

RESEARCH ARTICLE

# Accuracy of Pulse Oximeters in Detecting Hypoxemia in Patients with Chronic Thromboembolic Pulmonary Hypertension

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## Abstract

### Purpose

Pulse oximetry is routinely used to continuously and non-invasively monitor arterial oxygen saturation (SaO<sub>2</sub>). When oxygen saturation by pulse oximeter (SpO<sub>2</sub>) overestimates SaO<sub>2</sub>, hypoxemia may be overlooked. We compared the SpO<sub>2</sub> - SaO<sub>2</sub> differences among three pulse oximeters in patients with chronic thromboembolic pulmonary hypertension (CTEPH) who spent their daily lives in a poor oxygen state.

### Material and Method

This prospective observational study recruited 32 patients with CTEPH undergoing elective cardiac catheterization. As we collected arterial blood samples in the catheter laboratory, SpO<sub>2</sub> values were simultaneously recorded. Three pulse oximeters were used on each patient, and SpO<sub>2</sub> values were compared with oximetry readings using a blood gas analyzer. To determine the optimal SpO<sub>2</sub> value by which to detect hypoxemia (SaO<sub>2</sub> ≤ 90%), we generated receiver operating characteristic (ROC) curves for each pulse oximeter.

### Result

The root mean square of each pulse oximeter was 1.79 (OLV-3100), 1.64 (N-BS), and 2.50 (Masimo Radical). The mean bias (SpO<sub>2</sub> - SaO<sub>2</sub>) for the 90%–95% saturation range was significantly higher for Masimo Radical (0.19 +/- 1.78% [OLV-3100], 0.18 +/- 1.63% [N-BS], and 1.61 +/- 1.91% [Masimo Radical]; p < 0.0001). The optimal SpO<sub>2</sub> value to detect hypoxemia (SaO<sub>2</sub> ≤ 90%) was 89% for OLV-3100, 90% for N-BS, and 92% for Masimo Radical.

### Conclusion

We found that the biases and precision with which to detect hypoxemia differed among the three pulse oximeters. To avoid hypoxemia, the optimal SpO<sub>2</sub> should be determined for each pulse oximeter.

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## Introduction

Pulse oximeters measure oxyhemoglobin saturation ( $SpO_2$ ).  $SpO_2$  is routinely used worldwide not only in the intensive care unit (ICU) [1] and operating room, but also in outpatients [2] to detect patients at risk for hypoxemia. Because a reduction of  $F_{I}O_2$  benefits patients with respiratory failure, it is recommended to maintain a  $SpO_2$  in mechanically-ventilated patients at approximately 90% [3]. The mechanical ventilation protocol summary by the ARDS network states that the oxygenation goal of patients with ARDS is 55–80 mmHg of  $PaO_2$  or 88–95% of  $SpO_2$ .

Because such recent oxygen therapies substitute the  $SpO_2$  for  $SaO_2$ , the accuracy of pulse oximeters around 90% is crucial to avoid hypoxemia, but some studies suggest that  $SpO_2$  overestimates  $SaO_2$ , especially in patients with critically illnesses. [4] [5]. In a retrospective study including patients with septic shock, Wilson et al. [6] reported that the mean bias ( $SpO_2 - SaO_2$ ) was positive and 2.75 +/- 3.1%. Wilson et al. [6] also showed that among patients with 90%–93%  $SpO_2$  value, 50% of patients were with hypoxemia ( $SaO_2 < 90\%$ ). Jubran et al. [7] retrospectively evaluated patients in the ICU and found that the cut-off value of  $SpO_2$  to detect hypoxemia ( $SaO_2 < 90\%$ ) should be 94%. These results alert the possibility that  $SpO_2$  overestimates  $SaO_2$  in the ICU, and a cut-off value of  $SpO_2 < 90\%$  may leave patients at risk for hypoxemia.

Because each pulse oximeter follows different algorithms, it is necessary to define optimal  $SpO_2$  values to avoid hypoxemia by gathering  $SaO_2$  and  $SpO_2$  data prospectively from patients in the ICU. Of note, patients in the ICU have different backgrounds and frequently have hemodynamic instability and hypoxemia. Studies have shown that these factors influence the  $SpO_2$  values [6] [8]. Therefore, patients with poor oxygenation and without hemodynamic instability, hypercapnia and acidosis may be ideal candidates for defining optimal  $SpO_2$  values to avoid hypoxemia.

In the current study we hypothesized that the accuracy of pulse oximeters can be evaluated in hypoxic patients without hemodynamic instability. For this purpose we recruited patients with chronic thromboembolic pulmonary hypertension (CTEPH) because these patients were considered to live with poor oxygenation. When patients with CTEPH underwent elective cardiac catheterization, we attached 3 different pulse oximeters on their fingers. We measured  $SpO_2$  using three pulse oximeters and  $SaO_2$  simultaneously, and calculated biases ( $SpO_2 - SaO_2$  differences).

## Materials & Methods

### Study Design and Data Collection

This prospective observational study was conducted at Kyorin University Hospital in Tokyo, Japan. This study protocol was approved by our Institutional Review Board on Human Research (number H25-028). Written informed consent of this study was obtained from all patients. The study period was between September 2013 and February 2014. Thirty-two patients with CTEPH who underwent elective cardiac catheterization were recruited in this study.

When right heart catheterization and percutaneous transluminal pulmonary angioplasty [9] are performed in the catheterization laboratory, we routinely monitor  $SpO_2$  and  $SaO_2$  in all patients. For the current study, to compare the accuracy of different pulse oximeters, we used three pulse oximeters from three different companies, as follows: OLV-3100 (Nihonkohden, Nishiochiai, Tokyo, Japan); N-BS (Nellcor Puritan Bennett, Pleasanton, CA, USA); and Masimo Radical (Masimo, Irvine, CA, USA). The finger probes used were TL-273T3 (Nihonkohden), D-25 (Nellcor Puritan Bennett), and LNOP Neo-L (Masimo Radical). Each patient

was randomly mounted with a total of 3 finger probes from each pulse oximeter on the 2nd, 3rd, and 4th fingers.

The arterial catheter was placed into the radial artery ipsilateral to the pulse oximeter probe. Arterial blood samples were collected anaerobically through the arterial line when patient's condition was stable and SpO<sub>2</sub> values were stable for > 30 seconds. Each SpO<sub>2</sub> value was recorded simultaneously as we collected blood samples. The functional SaO<sub>2</sub> (HbO<sub>2</sub> / [hemoglobin+HbO<sub>2</sub>]) was determined using a blood gas analyzer (ABL 825; Radiometer, Copenhagen, Denmark). Fractional SaO<sub>2</sub> was calculated from the functional SaO<sub>2</sub> and the measured levels of carboxyhemoglobin and methemoglobin. Quality control standards were run each day. We tried to obtain 3 arterial blood samples from each patient at different time points.

In addition to patients with CTEPH, we enrolled 5 healthy volunteers to collect control data. Under room air condition, 5 healthy volunteers were mounted with 3 finger probes from 3 pulse oximeters, and arterial blood samples were collected anaerobically from their radial artery.

## Statistical Analysis

Assuming an SD of SpO<sub>2</sub> to be 2 to 3%, we estimated that a sample of 30 patients would need to be enrolled in order for the study to have 90% power, at a two-tailed significance level of 0.05, to detect a mean between-group difference of 1 SD. Data are expressed as the mean +/- standard deviation (SD) and root-mean-square (RMS), as the international standard of pulse oximeter equipment (ISO 9919) states the accuracy of the pulse oximeter equipment in terms of the RMS difference [10]. Data were also analyzed in 3 subgroups of SaO<sub>2</sub> (85% < SaO<sub>2</sub> ≤ 90%, 90% < SpO<sub>2</sub> ≤ 95%, and 95% < SaO<sub>2</sub> ≤ 100%). Statistical analysis was performed by one-way analysis of variance followed by Tukey's test. To assess agreement between SpO<sub>2</sub> and SaO<sub>2</sub>, a Bland-Altman plot was created, and the mean difference as bias, SD as precision, and the 2SD of difference as 95% limits of agreement were calculated. To assess the accuracy of each pulse oximeter to detect hypoxemia, the sensitivity, specificity, and positive and negative predictive values (PPV and NPV) were calculated. Receiver operating characteristic (ROC) curves were constructed. The closest value to the best specificity and sensitivity point on the ROC curve was identified, and the optimal SpO<sub>2</sub> value for each pulse oximeter was determined. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Omiya, Japan) which is a graphical user interface for R (The R Foundation for Statistical Computing, version 3.1.1) [11]. The levels of significance were set at a p = 0.05.

## Results

### Patient characteristics

We enrolled 32 patients in this study. Table 1 shows the demographics and results of blood gas sampling obtained immediately after arterial catheter placement. Although we tried to obtain three SpO<sub>2</sub> data by three pulse oximeters at the same time when we collected blood samples, we failed to collect some SpO<sub>2</sub> values. Therefore, we obtained 92 arterial blood samples, 88 SpO<sub>2</sub> data points by OLV-3100 (Nihonkohden), 80 data points by N-BS (Nellcor), and 75 data points by Masimo Radical (Masimo). At the beginning of right heart catheterization, the mean values with SD were 93.1% +/- 3.5% for SaO<sub>2</sub>. Fig 1 represents the SaO<sub>2</sub> data obtained immediately after arterial catheter placement. Of 32 patients with CTEPH, 21 (65.6%) had an initial SaO<sub>2</sub> < = 95%.

**Table 1. Demographics and laboratory data of the patients.**

Variable	Value
Gender (Male / Female)	8 / 24
Age (years)	62.9 +/- 14.7
Height (cm)	156.5 +/- 8.4
Weight (kg)	56.0 +/- 12.6
SaO <sub>2</sub> (%)	93.1 +/- 3.5
pH	7.432 +/- 0.024
PaCO <sub>2</sub> (mmHg)	35.3 +/- 3.4
PaO <sub>2</sub> (mmHg)	66.4 +/- 12.3
Hb (g/dL)	12.1 +/- 1.8
Fraction of Oxyhemoglobin (%)	90.4 +/- 3.3
Carboxyhemoglobin (%)	1.9 +/- 1.2
Deoxyhemoglobin (%)	6.6 +/- 3.0
Methemoglobin (%)	1.0 +/- 0.1

The demographics and results of blood gas sampling obtained immediately after arterial catheter placement are shown. Data are presented as the means ± SD.

SaO<sub>2</sub> oxyhemoglobin saturation measured by blood gas analyzer (ABL 825), PaO<sub>2</sub> partial pressure of oxygen in arterial blood, PaCO<sub>2</sub> partial pressure of arterial carbon dioxide, Hb hemoglobin

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### Calculated biases (SpO<sub>2</sub>—SaO<sub>2</sub>)

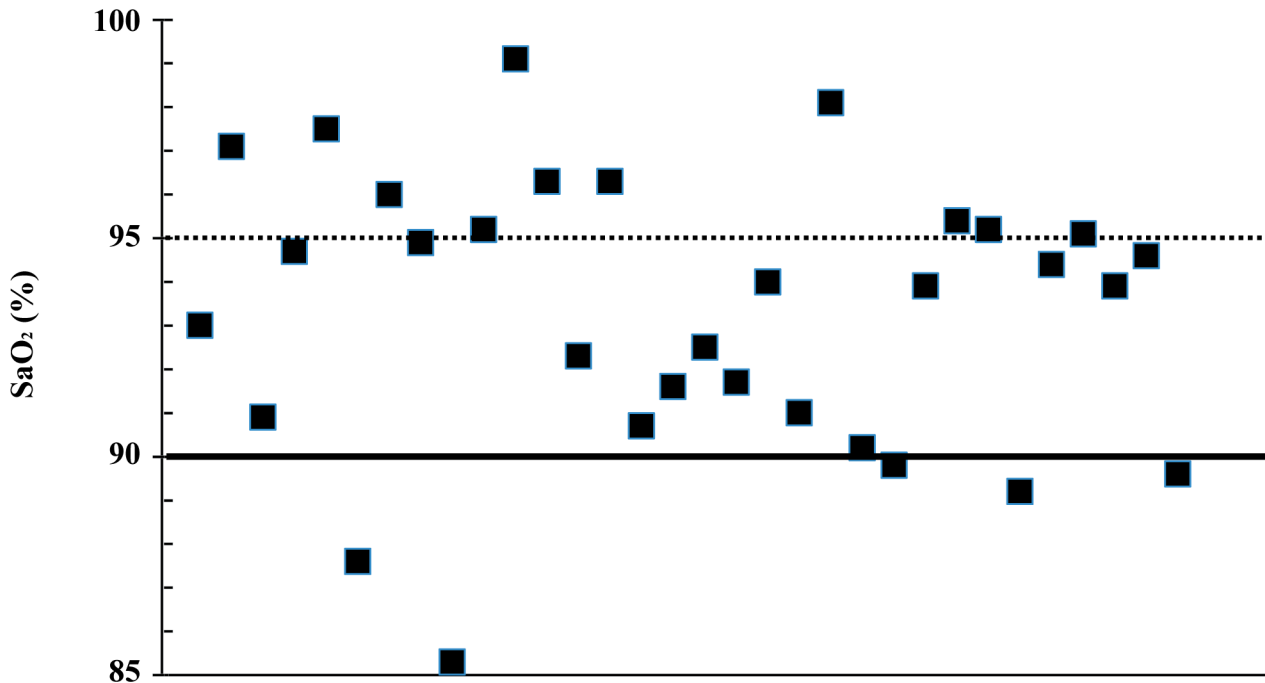
We collected control data from 5 healthy volunteers. [Table 2](#) summarizes data from healthy controls mounted with 3 finger probes from 3 pulse oximeters under room air condition. In 5 patients tested, all the 3 pulse oximeters qualified  $RMS \leq 4$  (the ISO 9919).

[Table 3](#) shows the calculated mean biases (SpO<sub>2</sub>—SaO<sub>2</sub>) measured by 3 pulse oximeters for the 85%–100% saturation range. All three pulse oximeters showed positive biases, suggesting that SpO<sub>2</sub> overestimated SaO<sub>2</sub>. The mean bias by Masimo Radical was significantly higher than the mean bias by Nihonkohden OLV-3100 and Nellcor N-BS ( $P < 0.0001$ ). Although all 3 pulse oximeters qualified for the ISO 9919 ( $RMS \leq 4$ ); the RMS by Masimo Radical had the highest value. [Fig 2](#) is the Bland Altman plot indicating a bias and limits of agreement.

Some patients had oxygen administered to avoid hypoxemia during the procedure. Actually, 35/92 blood samples were collected from patients with oxygen inhalation. [Table 4](#) shows data from patients under room air condition.

### Subgroup analysis

We questioned whether or not the biases of pulse oximeters are influenced by the SaO<sub>2</sub> range. [Fig 3](#) shows the calculated biases (SpO<sub>2</sub>—SaO<sub>2</sub>) in the 5% range of SaO<sub>2</sub>. Because the number of samples was small ( $n = 17$ ), SD values tended to be higher in the  $85\% < SaO_2 \leq 90\%$  range. The mean bias by the Masimo Radical for the  $90\% < SpO_2 \leq 95\%$  saturation range was significantly higher compared with the mean bias by the Nihonkohden OLV-3100 and Nellcor N-BS (0.19 +/- 1.99 for Nihonkohden OLV-3100, 0.34 +/- 1.52 for Nellcor N-BS, and 2.26 +/- 1.53 for Masimo Radical;  $p < 0.0001$  vs. Nihonkohden 3100 and Nellcor N-BS). There were no significant differences in the other 2 ranges ( $85\% < SpO_2 \leq 90\%$  and  $95\% < SpO_2 \leq 100\%$  saturation range).



**Fig 1. SaO<sub>2</sub> (oxyhemoglobin saturation) data of 32 patients obtained immediately after arterial catheter placement.** Before right heart catheterization, each patient had an arterial catheter placed into their radial artery ipsilateral to the pulse oximeter probes. Arterial blood was sampled, and the SaO<sub>2</sub> was measured by blood gas analyzer (ABL 825). Closed squares indicate initial SaO<sub>2</sub> values of 32 patients enrolled in this study.

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### Cut-off value of SpO<sub>2</sub>

We hypothesized that the cut-off value of each pulse oximeter to detect hypoxemia (SaO<sub>2</sub> ≤ 90% or PaO<sub>2</sub> ≤ 60 mmHg) was different. We calculated the sensitivity, specificity, PPV, and NPV of each pulse oximeter to detect hypoxemia (Table 5 and Table 6). As shown in Table 5, the specificity ([patients with SaO<sub>2</sub> > 90 and SpO<sub>2</sub> > 90] / [patients with SaO<sub>2</sub> > 90]) by Masimo Radical was 45.5% and the NPV ([patients with SaO<sub>2</sub> > 90 and SpO<sub>2</sub> > 90] / [patients with SpO<sub>2</sub> > 90]) by Nihonkohden 3100 was 65.0%.

Next, we calculated the optimal SpO<sub>2</sub> value to detect hypoxemia by constructing ROC curves. The optimal SpO<sub>2</sub> value was 89% for Nihonkohden 3100, 90% for Nellcor N-BS, and 92% for Masimo Radical. Using the optimal SpO<sub>2</sub> value of each pulse oximeter, the sensitivity, specificity, PPV, and NPV were re-calculated. The specificity by Masimo Radical increased from 45.5% to 81.8%, although the NPV decreased from 100% to 69.2%. The NPV by Nihonkohden 3100 increased from 65.0% to 86.7%, and the sensitivity also increased from 90.3% to 97.2%.

**Table 2. Calculated biases between SaO<sub>2</sub> (oxyhemoglobin saturation measured by blood gas analyzer [ABL 825]) and SpO<sub>2</sub> (oxyhemoglobin saturation measured by 3 pulse oximeters) among 5 healthy volunteers.**

	Nihonkohden OLV-3100	Nellcor N-BS	Masimo Radical
Number of samples	5	5	5
SpO <sub>2</sub> —SaO <sub>2</sub>	0.54 +/- 1.14	0.74 +/- 1.55	1.70 +/- 1.41
RMS of (SpO <sub>2</sub> —SaO <sub>2</sub> )	1.16	1.56	1.70

The calculated mean biases (SpO<sub>2</sub>—SaO<sub>2</sub>) measured by 3 pulse oximeters are shown. Data are presented as the mean ± SD.

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**Table 3. Calculated biases between SaO<sub>2</sub> (oxyhemoglobin saturation measured by blood gas analyzer [ABL 825]) and SpO<sub>2</sub> (oxyhemoglobin saturation measured by 3 pulse oximeters).**

	Nihonkohden OLV-3100	Nellcor N-BS	Masimo Radical
Number of samples	88	80	75
SpO <sub>2</sub> —SaO <sub>2</sub>	0.19 +/- 1.78	0.18 +/- 1.63	1.61 +/- 1.91 *
RMS of (SpO <sub>2</sub> —SaO <sub>2</sub> )	1.79	1.64	2.50

The calculated mean biases (SpO<sub>2</sub>—SaO<sub>2</sub>) measured by 3 pulse oximeters for the 85%–100% saturation range are shown. Data are presented as the mean ± SD and analyzed by one-way analysis of variance followed by Tukey's test.

\*p<0.0001 vs. Nihonkohden OLV-3100 and Nellcor N-BS

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## Discussion

### Key findings

In this study we evaluated the accuracy of three pulse oximeters to detect hypoxemia in patients with CTEPH who spend their daily life in a poor oxygen state. Among 32 patients enrolled in this study, 21 (65.6%) had a SaO<sub>2</sub> < = 95%. We found that all three pulse oximeters had positive biases, suggesting that all SpO<sub>2</sub> values overestimated SaO<sub>2</sub> values. Among 3 pulse oximeters, significant differences were detected in calculated biases (SpO<sub>2</sub>—SaO<sub>2</sub>), especially in the 90% < SaO<sub>2</sub> ≤ 95% range. We also found that the optimal cut-off values to detect hypoxemia were slightly different among the 3 pulse oximeters (89% for Nihonkohden 3100, 90% for Nellcor N-BS, and 92% for Masimo Radical). Our results suggest that when we substitute SpO<sub>2</sub> for SaO<sub>2</sub>, the optimal SpO<sub>2</sub> should be determined for each pulse oximeter to avoid hypoxemia.

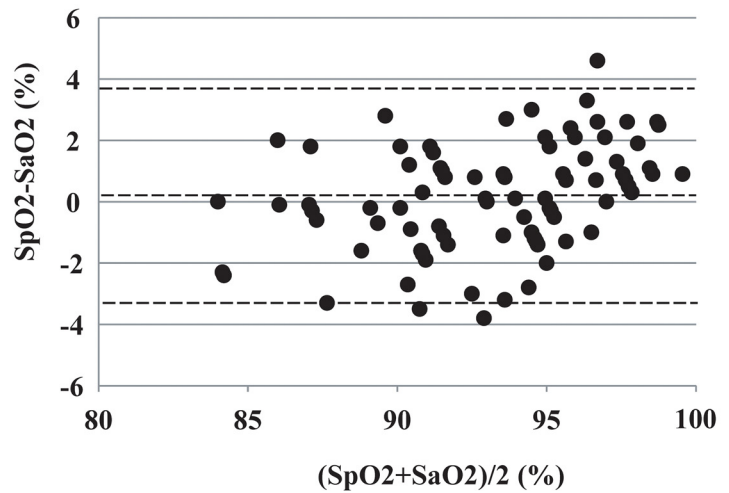
### Relationship to previous studies

Several data suggest that SpO<sub>2</sub> overestimates SaO<sub>2</sub> in patients with critically illnesses. In an observational prospective study involving patients admitted to the ICU, Van de Louw et al. [1] reported that the accuracy of SpO<sub>2</sub> appeared to be influenced by the type of oximeter, the presence of hypoxemia, and the requirement for vasoactive drugs. Van de Louw et al. [1] suggested that a SpO<sub>2</sub> > 94% appears necessary to ensure a SaO<sub>2</sub> of 90%. In a retrospective study, Wilson et al. [6] showed that pulse oximetry overestimated the SaO<sub>2</sub> by a mean of 2.75% in emergency department patients with severe sepsis and septic shock. Wilson et al. [6] found that the overestimation was exacerbated by the presence of hypoxemia. Of ICU patients, Ghayumi et al. [12] showed that a SpO<sub>2</sub> cut-off value ≤ 94% could predict hypoxemia (PaO<sub>2</sub> < 60 mmHg) with a sensitivity of 100% and a specificity of 95% in liver transplant candidates. The Ghayumi et al. [12] study included patients with a mean SaO<sub>2</sub> value of 95.19%, in contrast to the 93.1% mean SaO<sub>2</sub> value in our study, with more stable conditions of patients. Our results are consistent with previous studies that showed SpO<sub>2</sub> overestimates SaO<sub>2</sub>. (1,6)

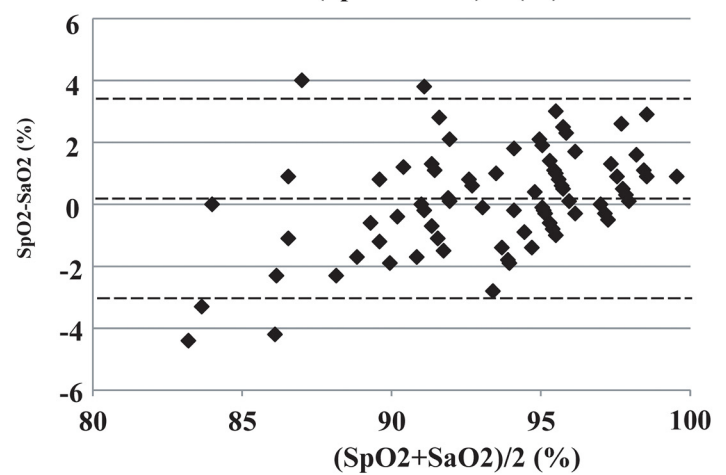
### Significance and implications

In this study we put more emphasis on the ability of pulse oximeters to detect hypoxemia rather than RMS differences (SpO<sub>2</sub>—SaO<sub>2</sub>) that is an international standard parameter of the accuracy of SpO<sub>2</sub>. We found that Masimo Radical had 100% of sensitivity and NPV with lowest specificity (Table 5). These statistical parameters suggest that Masimo Radical is most reliable when patients have a SaO<sub>2</sub> < = 90%. In the clinical setting, especially in ICU, the purpose of monitoring SpO<sub>2</sub> is to avoid hypoxemia, keeping the SaO<sub>2</sub> > 90%. After applying a calculated optimal SpO<sub>2</sub> (92% for the Masimo Radical), the specificity increased from 45.5% to 81.8%, while the NPV decreased from 100% to 69.2%. These changes in statistical parameters are

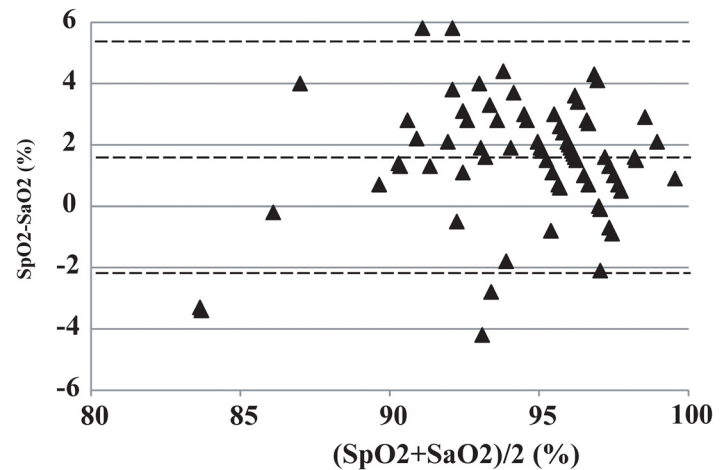
Nihonkohden  
OLV-3100



Nellcor  
N-BS



Masimo  
Radical



**Fig 2. Bland Altman plot comparing SaO<sub>2</sub> (oxyhemoglobin saturation measured by blood gas analyzer (ABL 825)) and SpO<sub>2</sub> (oxyhemoglobin saturation measured by 3 pulse oximeters).** For each data point, the mean value  $[(SpO_2 + SaO_2)/2]$  is presented on the x-axis, and the difference value  $(SpO_2 - SaO_2)$  on the y-axis. *Black lines* represent the 95% confidence interval for SpO<sub>2</sub> [bias  $\pm$  2 standard deviation (SD)]. The mean difference value  $(SpO_2 - SaO_2)$  represents the bias, and SD represents the precision. Oximeters are: A. Nihonkohden OLV-3100, B. Nellcor N-BS, and C. Masimo Radical. Bias was 0.19%  $\pm$  1.79% (mean  $\pm$  SD) by Nihonkohden oximeter, 0.18%  $\pm$  1.64% by Nellcor oximeter, and 1.61%  $\pm$  1.93% by Masimo oximeter.

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**Table 4. Calculated biases between SaO<sub>2</sub> (oxyhemoglobin saturation measured by blood gas analyzer [ABL 825]) and SpO<sub>2</sub> (oxyhemoglobin saturation measured by 3 pulse oximeters) among patients under room air condition.**

	Nihonkohden OLV-3100	Nellcor N-BS	Masimo Radical
Number of samples	54	50	51
SpO <sub>2</sub> —SaO <sub>2</sub>	0.15 +/- 1.94	0.05 +/- 1.95	1.55 +/- 1.55*
RMS of (SpO <sub>2</sub> —SaO <sub>2</sub> )	1.93	1.83	2.63

The calculated mean biases (SpO<sub>2</sub>—SaO<sub>2</sub>) measured by 3 pulse oximeters for the 85%–100% saturation range are shown. Data are presented as the mean ± SD and analyzed by one-way analysis of variance followed by Tukey’s test.

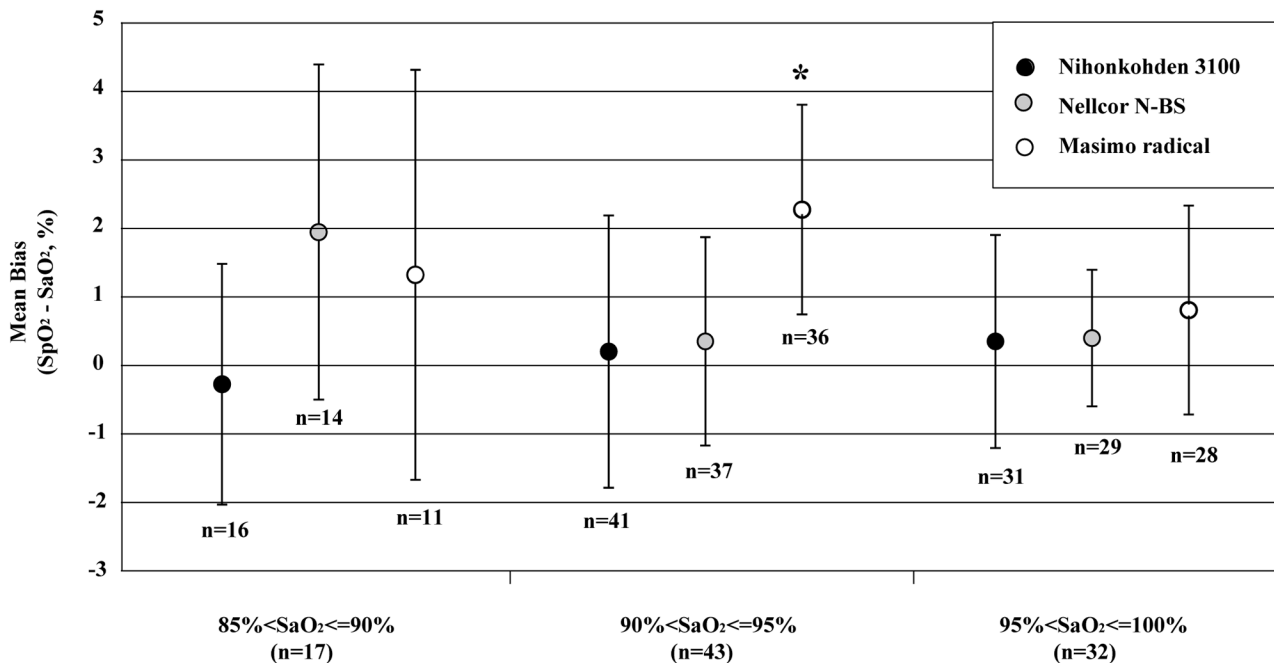
\*p<0.0001 vs. Nihonkohden OLV-3100 and Nellcor N-BS

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more favorable in keeping the SaO<sub>2</sub> > 90%, and beneficial in the clinical setting. These results imply that when we define a statistical “optimal value” for medical monitors, we must consider the clinical purpose of each monitor.

### Strengths and Limitations

There were several limitations in this study. First, because this study was performed in Japan and only included patients with CTEPH, all of the patients were Asian (Japanese) and 75% of the patients were female. Because Feiner et al. [13] reported that skin color and gender are predictive of errors in SpO<sub>2</sub> estimates at low SaO<sub>2</sub> levels (< 80%), our results may not be applicable to patients of general. In addition, some data were gathered during the catheter procedure. These procedures might have affected hemodynamics and resulted in increased biases. Although several factors might have influenced the accuracy of SpO<sub>2</sub>, we speculate that the



**Fig 3. Bias (mean ± SD) for the 3 oximeters in the 5% range of SaO<sub>2</sub> (oxyhemoglobin saturation measured by blood gas analyzer [ABL 825]).** Bias is calculated as SpO<sub>2</sub> (oximeter-measured value of oxyhemoglobin saturation) minus SaO<sub>2</sub>. SpO<sub>2</sub> measured by Nihonkohden 3100 are indicated with closed circles, SpO<sub>2</sub> by Nellcor N-BS with gray circles, and SpO<sub>2</sub> by Masimo radical with open circles. Data are presented as the mean ± SD and analyzed by one-way analysis of variance followed by Tukey’s test: \* p<0.0001 vs. Nihonkohden 3100 and Nellcor N-BS.

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**Table 5. Optimal SpO<sub>2</sub> value and ability of 3 pulse oximeters to detect hypoxemia (SaO<sub>2</sub> ≤ 90%).**

	Cut-off value of SpO <sub>2</sub> (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Nihon-kohden OLV-3100	90	90.3	81.2	95.6	65.0	88.6
Nellcor N-BS	90	93.9	85.7	96.9	75.0	92.5
Masimo Radicalp	90	100	45.5	91.4	100	92.0
	Optimal SpO <sub>2</sub> (%) <sup>#</sup>					
Nihon- kohden OLV-3100	89	97.2	81.2	95.9	86.7	94.3
Nellcor N-BS	90	93.9	85.7	96.9	75.0	92.5
Masimo Radical	92	93.8	81.8	96.8	69.2	92.0

The sensitivity, specificity, positive predictive values, and negative predictive values of each pulse oximeter to detect hypoxemia are shown with the calculated optimal SpO<sub>2</sub> value to detect hypoxemia.

PPV positive predictive values, NPV negative predictive values

Sensitivity = (patients with SaO<sub>2</sub> < 90 and SpO<sub>2</sub> < 90) / (patients with SaO<sub>2</sub> < 90)

Specificity = (patients with SaO<sub>2</sub> > 90 and SpO<sub>2</sub> > 90) / (patients with SaO<sub>2</sub> > 90)

PPV = (patients with SaO<sub>2</sub> < 90 and SpO<sub>2</sub> < 90) / (patients with SpO<sub>2</sub> < 90)

NPV = (patients with SaO<sub>2</sub> > 90 and SpO<sub>2</sub> > 90) / (patients with SpO<sub>2</sub> > 90)

<sup>#</sup>Optimal SpO<sub>2</sub> represents the best compromise between sensitivity and specificity to detect hypoxemia (SaO<sub>2</sub> ≤ 90%)

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unified backgrounds and stable conditions of the patients trump these drawbacks; however, further studies are needed including patients with different races.

Second, we put too much emphasis on detecting SaO<sub>2</sub> values < 90%. SpO<sub>2</sub> is simply a non-invasive monitor substituting SaO<sub>2</sub>. In the clinical situation, especially in the general ward, clinicians have a tendency to expect a safer SpO<sub>2</sub> range, not approximately 90%, but > 95%. With that point of view, there were no significant differences among the 3 pulse oximeters in the 95 < SaO<sub>2</sub> ≤ 100% range. Thus, keeping patients in the 95 < SaO<sub>2</sub> ≤ 100% range, all the pulse oximeters were reliable and there was no need for detecting the optimal SpO<sub>2</sub>. However, recent evidence suggests that conservative oxygen (targeting a SpO<sub>2</sub> between 90% and 92%) therapy may be beneficial to critically ill patients [14]. Indeed, the accuracy of a SpO<sub>2</sub> of approximately

**Table 6. Optimal SpO<sub>2</sub> value and ability of 3 pulse oximeters to detect hypoxemia (PaO<sub>2</sub> ≤ 60 mmHg).**

	Cut-off value of SpO <sub>2</sub> (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Nihon Kohden OLV-3100	90	98.2	61.3	82.4	95.0	85.2
Nellcor N-BS	90	100	57.1	81.2	100	85.0
Masimo Radical	90	100	23.8	77.1	100	78.7
	Optimal SpO <sub>2</sub> (%) <sup>#</sup>					
Nihon Kohden OLV-3100	92	86.0	96.8	98.0	78.9	89.8
Nellcor N-BS	93	82.7	100	100	75.7	88.8
Masimo Radical	95	97.8	95.2	97.8	95.2	97.0

The sensitivity, specificity, positive predictive values, and negative predictive values of each pulse oximeter to detect hypoxemia are shown with the calculated optimal SpO<sub>2</sub> value to detect hypoxemia.

PPV positive predictive values, NPV negative predictive values

Sensitivity = (patients with PaO<sub>2</sub> < 60 and SpO<sub>2</sub> < 90) / (patients with PaO<sub>2</sub> < 60)

Specificity = (patients with PaO<sub>2</sub> > 60 and SpO<sub>2</sub> > 90) / (patients with PaO<sub>2</sub> > 60)

PPV = (patients with PaO<sub>2</sub> < 60 and SpO<sub>2</sub> < 90) / (patients with SpO<sub>2</sub> < 90)

NPV = (patients with PaO<sub>2</sub> > 60 and SpO<sub>2</sub> > 90) / (patients with SpO<sub>2</sub> > 90)

<sup>#</sup>Optimal SpO<sub>2</sub> represents the best compromise between sensitivity and specificity to detect hypoxemia (PaO<sub>2</sub> ≤ 60 mmHg)

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90% may be important for future oxygen therapy. We suggest that further studies are warranted to evaluate “optimal” oxygen therapy on the assumption that SpO<sub>2</sub> overestimates SaO<sub>2</sub>, and optimal SpO<sub>2</sub> to detect hypoxemia differs among pulse oximeters.

Third, because this study was limited to patients with CTEPH, these results should be limited to normo/or hypocapnic patients, and may not be applicable to patients with hypercapnia, acidosis and hemodynamic instability. As oxygen dissociation curve clearly illustrates, the SaO<sub>2</sub> sure changes according to PaCO<sub>2</sub> level and pH. It is also well-known that hemodynamic instability affects the accuracy of pulse oximeters [6]. Further studies are recommended including patients with COPD, who spend their daily life with hypercapnia, and patients with septic shock.

## Conclusions

In conclusion, we found that SpO<sub>2</sub> measured by 3 pulse oximeters overestimated the SaO<sub>2</sub>, and the optimal cut-off value to detect hypoxia was slightly different among 3 pulse oximeters (89% for Nihonkohden 3100, 90% for Nellcor N-BS, and 92% for Masimo Radical). We suggest that when SpO<sub>2</sub> is substituted for SaO<sub>2</sub>, optimal SpO<sub>2</sub> should be determined for each pulse oximeter to avoid hypoxemia.

## Author Contributions

Conceived and designed the experiments: KM TY. Performed the experiments: TK RK MK KU TS. Analyzed the data: KM. Contributed reagents/materials/analysis tools: KM. Wrote the paper: TK KM TS TY.

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