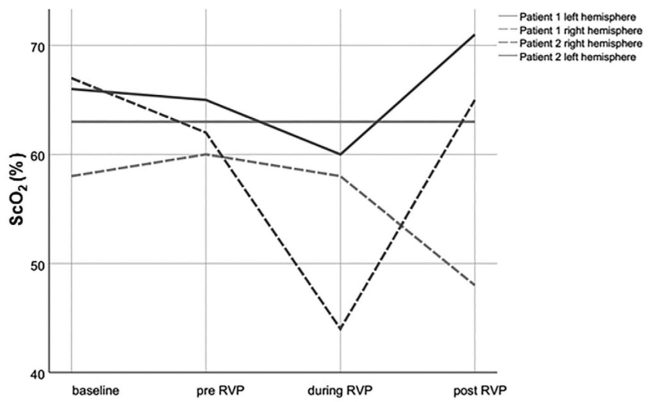

FIGURE 3 Correlation of rapid one-sided ScO_2 decline and neurological complication. Patient 1 developed a transient tremor of the left arm (TIA, new hemorrhagic or ischemic event ruled out by cerebral CT scan) and Patient 2 a left-sided hemiplegia (fatal stroke, later verified by cerebral CT scan). In both cases, an abnormal sudden ScO_2 decline was observed, monitored by the corresponding right hemispheric NIRS sensor. ScO_2, cerebral oxygen saturation; NIRS, near-infrared spectroscopy; RVP, rapid ventricular pacing; TAVI, transcatheter aortic valve implantation

pre RVP ScO_2 values, lower minimal ScO_2 values as well as larger deltas highest-to-lowest ScO_2 values (maximal ScO_2 drop) compared to patients without postoperative delirium. Additionally, an evaluable NIRS signal could be generated in all cases, underlining the easy to implement technique and viability of this diagnostic tool.

The pathophysiology of sudden cerebral oxygen saturation decline during RVP has been described by Paarmann et al. in a small patient cohort (*n* = 20) undergoing transapical TAVI in general anesthesia.[5] In our study, patients underwent transfemoral TAVI in analgosedation with spontaneous breathing but not general anesthesia. We observed a mean drop of 7.7% during RVP. Patients with an intraprocedural ScO_2 decline of >20% had a higher EuroSCORE II and lower LVEF at baseline.

Importantly, ScO_2 correlates with mixed venous saturation, invasively measured in the pulmonary artery and a valuable parameter for the patient's tissue oxygen extraction.[5] However, ScO_2 drops earlier than mixed venous saturation during RVP and might therefore be a more suitable parameter for monitoring quick hemodynamic changes, as observed during RVP. The underlying pathophysiology of a ScO_2 drop during RVP may be explained by the state of low-flow and low-perfusion during RVP. Known as cerebral blood flow autoregulation, the cerebral perfusion is kept stable between a mean blood pressures of the order of 60 and 150 mmHg.[19] In a state of low (to no) cardiac output and low vascular resistance a sufficient cerebral perfusion cannot be facilitated despite autoregulation. As ScO_2 drops rapidly and earlier than the mixed venous saturation during RVP, ScO_2 might be a more accurate and predictive parameter to evaluate the risk for systemic as well as cerebral low flow.

The number of RVP itself might have a relevant impact on cerebral oxygen saturation. We determined a moderate correlation between ScO_2 decline and number of RVP per patient. Fefer et al. recently described in a retrospective cohort, that multiple rapid ventricular pacing episodes and prolonged RVP duration are associated with adverse outcomes including increased short- and long-term mortality.[20] However, we did not survey the exact ScO_2 change over time but measured at pre-determined time-points immediately and 5 min after the conducted RVP. Further studies are needed to evaluate the specific impact of repetitive RVP on ScO_2 change over time. Nevertheless, RVP is often not avoidable during TAVI procedure, even essential for the implantation of self-expandable valves. Despite our finding, that repetitive RVP might correlate with ScO_2 decline and consequently with poorer neurocognitive outcome in certain patients, we strongly recommend to perform RVP if required for hemodynamic reasons, such as post-dilatation to reduce paravalvular leakage or prosthesis insufficiency.

Delirium is a potentially preventable cause of cognitive impairment and dementia. It is associated with prolonged in hospital stay,

TABLE 3 Characteristics of patients with pathological drop of cerebral oxygen saturation

Patients characteristic (n = 55)	ΔScO_2 < 20% (n = 37)	ΔScO_2 > 20% (n = 13)	p-Value
Female (n)	23 (82.1%)	5 (17.9%)	.198
Age (years)	81.1 ± 7.2	80.3 ± 4.5	.718
Mini mental state examination (pts)	27 25.5–28.0	26 25.5–27	.072
Baseline ScO_2 (%)	61.8 ± 5.3	52 ± 8.6	.002
EuroSCORE II (%)	3.42 (1.9–5.8)	5.7 (3.9–17.9)	.020
STS PROM	3.7 (2.1–5.6)	4.3 (3.4–6.6)	.144
STS PROMM	19.2 (13.3–23.8)	24.8 (17.6–31.5)	.124
BMI kg/m^2	28.5 ± 5.1	27.5 ± 9.3	.644
LVEF (%)	55.5 ± 9.9	45.8 ± 12.7	.007
Aortic valve area (cm^2)	0.69 ± 0.18	0.69 ± 0.21	.971
NT-proBNP (ng/l)	2,709 ± 3,606	7,707 ± 9,410	.133
Hemoglobin (g/dl)	11.94 ± 1.8	11.74 ± 2.5	.757
High-sensitive troponin-T (ng/ml)	31.6 ± 33.3	42.5 ± 26.2	.355
Postoperative delirium (n)	9 (24.3)	8 (61.5%)	.015
Hypertension (n)	36 (92.3%)	11 (84.6%)	.098
Chronic kidney disease (n)	13 (35.1%)	9 (69.2%)	.033
Diabetes mellitus (n)	13 (35.1%)	2 (15.4%)	.181
Atrial fibrillation (n)	11 (29.7%)	5 (38.5%)	.602
Coronary heart disease	24 (64.9%)	10 (76.9%)	.423
Cerebral arterial disease	14 (37.8%)	5 (38.5%)	.968
Previous stroke (n)	5 (13.5%)	5 (38.5%)	.053
New postoperative stroke or TIA (n)	0 (0%)	3 (23.1%)	.003
30-Day mortality (n)	0 (0%)	1 (7.7%)	.260

Note: Data shown as n (percentage) or mean ± SD. BMI, body mass index; EuroSCORE II, MMSE and STS Scores are presented as median (interquartile range). LVEF, left ventricular ejection function; MMSE, mini mental state examination; PCI, percutaneous coronary intervention; ScO_2, cerebral oxygen saturation; STS PROM/PROMM, Society of Thoracic Surgeons risk model score for mortality/mortality and morbidity; TIA, transient ischemic attack.

increased risk of hospital readmissions and increased 180-day mortality.[3,21] A meta-analysis conducted by Tilley et al. reports an incidence of delirium following TAVI of 23%.[22] In our cohort we observed a higher incidence of post interventional delirium of 34%. We found that the incidence of postoperative delirium is 2.5 times as high in patients with an intraprocedural ScO_2 drop of >20% (incidence 61.5%) compared to counterparts with ScO_2 drops <20% (incidence 24.3%). Furthermore, patients who experienced delirium had significant lower pre RVP and larger intraprocedural ScO_2 drops compared to non-delirious patients. Our results support the findings of Schoen et al who described a correlation of low pre- and intraoperative ScO_2 values with postoperative delirium in patients undergoing on-pump cardiac surgery.[7] Consequently, ScO_2 may be a valid screening parameter for patients at risk for postoperative delirium. Indirectly, avoidance of RVP in patients at risk by the choice of self-expanding valve prosthesis may be a strategy that needs further investigation. Patients with an intraprocedural ScO_2 drop of >20% may benefit from a consequent delirium prophylaxis (such as early mobilization, cognitively stimulation activities, hydration protocols, nonpharmacological sleep) in order to reduce delirium associated complications.

A further possible implication of NIRS during transfemoral TAVI procedure is the early detection of cerebrovascular incidences such as stroke or TIA. In two cases, we observed a rapid one-sided ScO_2 decline accompanied by new neurological complications. As under general anesthesia or sedation the new onset of neurological symptoms is not easy to detect, ScO_2 measurement may be helpful in the detection of a neurological complication and contribute to start diagnostic and specific therapy as early as possible. Based on our findings a rapid, strict one-sided decline may be a valuable indicator for a one-sided stroke/TIA in frontal parts of the cerebrum and requires immediate neurological diagnostic steps and initiation of treatment if required. However, severe cerebral ischemia localized outside of the frontal lobes is not detected by the NIRS configurations used in clinical practice. Consequently, uneventful NIRS measurements do not exclude potential cerebral ischemia in other brain regions than the frontal lobes.[11]

Carotid artery disease, impaired cognitive status and dementia are risk factors for neurological complications during TAVI procedure.[23,24] Against our expectation, in our cohort, preoperative MMSE and known cerebral artery disease did not correlate with intraprocedural ScO_2 changes. However, we noted a trend for a higher

TABLE 4 Risk factors for postoperative delirium

Variable	*p*-Value	OR (95% CI)
Age[a]	.021	1.25 (1.04–1.52)
Sex (male)[a]	.425	0.56 (0.13–2.52)
EuroSCORE II[a]	.51	0.96 (0.86–1.08)
Δ highest-lowest ScO_2	.006	1.26 (1.07–1.48)

Note: Multivariable Logistic Regression analysis for risk of postoperative delirium.
[a]Variables were fixed in the model for adjustment. ScO_2, regional cerebral oxygen saturation.

prevalence of pathological ScO_2 declines >20% in patients with a history of stroke (13.5% vs. 38.5%, p = .053).

Taken together our results underline the benefit of NIRS measurement in high risk patients (high EuroSCORE and STS Score) as well as patients with impaired LV-function and pre-existing comorbidities such as previous stroke or sub-clinical dementia. A clear benefit of NIRS diagnostic is the easy implementation, interpretation and rather low costs. Postoperative delirium is costly and prolongs the stay on ICU/in hospital impeding morbidity and even mortality in TAVI patients.[3,21] Our data demonstrates a clear trend of a higher incidence for postinterventional delirium in patients with pathologic decline of cerebral oxygenation saturation > 20% during the procedure. Thus, NIRS diagnostic might be a helpful tool to improve the general outcome in old and frail TAVI patients. Especially in patients with a pathological decline of cerebral oxygen saturation > 20% you must be aware of neurological complications and the development of postoperative delirium and cognitive dysfunction. Certainly, prospective studies with longer follow-up are needed to determine the ability of NIRS measurements to have an impact on long-term survival and cognitive function.

Our study has several limitations. First, we conducted a single center pilot study with a rather small and heterogenous all-comer patient cohort. Second, although mainly Fentanyl was used for analgo-sedation, sedation level varied and the impact of sedation depth on cerebral oxygenation itself may lead to certain bias. Third, measurements with different brands of oximeters are not comparable and our results with the Masimo oximeter may not be transferrable to other cerebral oximetry systems. Furthermore, the duration of RVP itself might have a relevant impact on the drop of the cerebral oxygen saturation, by generating a state of cardiac low flow. However, we did not measure the exact duration of RVP, but in most cases time was presumably below 10 s. Fourth, we did not determine partial pressures of oxygen and carbon dioxide as well as end-tidal carbon dioxide, all known to influence cerebral blood flow.

5 | CONCLUSION

During RVP of transfemoral TAVI procedure under analgo-sedation ScO_2 decreases significantly compared to baseline values. A drop of ScO_2 > 20% was associated with a higher incidence of postinterventional delirium and stroke and is a reliable cut-off value to screen for these complications. Measurement of ScO_2 during TAVI procedure may become an important and easy to implement diagnostic tool to detect patients at high risks for cerebrovascular complications and postoperative delirium. Further and larger studies are needed to determine whether patients with a pathological ScO_2 drop during TAVI procedure benefit from specific therapeutic algorithms to prevent postoperative delirium.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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REFERENCES

1. Zakkar M, Bryan AJ, Angelini GD. Aortic stenosis: diagnosis and management. BMJ. 2016;355:i5425.
2. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380:1695-1705.
3. Eide LSP, Ranhoff AH, Fridlund B, et al. Readmissions and mortality in delirious versus non-delirious octogenarian patients after aortic valve therapy: a prospective cohort study. BMJ Open. 2016;6:e012683.
4. Werner N, Zeymer U, Schneider S, et al. German transcatheter aortic valve interventions-registry investigators. Incidence and clinical impact of stroke complicating transcatheter aortic valve implantation: results from the German TAVIRegistry. Catheter Cardiovasc Interv. 2016;88:644-653.
5. Paarmann H, Heringlake M, Heinze H, et al. Non-invasive cerebral oxygenation reflects mixed venous oxygen saturation during the varying haemodynamic conditions in patients undergoing transapical transcatheter aortic valve implantation. Interact Cardiovasc Thorac Surg. 2012;14:268-272.
6. Paarmann H, Heringlake M, Sier H, Schön J. The association of non-invasive cerebral and mixed venous oxygen saturation during cardiopulmonary resuscitation. Interact Cardiovasc Thorac Surg. 2010;11:371-373.
7. Schoen J, Meyerrose J, Paarmann H, Heringlake M, Hueppe M, Berger K-U. Preoperative regional cerebral oxygen saturation is a predictor of postoperative delirium in on-pump cardiac surgery patients: a prospective observational trial. Crit Care. 2011;15:R218.
8. Heringlake M, Garbers C, Käbler J-H, et al. Preoperative cerebral oxygen saturation and clinical outcomes in cardiac surgery. Anesthesiology. 2011;114:58-69.
9. Watzman HM, Kurth CD, Montenegro LM, Rome J, Steven JM, Nicolson SC. Arterial and venous contributions to near-infrared cerebral oximetry. Anesthesiology. 2000;93:947-953.
10. Davie SN, Grocott HP. Impact of extracranial contamination on regional cerebral oxygen saturation: a comparison of three cerebral oximetry technologies. Anesthesiology. 2012;116:834-840.
11. Erdoes G, Rummel C, Basciani RM, et al. Limitations of current near-infrared spectroscopy configuration in detecting focal cerebral ischemia during cardiac surgery: an observational case-series study. Artif Organs. 2018;42:1001-1009.
12. Mitchell AJ, Shukla D, Ajumal HA, Stubbs B, Tahir TA. The mini-mental state examination as a diagnostic and screening test for delirium: systematic review and meta-analysis. Gen Hosp Psychiatry. 2014;36:627-633.
13. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA. 2001;286:2703-2710.

14. Edmonds HL. Protective effect of neuromonitoring during cardiac surgery. Ann N Y Acad Sci. 2005;1053:12-19.
15. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. Ann Thorac Surg. 2009;88:S23-S42.
16. Nashef SAM, Roques F, Sharples LD, et al. EuroSCORE II. Eur J Cardio-Thorac Surg. 2012;41:734-745.
17. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-198.
18. Quinn TJ, Dawson J, Walters MR, Lees KR. Functional outcome measures in contemporary stroke trials. Int J Stroke. 2009;4:200-205.
19. Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. Cerebrovasc Brain Metab Rev. 1990;2:161-192.
20. Fefer P, Bogdan A, Grossman Y, et al. Impact of Rapid Ventricular Pacing on Outcome After Transcatheter Aortic Valve Replacement n.d.
21. Huded CP, Huded JM, Sweis RN, et al. The impact of delirium on healthcare utilization and survival after transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2017;89:1286-1291.
22. Tilley E, Psaltis PJ, Loetscher T, et al. Meta-analysis of prevalence and risk factors for delirium after transcatheter aortic valve implantation. Am J Cardiol. 2018;122:1917-1923.
23. Thirumala P, Muluk S, Udesh R, et al. Carotid artery disease and periprocedural stroke risk after transcatheter aortic valve implantation. Ann Card Anaesth. 2017;20:145-151.
24. Yanagisawa R, Tanaka M, Yashima F, et al. Frequency and consequences of cognitive impairmentin patients underwent transcatheter aortic valve implantation. Am J Cardiol. 2018;122:844-850.

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