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Significance of tissue oxygenation in patients connected to a mechanical ventilator

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Abstract

The aim of this study is to investigate whether the follow-up of patients on a mechanical ventilator using a tissue oxygenation device is superior to that using an O2 saturation probe. Our study was conducted at the Necmettin Erbakan University Meram Medical School Emergency Medicine Critical Care Unit between 01/04/2016 and 01/06/2016. Patients over the age of 18, non-pregnant, and followed up on mechanical ventilators were prospectively recruited, and the saturations of the patients with tissue oxygenation devices and pulse oximetry were evaluated and compared. SPSS (ver. 19.0) was used for the statistical analysis of the collected data, and the descriptive measures of all the obtained variables were calculated. The collected data revealed a statistically significant positive correlation between oxygen saturation measured by pulse oximetry and tissue oxygen saturation (StO2) in the patient group (n = 53), in which deceased and discharged patients were evaluated together. Both the hemoglobin levels and StO2 were low in the sepsis patients. It is important to follow tissue perfusion in intensive care patients, and this can be done with a noninvasive method. The results of our study reveal that perfusion should be followed with tissue oxygenation in patients on mechanical ventilators because low tissue oxygenation indicates increased patient mortality.

Keywords: saturation, tissue oxygenation, mechanical ventilator, hypoperfusion

1. Introduction

Monitoring tissue oxygenation adequacy is important for ensuring organ functions in the follow-up and treatment of critically ill patients (1). An important factor affecting morbidity and mortality in sepsis and critically ill patients is tissue hypoxia, which is caused by an imbalance between oxygen delivery and tissue oxygen utilization (2). A tissue oxygenation device is used alongside infrared spectroscopy to measure the local oxygen saturation of hemoglobin and the total hemoglobin index in the tissue (StO_2). With the rotating light absorption spectrum of a tissue sample, the concentrations of oxyhemoglobin and deoxyhemoglobin vary substantially. The percentage of StO_2 is determined by hemoglobin oxygen saturation, which is limited by the tissue value in the blood.

The most important technological progress in oxygenation monitoring is the introduction of pulse oximeters (PO). Oximeters are used for the frequent monitoring of SO_2 owing to the regular occurrence of hypoxemia in ICU patients, the necessity of adjusting the O_2 concentration frequently given to avoid inadequate treatment or O_2 toxicity, and the inability to clinically detect mild hypoxemia (3). PO was developed based on the pulsation of arterial blood flow and the absorption of light of two different wavelengths by oxyhemoglobin and reduced hemoglobin (4). It mathematically calculates arterial SO_2 from the hemoglobin saturation it measures during systole and diastole. Although the measurements made with PO are quite reliable, it is necessary to consider some factors to check this reliability. The fact that the peripheral pulse or ECG rhythm and the oximeter pulse wave are identical suggests that the measurement is reliable. If the SO_2 is between 70% and 92%, there is a ±4% variation range; if it is below 70%, its reliability decreases (5); If it is over 92%, it is generally accepted as correct and parallel with PaO_2 (6). Therefore, it is necessary to keep SO_2 above 92% in monitoring oxygen therapy.

The aim of this study was to investigate whether follow-up with a device that measures the tissue oxygenation of patients on a mechanical ventilator is superior to the O_2 saturation probe.

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2. Materials and Methods

The study was carried out with the permission of University of Necmettin Erbakan Meram Faculty of Medicine Ethichs Comite (Date 30.03.2016, Decision no: 2016/124). All procuderes were carried out in accordance with the etical rules and the principles of the Declaration of Helsinki.

2.1. Study design

Our study was conducted in the Necmettin Erbakan University Meram Emergency Medicine Critical Intensive Care Unit between 01/04/2016 and 01/06/2016. Patients over the age of 18, who were not pregnant and on mechanical ventilators, were recruited prospectively. A voluntary consent form was signed by the relatives of the patients, and the patients who would participate in the study were determined after their consent was obtained.

2.2. Study population

The conditions for inclusion in the study were that the patients should be connected to a mechanical ventilator and be women over the age of 18 who were not pregnant. Men and women were included in the study regardless of gender. Patients were included in the study with permission from their relatives.

2.3. Data collection

The names, ages, genders, and file numbers of the patients included in the study were recorded. The blood gases of the patients were collected using a tissue oxygenation device, and measurements were made with pulse oximetry. Measurements were made with a tissue oxygenation device in the right and then in the left hands of the patients, a total of two times. The patients' blood pressure, heart rate, and whether they took any vasodilator or vasoconstrictor drugs at the time of measurement were included in the study. In addition, it was determined whether the diseases in the patients' histories and smoking affected the tissue oxygenation. The pH, $PaO2,$ and saturation measured by pulse oximetry were determined from the blood gases taken from the patients using a tissue oxygenation device. Based on the user manual of the tissue oxygenation device, the device is used alongside infrared spectroscopy to measure the local oxygen saturation of the tissue hemoglobin and StO_2. The light absorption spectrum of a tissue sample varied mainly according to the concentration of oxyhemoglobin and deoxyhemoglobin. The percentage of StO_2 was measured by hemoglobin oxygen saturation, which is limited by the tissue value in the blood. The Inspectra StO_2 Spot Checker (Hutchinson Technology Inc., United States) has a non-invasive imaging system that measures the percentage of the estimated value of hemoglobin oxygen saturation in thenar skeletal muscle tissue (StO_2). We determined whether the tissue oxygenation of the patients affected their length of stay in the hospital and its effects on the patients' discharge and exit. Although the diagnoses of the patients participating in this study were followed up, they were not taken into account for inclusion in this study.

2.4. Statistical analysis

Our study was designed in a prospective manner, with a total of 61 patients admitted to the emergency department. The dataset comprised data on tissue oxygen saturation and various vital signs from the patients, and SPSS (ver. 19.0) was used for the statistical analysis of the data. The descriptive measures of all the obtained variables were calculated, and the categorical variables were frequency and percentage. Additionally, the proportional scale numerical variables were presented as mean ± SD or (median, min, max) in Table 1. The Kolmogorov–Smirnov test was used to analyze whether the continuous numerical values among the proportional scale variables conformed to the normal distribution. The StO_2, blood pressure, pulse, and hemoglobin values followed the normal distribution, whereas the SO_2 values did not conform to the normal distribution. Hence, parametric comparison methods were used in cases where there were sufficient observation values in the group numbers, and non-parametric tests were used for group comparisons in other cases. Moreover, the Student's t-test was used in the case of two independent groups, and a one-way analysis of variance was used in multiple groups. For non-parametric cases, Mann–Whitney U tests were preferred in the case of the two groups, whereas Kruskal–Wallis tests were preferred for multiple groups. Pearson's or Spearman's correlation analysis was used to determine the relationship between the proportional scale variables. The relationship between the categorical variables was determined using the Monte Carlo-corrected chi-square analysis method. Significant results of pairwise comparisons are shown in Fig. 1 and presented in Table 2 with the same lowercase letters. In the study, the Type-I error value was taken as 5%, and the result was considered statistically significant at $p < 0.05$.

3. Results

In this study, 50.8% of the 61 patients admitted to the emergency department were males, whereas 49.2% were females. Meanwhile, more than half of the patients (54.1%; n=33) died. Among the patients who died, chest disease had the highest rate (37.7%; n=23). Sepsis also had a high rate (26.2%), as well as neurological problems and intracranial hemorrhage (Table 1).

Two-thirds of the patients were non-smokers, and 54.1% of 33 patients used noradrenaline. Meanwhile, the number of patients using dopamine was lower (11.5%; n = 7). Additionally, no patient used dobutamine and esmolol, and only one patient used nitroglycerin. Because the final status of the patients transferred to other centers was not known, eight patients were excluded, and a recomparison was made. In this case, the heart rate and StO_2 value were significantly different between the discharged and excluded patients (p = 0.041). While the pulse rate was high in patients with Ex, the StO_2 value was higher in discharged patients (Table 2).

The patients were grouped into middle and advanced age categories based on the baseline age of 40 years, and the difference in the mean StO_2 (p = 0.043) between the groups was significant. The measurement results showed that the values decreased in patients of advanced age. While the mean PaO_2 had a higher value in middle-aged patients, no significant difference was found between the groups (Table 3).

Table 1. Descriptive measures of patients according to their discharge status (including those who were referred)

Vital measurements **Average ±SS**	Units	Discharge n=20	Exitus n=33	To transfer n=8	P
AGE	Year	62.45±22.33	67.09±18.26	71.5±21.23	*0.106*
Systolic blood pressure	mmHg	117.4±24.46	103.73±33.34	110.5±21.33	*0.233*
Diastolic blood pressure	mmHg	57.5±11.62	55.67±15.09	63.13±13.31	*0.368*
MAP	mmHg	77.46±12.60	71.68±18.52	78.91±14.53	*0.412*
Pulse	beats/min	90.65±19.12^{a,b}	114.48±24.98^{a}	117.5±33.54^{b}	*0.004**
Blood sugar	*Mg/dl*	161.5±72.98	154.67±72.74	165±62.81	*0.814*
Hemoglobin	*G/L*	12.3±2.13	11.26±2.48	13.05±2.65	*0.095*
Pulse O_2	*%*	95.75±2.31	93.61±9.82	97.13±3.09	*0.120*
StO_2	*%*	82.97±8.19	76.21±11.65	76.00±7.47	*0.084*
Ph		7.36±0.09	7.33±0.11^{a}	7.49±0.15^{a}	*0.014**
PaO_2	*%*	106.11±34.85	113.34±36.53	126.05±33.04	*0.390*
Length of hospital stay	day	22.5±16.45^{a}	17.55±20.47	9.13±13.91^{a}	*0.041**

Table.2. Descriptive measures according to the discharge status of the patients

Vital measurements **Average ±SS**	Units	Discharge n=20	Exitus n=33	P
Age	Year	62.45±22.33	67.09±18.26	*0.509*
systolic blood pressure	mmHg	117.4±24.46	103.73±33.34	*0.106*
Diastolic blood pressure	mmHg	57.5±11.62	55.67±15.09	*0.876*
MAP	mmHg	77.46±12.60	71.68±18.52	*0.393*
Pulse	beats/min	90.65±19.12	114.48±24.98	*0.001**
Blood sugar	*Mg/dl*	161.5±72.98	154.67±72.74	*0.700*
Hemoglobin	*G/L*	12.3±2.13	11.26±2.48	*0.095*
SO_2	*%*	95.75±2.31	93.61±9.82	*0.677*
StO_2	*%*	82.97±8.19	76.21±11.65	*0.041**
Ph		7.36±0.09	7.33±0.11	*0.633*
PaO_2	*%*	106.11±34.85	113.34±36.53	*0.419*
Length of hospital stay	day	22.5±16.45	17.55±20.47	*0.046**

Table 3. Descriptive measures of patients according to middle and advanced age

Vital measurements **Average ±SS**	Units	Age 40 and below (n=9)	Age over 40 (n=52)	P
Age	Year	26.22±8.33	73.06±11.24	*<0.001**
systolic blood pressure	mmHg	108.38±18.29	109.29±31.24	*0.846*
Diastolic blood pressure	mmHg	61.00±10.41	56.65±14.33	*0.281*
MAP	mmHg	76.66±11.92	74.16±17.08	*0.614*
Pulse	beats/min	101.89±28.85	107.95±26.53	*0.943*
Blood sugar	*Mg/dl*	165.11±71.04	157.08±71.16	*0.839*
Hemoglobin	*G/L*	12.17±2.71	11.77±2.42	*0.684*
SO_2	*%*	97.22±1.64	94.35±8.01	*0.098*
StO_2	*%*	84.55±8.16	77.33±10.57	*0.043**
Ph		7.34±0.09	7.36±0.12	*0.569*
PaO_2	*%*	125.22±49.18	110.47±32.76	*0.259*
Length of hospital stay	day	9.22±6.85	19.60±19.68	*0.210*

Noradrenaline drug use had an effect on blood pressure and heart rate. The systolic and diastolic blood pressures of the patients who used the drug were lower, whereas their heart rates were higher. The use of noradrenaline significantly decreased the StO_2 (p = 0.012) and SO_2 measurements (Table 4). Dopamine use was effective only on systolic blood pressure (p = 0.036) and hospital stay (p = 0.028). Furthermore, StO_2 or SO_2 measurements had lower values in patients using dopamine, but no difference was detected between the groups.

The StO_2 measurements taken from the right hand had a positive and significant correlation (R = 0.344; p = 0.007) with systolic blood pressure and a negative and significant correlation with pulse rate (R = −0.388; p = 0.002). A higher positive correlation was found with SO_2 values (R = 0.498; p < 0.001). While the StO2 rates were concentrated between 80% and 90%, the SO_2 values were concentrated between 90%–99%. No significant correlation was found between diastolic blood pressure, blood glucose, hemoglobin, PaO_2, and StO_2.

Approximately 50% positive correlation was calculated between the StO_2 measurements taken from the left hand and the systolic, diastolic, and SO_2 values.

Table 4. Descriptive measures according to noradrenaline use status

Vital measurements **Average ±SS**	Units	YES (n=33)	NO (n=28)	P
Age	Year	68.03±15.08	63.93±24.57	*0.813*
Systolic blood pressure	mmHg	97.24±27.43	123.07±26.02	*0.001**
Diastolic blood pressure	mmHg	53.03±13.78	62.21±12.32	*0.010**
MAP	mmHg	67.76±15.80	82.50±13.31	*0.112*
Pulse	beats/min	114.91±27.11	97.82±23.51	*0.012**
Blood sugar	*Mg/dl*	161.3±70.7	154.68±71.63	*0.487*
Hemoglobin	*G/L*	11.42±2.24	12.32±2.62	*0.134*
SO_2	*%*	93.42±9.73	96.36±2.72	*0.047**
StO_2	*%*	75.48±11.10	81.83±8.77	*0.012**
Ph		7.34±0.13	7.39±0.1	*0.100*
PaO_2	*%*	106.95±31.49	119.34±39.29	*0.284*
Length of hospital stay	day	17.03±18.6	19.29±19.05	*0.256*

Furthermore, the StO_2 values had a positive and significant correlation ($R = 0.269$; $p = 0.036$) with systolic blood pressure and a negative and significant correlation with pulse rate ($R = -0.324$; $p = 0.011$). There was a significant correlation between StO_2 and mean arterial pressure (MAP) ($R = 0.507$; $p < 0.001$). Meanwhile, there was no significant correlation between SO_2, diastolic blood pressure, blood glucose, hemoglobin, PaO_2, and StO_2. Moreover, StO_2 did not change with the length of hospital stay. When the referred patients were excluded, there was no significant correlation between StO_2, SO_2, and MAP among the discharged patients, whereas a significant and positive correlation was found between all three variables in the ex-patient group (R MAP − $StO_2 = 0.529$; $p = 0.002$). When both the Ex and discharged patients were considered ($n = 53$), the correlation between pulse O_2 and StO_2 was positive and significant ($R = 0.597$; $p < 0.001$) (Table 5).

Table.5. Relationship between SpO2 measurement values and vital signs

Sto2 (n=61)	AGE (YEAR)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Pulse (beats/min)	Blood sugar *(Mg/dl)*	Hb (g/L)
R	-0.165	0.269	0.020	-0.324	-0.010	0.197
P	*0.203*	*0.036**	*0.880*	*0.011**	*0.940*	*0.128*
	MAP (mmhg)	Pulse O2 (%)	Ph	PaO_2 (%)	Length of hospital stay(day)	
R	*0.507*	0.054	0.024	0.066	0.188	
P	*<0.001**	*0.678*	*0.852*	*0.614*	*0.146*	

4. Discussion

In our study, it was aimed to investigate whether the follow-up with a device that measures tissue oxygenation of patients followed on mechanical ventilator is superior to the O_2 saturation probe. The StO_2 measurements taken from the right hand had a positive and significant correlation ($R = 0.344$; $p = 0.007$) with systolic blood pressure and a negative and significant correlation with pulse rate ($R = -0.388$; $p = 0.002$). A higher positive correlation was found with SO_2 values ($R = 0.498$; $p < 0.001$). While the StO_2 rates were concentrated between 80% and 90%, the SO_2 values were concentrated between 90% and 99%. Meanwhile, no significant correlation was found between diastolic blood pressure, blood glucose, hemoglobin, PaO_2, and StO_2. Approximately 50% positive correlation was found between the StO_2 measurements taken from the left hand and the systolic, diastolic, and SO_2 values, and no significant correlation was found between blood sugar, hemoglobin, PaO_2, and StO_2. However, no correlation was found between the mean StO_2 value and SO_2. When both the Ex and discharged patients were considered ($n = 53$), the correlation between pulse O_2 and StO_2 values was positive and significant.

Kır et al. (7) found that mixed and central venous oxygen saturation are useful for determining disease severity and evaluating the response to treatment in various critically ill conditions in which the cardiovascular system is affected. In line with current knowledge, SvO_2, and $ScvO_2$ are considered useful tools for evaluating and managing tissue perfusion in critically ill patients (7). However, these are invasive procedures for tissue perfusion measurement. The tissue oxygenation device we used in our study is a non-invasive tool with no contraindications. With this device, we have also provided information about tissue perfusion without any harm to the patients. In a clinical study by Lima et al., the normal range of StO_2 was 75%–91%. StO_2 measurements below 75% can consistently be considered an important indicator of a patient's hypoperfusion. High StO_2 levels (> 91%) were found to be measurable when oxygen delivery was well above use (8). In our study, the StO_2 value was found to be 79%, and it was lower in patients with impaired tissue perfusion and ex. In the studies of Myers et al. (9) and Gomer et al. (10), while StO_2

was used for the resuscitation of peripheral organs, it emerged as a covert detector of hypoperfusion. This result prompted the researchers to focus on the usefulness of StO_2 measured from skeletal muscle in critically ill patients. StO_2 measurements can be made from various muscles in the intensive care unit, and it has been thought that StO_2 measurements may be affected by local edema and adipose tissue. In our study, the StO_2 value was found to be higher in men than in women. The high StO_2 value in men was not associated with any of the measured values, such as Hemoglobin (Hb), blood sugar, blood pressure, and pulse. From this point of view, since tissue oxygenation is related to tissue perfusion and muscle mass is greater in men than in women, StO_2 measurement should be taken from the thenar region because women have more adipose tissue than men and StO_2 may be affected by muscle mass and adipose tissue.

Because perfusion is known to be impaired in sepsis, the work of Lima et al. supports our study. In the studies of Colin et al., Leone et al., and Shapiro et al., the StO_2 value was also commonly investigated in patients with severe sepsis and septic shock. Although StO_2 values have robust prognostic implications in trauma patients, they appear to be more complex in septic conditions (11–12). In a study by Creteur et al., the StO_2 value was found to be lower in septic patients (13). In our study, when all patients were considered, the lowest StO_2 ratio was found in sepsis patients. Tissue perfusion was impaired in sepsis patients, and StO_2 is low, which confirmed this fact. The StO_2 value was low in patients with low systolic blood pressure and high in patients with high systolic blood pressure, confirming that hypoperfusion has an effect on tissue oxygenation.

In our study, the StO_2 and SO_2 values were low in patients using noradrenaline and dopamine. Thus, noradrenaline and dopamine disrupted tissue perfusion, thereby decreasing the StO_2 value. This highlights the importance of measurements taken with the tissue oxygenation device for monitoring the general condition and tissue perfusion of patients. In addition, while the StO_2 value was high for patients under the age of 40, it was low for patients over the age of 40. As age progresses, tissue perfusion deteriorates; hence, tissue oxygenation was lower in patients over the age of 40. Additionally, StO_2 was higher in discharged patients. Hence, it was determined that patients with high StO_2 values are less likely to die because their tissue perfusion is not impaired.

Although our study supports the idea that tissue oxygenation is an indicator of perfusion, its shortcoming is that we did not consider the ejection fraction (EF) of our patients. In this study, EF could be determined in patients with heart failure, and its effects on tissue oxygenation could be evaluated. While our perfusion evaluation of the patients was adequate, a secondary evaluation was needed because we could not follow up our referral patients for a long time.

It is important to follow tissue perfusion in intensive care patients, and this can be done with a noninvasive method. The results of our study reveal that perfusion should be followed with tissue oxygenation in patients on mechanical ventilators because low tissue oxygenation indicates increased patient mortality.

Conflict of interest
The authors declared no conflict of interest.

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Authors' contributions
Concept: F.K., A.S.G., Design: F.K., Data Collection or Processing: F.K., B.G., H.A., M.G., Analysis or Interpretation: F.K., Literature Search: F.K., Writing: F.K., A.S.G., Z.D.D.

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