Article Title:

Near-infrared spectroscopy underestimates cerebral oxygenation in hemodialysis patients

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Abstract

Regional cerebral oxygen saturation (rSO_2) measured using near-infrared spectroscopy has been reported to be significantly lower in hemodialysis (HD) patients than in non-HD ones, but the mechanisms are unknown. The aim of this prospective study was to assess the accuracy of near-infrared spectroscopy to estimate cerebral oxygenation in HD patients undergoing cardiovascular surgery. Our hypothesis was that rSO_2 values would underestimate cerebral oxygenation in HD patients. This study included 113 patients (7 HD patients and 106 non-HD ones) undergoing cardiac or major aortic surgery between December 2015 and November 2017. We evaluated the validity of rSO_2 by comparing it with ipsilateral jugular venous oxygen saturation ($SjvO_2$). In HD and non-HD patients, rSO_2 and $SjvO_2$ showed a weak correlation (R^2: 0.46 and 0.28 in HD and non-HD patients, respectively). Bland–Altman analysis revealed that bias (95% limits of agreement) of rSO_2 compared to $SjvO_2$ was −19.2% (−41.7% to 3.3%) in HD patients and −1.9% (−19.3% to 15.5%) in non-HD ones. The large negative bias suggests that the rSO_2 values measured using near-infrared spectroscopy substantially underestimate cerebral oxygenation in HD patients.

Introduction

Regional cerebral oxygen saturation (rSO_2) measured using near-infrared spectroscopy (NIRS) provides non-invasive and real-time estimation of cerebral oxygenation and has been increasingly used in a variety of clinical settings, e.g., cardiac surgery [1]. The use of NIRS to measure cerebral oxygenation has been validated in healthy adults [2]. However, rSO_2 measurement using NIRS technology is influenced by various factors, including cerebral arterial/venous blood partitioning, skull thickness, and cerebrospinal fluid (CSF) area [1].

Some reports, including our own, have demonstrated that rSO_2 values are significantly lower in hemodialysis (HD) patients when compared to non-HD ones [3-5]. Although there are several possible explanations for low rSO_2 levels in HD patients, including decreased cerebral perfusion [3, 6], metabolic acidosis [7], and increased area of the CSF layer due to cerebral atrophy [8], the specific cause of the reduced rSO_2 values in HD patients remains unknown.

The primary aim of the study was to assess the accuracy of NIRS to estimate cerebral oxygenation in HD patients undergoing cardiovascular surgery. Preoperative rSO_2 values were compared to jugular venous oxygen saturation ($SjvO_2$), an indirect indicator of global cerebral oxygenation [9], in HD and non-HD patients. We hypothesized that rSO_2 values would underestimate cerebral oxygenation in HD patients.

Methods

This prospective study was approved by the ethics committee at Kyoto University. All participants provided written, informed consent to participate. Adults aged ≥20 years who underwent cardiac or major aortic surgery at Kyoto University Hospital between December 1, 2015 and November 30, 2017 were included. Based on previous research [5], we estimated that about 180 patients met the inclusion criteria during the 2-year study period, of which approximately 30 were dependent on HD. Additionally, other investigations have shown that the standard deviation (SD) of the difference between rSO_2 and $SjvO_2$ (ΔSO_2) is estimated to be 10% [2]. With the probability of type I error set at 0.05 and a sample size of 180, the chance of detecting a 5% and 10% difference in ΔSO_2 between HD and non-HD patients is 70.1% and 99.9%, respectively. Considering that a ΔSO_2 >10% is clinically significant, this sample size would be considered adequate for the purpose of this investigation.

Data collected from the electronic medical records of participants, included age, gender, weight, height, other comorbidities, and preoperative examination findings. In patients who preoperatively underwent computed tomography (CT) scans, the area of frontal CSF layer [10] and skull thickness [8] were calculated from CT images, which included the anterior horn of the lateral ventricle.

Upon entering the operating room, the rSO_2 values were obtained using the INVOS 5100C system (Somanetics, Troy, MI). Probes containing light sources provided two continuous wavelengths of near-infrared light (730 and 810 nm), reaching a brain area corresponding to the junction between the anterior and middle cerebral artery vascularization territory. Two probes were attached to the right and left sides of the forehead with the inferior border approximately 1 cm above the eyebrow and the medial edge at midline. General anesthesia was induced, and patients were tracheally intubated and mechanically ventilated. Blood from the internal jugular vein was collected through cervical puncture of the pulmonary artery catheter or central venous catheter insertion. The $SjvO_2$ values were measured from internal jugular vein blood samples with RapidLab 1265 (Siemens, Erlangen, Germany) and the rSO_2 values were simultaneously recorded from the ipsilateral side.

Data were analyzed using JMP version 8.0 (SAS Institute Japan Ltd., Tokyo, Japan). Continuous data were presented as median (interquartile range), and categorical variables as number (percentage). Differences between groups were compared using the Mann–Whitney U test for continuous variables, and Pearson's chi-square or Fisher's exact tests for categorical variables. Linear regression analysis was used to assess the association between continuous variables. The agreement between rSO_2 and $SjvO_2$ values across all subjects was assessed using a Bland–Altman plot. The degree of error, defined as the difference between rSO_2 and $SjvO_2$ values, was assessed in terms of parametric analysis of the errors, including bias (mean of the difference between rSO_2 and $SjvO_2$ values), SD, and 95% limits of agreement. All statistical tests were two-tailed, and the probability of type I error was set at 0.05. This manuscript adheres to the Guidelines for Reporting Reliability and Agreement Studies [11].

Results

A total of 180 patients underwent cardiac or major aortic surgery during the study period. Of these, 27 did not provide written informed consent and were excluded. Additionally, 23 patients whose $SjvO_2$ was not measured and 17 whose rSO_2 values were not properly collected were excluded; the remaining 113 were included in the analysis. Among these 113, 7 (5.9%) preoperatively received HD. All HD patients had been on dialysis for at least 1 year at the time of surgery (median: 8 years). HD patients had significantly lower rSO_2 values than non-HD ones [44.6% (31.1%–58.0%) vs. 67.4% (65.7%–69.1%); $P < 0.01$]. The area of CSF layer was significantly greater in HD patients than non-HD ones [4.8 (3.8–5.8) vs. 3.6 (3.2–4.0); $P = 0.032$]. There was no statistically significant difference in skull thickness between groups (Table 1).

Linear regression analysis showed that the average slope and intercept for rSO_2 versus $SjvO_2$ were 0.66 and 34.4, respectively, in HD patients and 0.59 and 29.2, respectively, in non-HD patients (Supplementary Figure 1). In HD and non-HD patients, rSO_2 and $SjvO_2$ showed a weak correlation (R^2: 0.46 and 0.28 in HD and non-HD patients, respectively; Supplementary Figure 1). Bland–Altman analysis revealed a significantly greater bias for rSO_2 compared to $SjvO_2$ in HD patients compared to non-HD patients (HD, −19.2%; non-HD, −1.9%; $P < 0.001$; Figure 1). SDs of the error in HD and non-HD patients were 11.5% and 8.9%, respectively; 95% limits of agreement ranged from −41.7% to 3.3% and from −19.3% to 15.5% in HD and non-HD patients, respectively (Figure 1).

Finally, we assessed the association between the area of CSF layer or skull thickness and ΔSO_2 in a subsample of patients who had preoperative CT scans (n = 74). The correlation between the area of CSF layer and ΔSO_2 was weak but statistically significant (R^2, 0.05; $P = 0.047$; Supplementary Figure 2). No correlation was observed between skull thickness and ΔSO_2 (Supplementary Figure 3).

Discussion

In this study, we compared rSO_2 measured using NIRS to $SjvO_2$, a widely used marker of global cerebral oxygenation [9]. When compared to $SjvO_2$, rSO_2 substantially underestimated cerebral oxygenation in HD patients. To the best of our knowledge, this is the first report to assess the accuracy of NIRS in HD patients and demonstrate substantial underestimation of cerebral oxygenation by NIRS in HD patients.

Although several possible explanations for low rSO_2 in HD patients have been suggested [3, 6–8], the precise mechanisms are unknown. In this study, rSO_2 values were lower than $SjvO_2$ values by approximately 20% in HD patients, whereas ΔSO_2 in non-HD patients was −1.9%. These data suggest that underestimation of cerebral oxygenation by NIRS is, at least in part, responsible for the low rSO_2 values in HD patients, which brings into question the validity of cerebral oxygenation monitoring through NIRS in HD patients. Previous studies demonstrated that HD patients showed cerebral atrophy corresponding to approximately 10–20 years of chronological age [3] and an increase in CSF layer area [12] compared to controls. Further, Yoshitani et al. [8] demonstrated a negative correlation between the area of the CSF layer and rSO_2 value. Thus, these data would suggest that the mechanism for the underestimation of cerebral oxygenation by rSO_2 may be due to the increase in the area of the CSF layer, which reduces the intensity of near-infrared light that the detector receives. In our study, the correlation between the area of CSF layer and ΔSO_2 was significant but very weak. Additionally, the association between skull thickness and ΔSO_2 was assessed as skull thickness may influence the distance from the probe to surface of the brain, affecting the rSO_2 values. No significant correlation between skull thickness ΔSO_2 was observed. These data would suggest that neither the CSF layer area nor skull thickness play a large role in the underestimation of cerebral oxygenation seen using NIRS. Further research is required to elucidate the mechanisms, by which cerebral oxygenation is underestimated through NIRS in HD patients.

This study had various limitations. First, continuous monitoring of rSO_2 and $SjvO_2$ would have been preferred to estimate the reliability and accuracy of rSO_2. However, we only collected rSO_2 and $SjvO_2$ simultaneously at one time-point. Continuous monitoring of $SjvO_2$ through internal jugular vein retrograde catheterization is considered relatively invasive. Therefore, a blood sample collected through a single venipuncture was used. The small sample size is another limitation. However, it was sufficient to support our initial hypothesis, because ΔSO_2 was much larger than we expected before the study.

In conclusion, this study demonstrates that rSO_2 values measured using NIRS substantially underestimate cerebral oxygenation in HD patients. Further research is needed to elucidate the specific mechanism of this underestimation in cerebral oxygenation.

Acknowledgments

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Table 1. Patient characteristics stratified by HD.

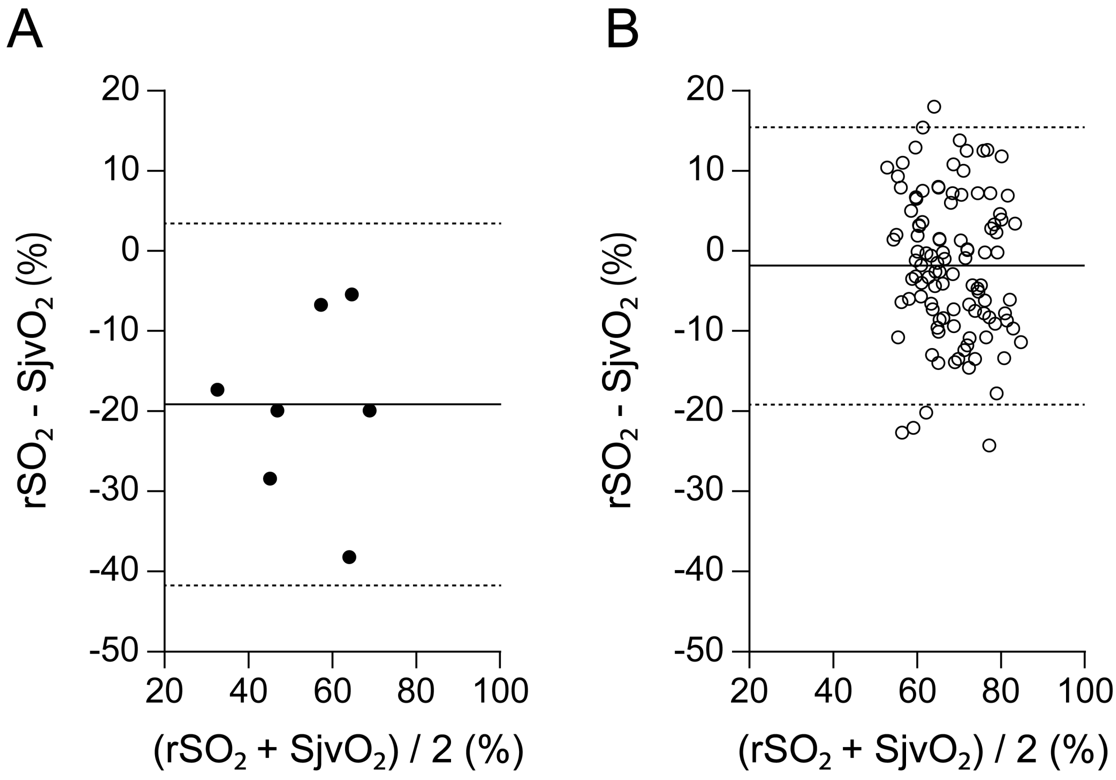
	Non-HD patients (n = 106)	HD patients (n = 7)	P value
Age (years)	67 (64–69)	73 (63–84)	0.027
Female gender	34 (32.1%)	3 (42.86%)	0.556
Wight (kg)	62.5 (59.8–65.1)	62.5 (52.2–72.8)	0.504
Height (m)	1.62 (1.60–1.65)	1.58 (1.50–1.67)	0.302
Hypertension	28 (73.7%)	9 (81.8%)	0.708
Diabetes mellitus	31 (29.3%)	3 (42.9%)	0.163
ASO	2 (1.9%)	1(14.3%)	0.048
LVEF (%)	60.4 (57.7–63.0)	56.2 (43.3–69.1)	0.236
Area of CSF layer (cm^2)	3.6(3.2–4.0)	4.8 (3.8–5.8)	0.032
Skull thickness (cm)	1.10 (1.00–1.19)	1.18(0.43–1.92)	0.800
Mean arterial pressure (mmHg)	75 (66–86)	67 (57–71)	0.047
Percutaneous oxygen saturation (%)	100 (99–100)	100 (99–100)	0.834
Internal jugular vein blood gas analysis			
pH	7.38(7.37–7.39)	7.36(7.33–7.39)	0.078
Partial pressure of carbon dioxide (mmHg)	45.7 (43.1–49.2)	48.1 (43.8–51.4)	0.374
Partial pressure of oxygen (mmHg)	42.4 (38.4–47.0)	39.4 (34.9–46.9)	0.656
Base Excess (mmol/L)	0.95(0.47–1.44)	0.51(-1.94–2.97)	0.34

Hemoglobin concentration (g/dL)	11.8(11.4–12.1)	10.7 (9.6–11.8)	0.025
$SjvO_2$ (%)	69.6 (61.7–77.2)	60.5 (56.7–78.7)	0.292
rSO_2 (%)	67.4 (65.7–69.1)	44.6 (31.1–58.0)	0.003
rSO_2 - $SjvO_2$ (%)	−1.7 (−8.3 to 4.7)	−19.7 (−28.2 to −6.5)	<0.001

Area of CSF layer and skull thickness measured in 6 HD and 68 non-HD patients who preoperatively underwent head computed tomography scan. Mean arterial pressure and percutaneous oxygen saturation at the timing of internal jugular vein blood sampling was recorded. HD, hemodialysis; ASO, arteriosclerosis obliterans; LVEF, left ventricular ejection fraction; rSO_2, regional cerebral oxygen saturation

Figure legend

Figure 1. Bland–Altman plots demonstrating the agreement between rSO_2 and $SjvO_2$ of HD patients (Figure 1A) and non-HD patients (Figure 1B). The y-axis represents the difference between rSO_2 and $SjvO_2$, and the x-axis represents the mean of rSO_2 and $SjvO_2$. The solid line represents mean bias between rSO_2 and $SjvO_2$, and the dashed lines represent limits of agreement. rSO_2, regional cerebral oxygen saturation; $SjvO_2$, jugular venous saturation; HD, hemodialysis



Supplementary materials

Supplement to: Matsukawa S, Kai S, Mizota T. Near-infrared spectroscopy underestimates cerebral oxygenation in hemodialysis patients. J Anesth.

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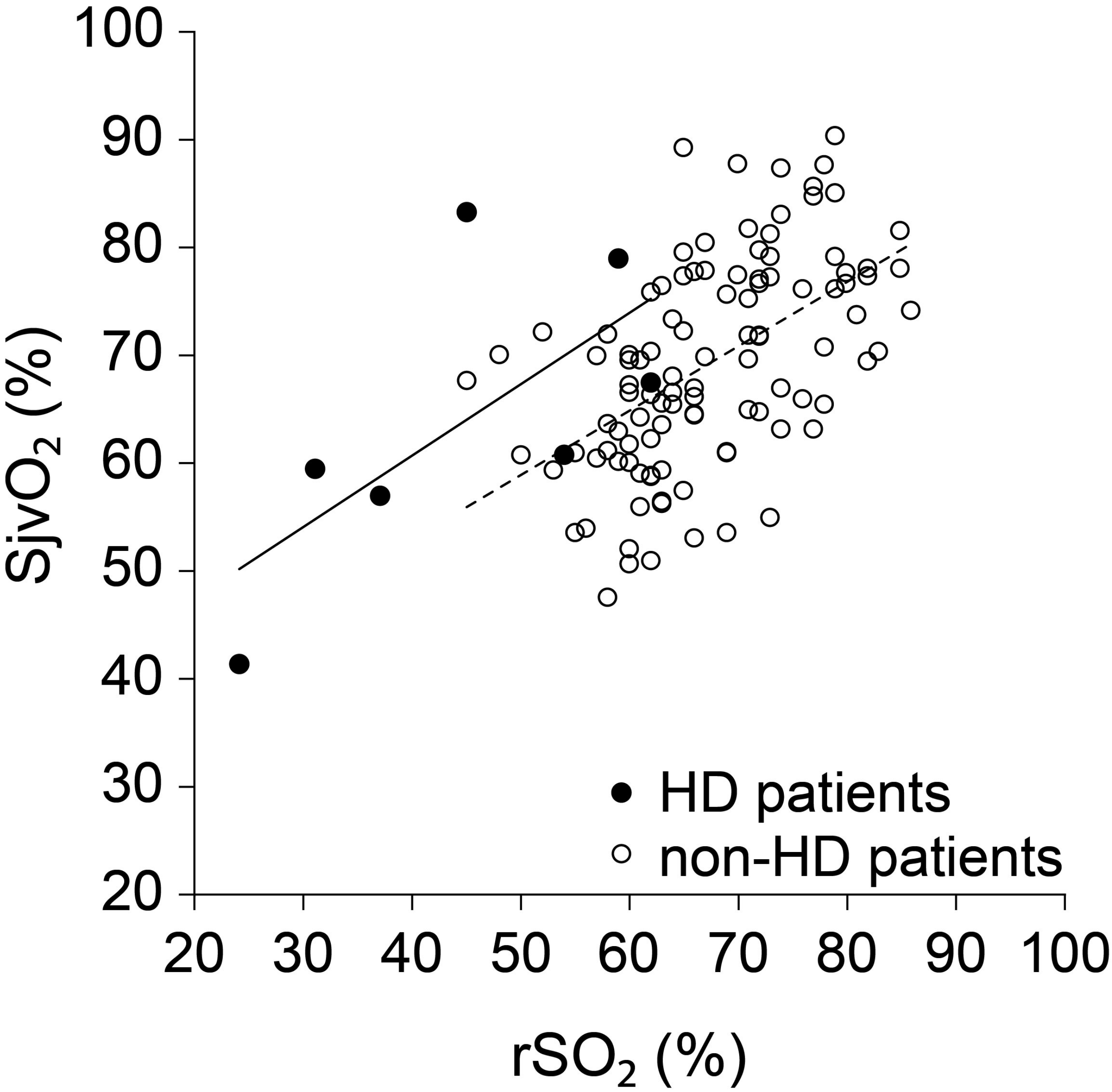
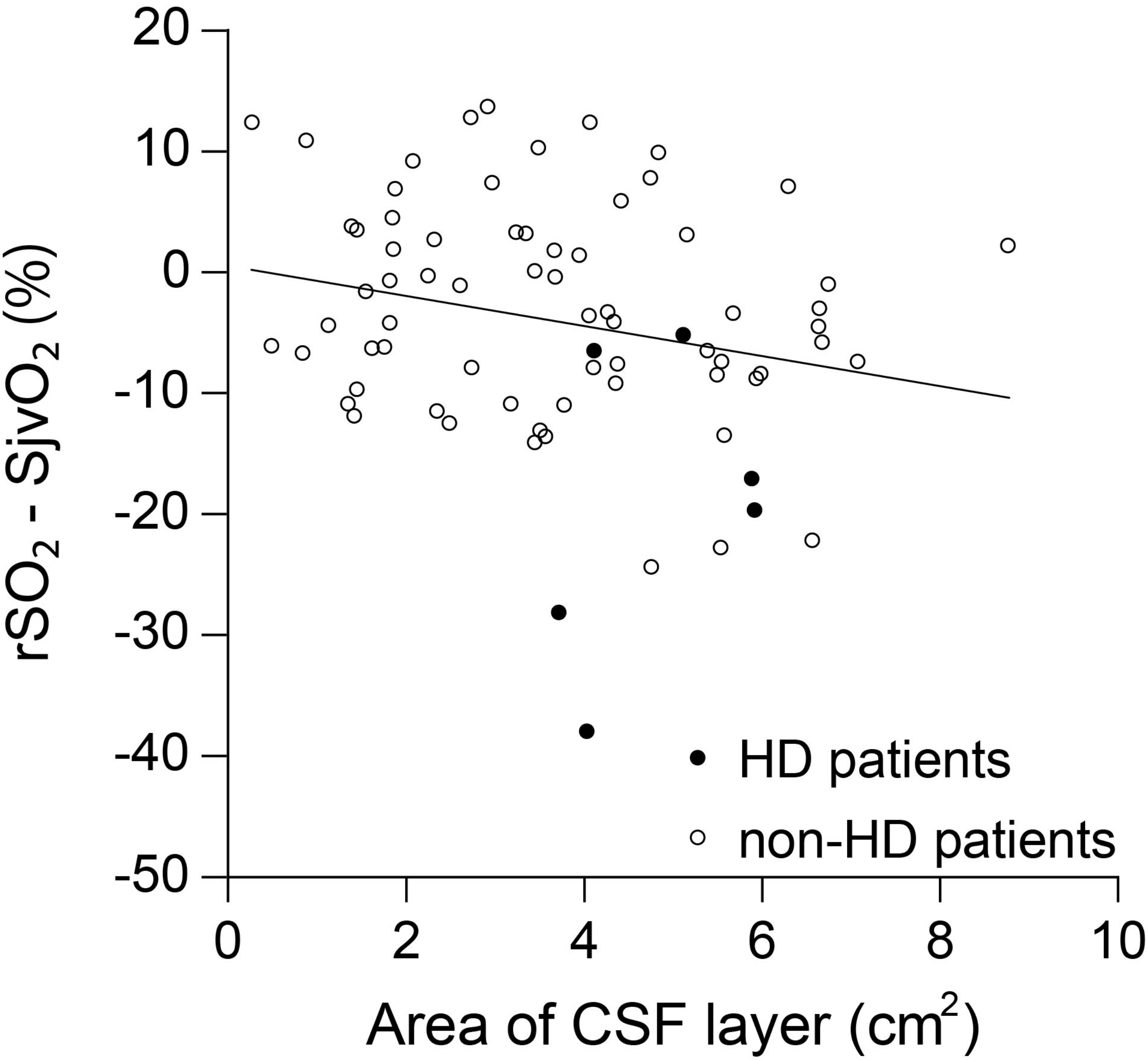
Supplementary Figure 1. Scatter plot of rSO_2 and $SjvO_2$. The solid line represents the linear regression line for HD patients, whereas the dashed line represents that for non-HD patients. rSO_2, regional cerebral oxygen saturation; $SjvO_2$, jugular venous saturation; HD, hemodialysis



Supplementary Figure 2. Scatter plot of area of CSF layer and the difference between rSO_2 and $SjvO_2$. Area of CSF layer measured in 6 HD and 68 non-HD patients who preoperatively underwent head computed tomography scan. The solid line represents the linear regression line for all patients. rSO_2, regional cerebral oxygen saturation; $SjvO_2$, jugular venous oxygen saturation; HD, hemodialysis



Supplementary Figure 3. Scatter plot of skull thickness and the difference between rSO_2 and $SjvO_2$. Skull thickness measured in 6 HD and 68 non-HD patients who preoperatively underwent head computed tomography scan. rSO_2, regional cerebral oxygen saturation; $SjvO_2$, jugular venous oxygen saturation; HD, hemodialysis