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THENAR OXYGEN SATURATION (StO_2) DURING WEANING FROM MECHANICAL VENTILATION: AN OBSERVATIONAL STUDY

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ABSTRACT

Question of the study: to determine whether thenar tissue oxygen saturation (StO_2) measured by non-invasive near-infrared spectroscopy, and its changes derived from an ischemic challenge, are associated to weaning outcome.

Patients and methods: Prospective observational study in a 26-bed medical-surgical intensive care unit. Patients receiving mechanical ventilation (MV) for >48 hours, and considered ready to wean by their physicians, underwent a 30-minute weaning trial (WT). StO_2 was measured continuously on the thenar eminence. A transient vascular occlusion test (VOT) was performed prior to and 30 minutes into the WT, in order to obtain StO_2 deoxygenation (DeO_2) and reoxygenation rates, and estimated local oxygen consumption ($nirVO_2$).

Results: Thirty-seven patients were studied. Patients were classified as weaning success (n=24) or weaning failure (n=13). No significant demographic, respiratory or hemodynamic differences were observed between both groups at inclusion. Patients who failed the overall weaning process showed a significant increase in DeO_2 and in $nirVO_2$ from baseline to 30 min of WT, whereas no significant changes were observed in the weaning success group.

Answer to the question: Failure to wean from mechanical ventilation was associated to higher relative increases in DeO_2 after 30 minutes of spontaneous ventilation.

Keywords: Near-infrared spectroscopy; Tissue oxygenation; Microcirculation; Regional blood flow; Mechanical ventilation; Weaning;

INTRODUCTION

Discontinuation of ventilatory support in critical care medicine might be a difficult challenge in about one third of patients[1]. Failure to wean from mechanical ventilation (MV) is difficult to predict[2]. Furthermore, failed extubation is associated with increased hospital mortality, prolonged ICU and hospital stays, and increased need for tracheostomy[3].

Since spontaneous ventilation is a form of cardiovascular stress test, failure to wean from MV often reflects cardiovascular insufficiency owing to the increased oxygen cost of breathing[4,5]. Normally, any increased oxygen cost of breathing is met by an increased respiratory muscle blood flow, which in flow-limited states will divert blood flow away from other tissues, such as the splanchnic and the peripheral circulation[6], and may lead to their hypoperfusion[7-11].

Recently, skeletal muscle oxygen saturation on the thenar eminence (StO_2) measured non-invasively using near-infrared spectroscopy (NIRS) has been proposed as an early and reliable measure of hypoperfusion states[12-14]. This proposal is based on the idea of the peripheral and splanchnic circulation shunting in low flow states, where blood flow is diverted from these less-vital to more-vital areas, like the heart, brain and respiratory muscles. In addition to reporting steady-state StO_2[15-17], functional monitoring using a transient total vascular occlusion allows for further assessment of cardiovascular state. The dynamic Vascular Occlusion Test (VOT) creates the novel StO_2 parameters Deoxygenation rate (DeO_2) and upon removal Reoxygenation rate (ReO_2) which improve predictive value of StO_2 in certain critically ill populations[18,19].

We postulated that NIRS monitoring would demonstrate significant hypoperfusion of peripheral skeletal muscle in patients during unsuccessful attempts to wean from mechanical ventilation. The purpose of this study was to analyze whether StO2 and its VOT-derived changes can be useful in predicting weaning outcome in critically ill patients.

MATERIAL AND METHODS

This prospective observational study was conducted in a 26-bed medical-surgical intensive care unit at a university hospital. This study was approved by the Institutional Review Board at the Hospital de Sabadell. Informed consent was obtained from the patient or their next of kin prior to the study initiation.

We included adult patients (≥18 years old) receiving invasive mechanical ventilation for >48 hours and considered ready to wean by their physicians according to the following criteria: partial or complete recovery from the underlying cause of acute respiratory failure; adequate gas exchange, as indicated by a partial pressure of arterial oxygen (PaO_2) >60 torr (7.99 kPa) to a fraction of inspired oxygen (FiO_2) < 0.4, with a positive end-expiratory pressure (PEEP) < 5 cmH_2O; a core temperature <38º C; a hemoglobin >8 g/dL; and no further need for vasoactive and/or sedative agents.

Exclusion criteria were: trauma in both upper limbs, and hematoma or skin lesions at the thenar eminence that could hinder placement of NIRS sensor probe.

Patients with altered level of consciousness that could lead to central hypoventilation and/or impaired secretions management were also excluded.

Study protocol

After inclusion, patients underwent a weaning trial (WT) for 30 minutes, defined as assisted spontaneous breathing with continuous positive airway pressure (CPAP) of 5 cm H_2O, or a T-tube trial, according to their medical team. Patients were in a semi-recumbent position, and the FiO_2 was kept constant during the trial.

The evaluation criteria for the WT failure was defined as the presence of one or more of the following criteria during the 30 minutes trial: a respiratory rate (RR) of more than 35 breaths/min for 5 minutes or longer; an arterial pulse-oxymetry saturation (SpO_2) <90%, heart rate (HR)>140 beats/min or sustained increase or decrease in heart rate of more than 20%; a systolic blood pressure >180 mmHg or <90 mmHg; increased anxiety and diaphoresis. The decision to remove the endotracheal tube was made independently of the study investigators at the end of a successful WT by their attending physicians, who did not have access to the specific StO_2 data. Weaning success was defined as patient remaining free of mechanical ventilatory support for >24 hours after passing the WT. Weaning failure was defined as either failure to pass the WT (WT failure) or reinstitution of MV within 24 hours of extubation (extubation failure) (figure 1).

Methods

We collected demographic data: age, sex, diagnosis, and days on mechanical ventilation. Hemodynamic, respiratory and oxygenation variables were monitored continuously and recorded just before starting and at 30 minutes into the WT. HR and

mean arterial pressure (MAP) were recorded by routine bedside monitoring (Monitor Intellivue MP 70; Phillips Medizinsystems, Boeblingen, Germany). RR, tidal volume (Vt), minute ventilation (V_E), FiO_2 and SpO_2 were recorded at start and 30 minutes into the WT (Monitor Intellivue MP 70; Phillips Medizinsystems, Boeblingen, Germany). Arterial blood gas analysis was done before and 30 minutes into the WT (ABL 700 series; Radiometer Medical, Copenhagen, Denmark). StO_2 was recorded continuously using the InSpectra 650 Tissue Spectrometer (Hutchinson Tech., Hutchinson, Minnessotta). The StO_2 15-mm optical surface probe was placed on intact skin on the thenar eminence; it was never placed adjacent to the site of radial artery cannulation. The InSpectra tissue spectrometer also measures relative hemoglobin concentration in the NIR field of view, which is presented as the tissue hemoglobin index (THI).

Vascular Occlusion Test (VOT). The VOT was performed as previously described by Gómez et al[23]. Briefly, a blood pressure cuff is placed proximal to the hand on the forearm and rapidly inflated at 40 mmHg above systolic pressure and kept inflated until StO_2 decreased to 40%. Then the cuff is rapidly deflated and the rate of increase in StO_2 is noted. The resulting DeO_2 and ReO_2 slopes are reported as change in O_2 saturation over time. We performed a VOT at the beginning of the WT and again at 30 minutes into the WT giving DeO_2 and ReO_2 data paired for each time point. Using the DeO_2 slope and the THI values at the beginning and at the end of the VOT we also calculated the NIRS-derived thenar muscle oxygen consumption ($nirVO_2$), as described by Skarda et al[20]: $nirVO_2 = (\text{DeOx slope})^{-1}/[\ (THI_{start}+THI_{end})/2]$. Relative changes in StO2 derived parameters were calculated as the quotient between values at minute 30 and baseline. Absolute StO_2 and VOT-derived variables were obtained automatically using the InSpectra Research Software® v4.01 (Hutchinson Technology).

Analysis

A descriptive analysis was performed. The Kolmogorov-Smirnov test was used to verify the normality of distribution of the studied variables. Continuous variables are presented as median values with interquartile ranges (IQR). Wilcoxon test was used to analyze changes over time in the paired variables. Mann-Whitney U test for continuous variables and Fisher exact test for categorical variables were used to compare failure and success groups. Data were analyzed using the SPSS 17.0 Software (Chicago, Il, USA). Statistical significance was defined as $p<0.05$ (two-tailed test).

RESULTS

Thirty-seven patients were studied. Patient baseline characteristics are summarized in table 1. Twenty-six patients succeed WT and were extubated. However, two of the patients who were extubated required re-instauration of MV within 24 hours (extubation failure). Eleven patients failed the WT (figure 1). No baseline differences in demographic, hemodynamic, and respiratory variables were observed when comparing success and failure groups (table 1), except for lower baseline HR in those patients who failed the weaning process (78 (71, 91) *vs.* 90 (77, 95), *p* 0.04).

The evolution of the main studied variables is shown in Table 2. After 30 minutes of WT, both, patients who succeed and patients who failed the overall weaning process, showed a significant increase in RR and HR, with no other changes in their hemodynamic, respiratory and oxymetric parameters.

StO_2 variables

No differences were observed in baseline StO_2 parameters between the two groups (table 2). When analyzing the evolution of NIRS-derived parameters, patients who succeed and patients who failed showed different patterns. The weaning success group showed no significant changes in steady-state StO_2, DeO_2, ReO_2, and $nirVO_2$ after 30 minutes of WT. Whereas the weaning failure group showed a significant decrease in their DeO_2 slope (from -11.2 %/min (-16.9, -7) to -13.7 %/min (-18.7, -7.9), p=0.04; figure 2), as well as an increase in $nirVO_2$ (from 92 U (76, 146) to 141 U (93, 212), p=0.04) after 30 minutes of WT. Changes in local Hb content (THI) were not different between success and failure groups (from 9.9 U (8.1, 11.9) to 10.5 U (8.5, 12.9), p<0.01, in the success group; and from 10.1 U (7.8, 11.1) to 10.4 U (7.7, 13), p=0.03, in the failure group).

The DeO_2 ratio (represented as the ratio of DeO_2 at 30 minutes to baseline DeO_2) was significantly higher in the failure group (1.03 (0.92, 1.22) in the success group vs. 1.27 (1.12, 1.49) in the failure group, p<0.01; figure 3). In addition, the $nirVO_2$ ratio (the increase in $nirVO_2$ during the WT, represented as the ratio of $nirVO_2$ at 30 minutes to baseline $nirVO_2$) was also higher in the failure group (1.1 (0.8, 1.3) in the success group vs 1.24 (1.21, 1.66) in the failure group, p=0.02).

DISCUSSION

The main result of the present study is that higher relative increases in StO2 deoxygenation rate (DeO_2) and in local skeletal muscle oxygen consumption ($nirVO_2$) after a 30min WT were associated to failure to wean from mechanical ventilation.

Changing from positive pressure ventilation to spontaneous breathing determines an increase in the work of breathing, and thus, an increase in the oxygen demand of the respiratory muscles. If the metabolic demand of transitioning from MV to spontaneous ventilation cannot be met by increasing cardiac output either because cardiovascular reserve is limited, the work cost of breathing excessive, or both, then the cardiovascular system addresses these excessive demands by increasing sympathetic tone which tries to maximize cardiac output[21], while redistributing blood flow away from the periphery and splanchnic circulation to the respiratory muscles[22,23]. Such increased sympathetic activity also increases tissue metabolic rate. Accordingly, blood flow redistribution and increased tissue oxygen consumption could co-exist in patients during a failed WT.

Assessing blood flow redistribution in the splanchnic bed via monitoring splanchnic tissue hypoxia has proven to be a useful tool to predict weaning outcome[9,11]. Despite some initial promising results[8-11], gastric tonometry was not evaluated in large studies. Furthermore, this technique did not become a routine standard of care due to its technological requirements and difficult application at the bedside. As occurs with the splanchnic area, non-invasive monitoring of the peripheral circulation might add potential benefits to cardiovascular performance assessment. In this study we hypothesized that presumed cardiovascular overload of excessive cost of breathing would be detected by non-invasive regional evaluation of skeletal muscle oxygenation using NIRS technology.

As we already expected, we did not observe significant changes in StO2 during the SBT in any of the two groups. Although steady-state StO_2 has been proposed as a marker of hypoperfusion states, especially in hemorrhagic shock[24], our group and others have already demonstrated the lack of sensitivity of the absolute StO_2 value[15,16,25], suggesting that absolute steady-state StO_2 might not detect less severe degrees of tissue hypoperfusion. We presumed that during the WT there would not be enough blood flow redistribution to be detected by static NIRS measurements.

However, dynamic NIRS-derived variables created by an ischemic challenge, DeO_2 and ReO2, provide more information about tissue wellness, exploring the local metabolic rate and the endothelial integrity, respectively. These novel parameters have been studied mostly in trauma and septic shock patients, were they have consistently shown prognostic implications, independently from other cardiovascular parameters [26,27].

In our set of patients, the relative increase in DeO_2 during a 30min WT was associated to weaning failure. DeO_2 is a dynamic parameter that depends on the local O_2 supply/demand relationship and mirrors local oxygen utilization. Increases in DeO_2 might be explained by two different, and cumulative, mechanisms: (a) by a local supply-demand dependency in low or inadequate flow states (such as blood flow redistribution), and (b) by an increased metabolic rate. During spontaneous breathing, if there was an increase in respiratory muscles demand, leading to sympathetically mediated peripheral vasoconstriction, and blood flow redistribution, inadequate local flow could led to increased local O_2 extraction. In such cases, in addition to higher DeO_2 rates, one would expect to see reduced THI values in the failure group, as compared to the successfully weaned patients, reflecting lower tissue hemoglobin

content in blood flow redistribution conditions. Indeed, in a nice paper, Bartels et al[17] demonstrated that thenar eminence THI decreased significantly during blood flow redistribution induced by simulated hypovolemia (i.e. lower body negative pressure). In our study though, we did not observe any differences in THI behavior during the WT between the two groups. Although, as occurs with absolute StO_2, THI might be not sensitive enough to detect mild decreases in local blood flow, during the SBT both groups showed a THI increase suggesting, if any, an increase in cardiac output in response to the reinitiation of spontaneous ventilation. Therefore, the observed increase in DeO_2 in the failure group might be mostly related to local oxygen consumption. This hypothesis was also supported by $nirVO_2$ evolution, an estimation of local oxygen consumption that corrects DeO_2 for the local Hb content[20]. This finding might reflect increased sympathetic outflow trying to compensate for the inadequate cardiovascular response, as supported by other studies that showed a significant increase in plasma catecholamine levels during WT, especially in failure to wean patients[35-37].

In summary, in the present observational study higher DeO2 and nirVO2 during a WT were associated with weaning failure. Our findings suggest that these functional parameters might detect increased local oxygen consumption secondary to increased sympathetic tone in failure to wean patients.

Study limitations

Some limitations of the present study should be acknowledged. First, it was carried out in a single center. Albeit we expect that similar patients should behave similarly, weaning approaches may vary across centers degrading the predictive value of these StO2 derived parameters. Thus, this study needs to be duplicated across other

centers. Second, our pilot study had a small sample size, and only 13 patients presented weaning failure (with only 2 extubation failures). It appears especially interesting to evaluate the predictive utility of these parameters in preventing extubation failure, which could not be addressed in our pilot study. Clearly, a larger study would allow refinement into the interactions of processes and calibration of the predictive parameters that were primarily identified in this study. Third, we did not determine the cause of weaning failure in patients who were considered to fail. We merely identified that they did fail. We can expect different behaviors of StO_2 parameters in patients who fail because of limited cardiovascular reserve from patients who fail because of upper airway obstruction and/or impaired secretions management. This issue must be taken into account in future studies exploring weaning failure.

Conclusions

Relative changes in StO_2 VOT-derived deoxygenation slopes and local oxygen consumption after 30 minutes of a weaning trial were associated to weaning outcome. Thus, StO_2 changes derived from a VOT might be a useful clinical tool to predict weaning outcome.

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Competing interests

The authors declare no competing interests.

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Table 1. Patient baseline characteristics prior to the Weaning Trial

	All patients (n=37)	Weaning success (n=24)	Weaning failure (n=13)	*p* value*
Age (years)	71 (56, 79)	71 (58, 79)	73 (48, 79)	1
Gender (M/F, n)	24/13	16/8	8/5	0.7
Pre-existent co-morbidities (n,%)				
· sleep apnea	4 (11)	4 (17)	0 (0)	0.6
· COPD	10 (27)	7 (29)	3 (15)	
· coronary disease	10 (27)	6 (25)	4 (31)	
· CHF	11 (30)	7 (29)	4 (31)	
No previous disease	15 (41)	8 (33)	3 (15)	
Etiology of ARF (n,%)				
· septic shock	20 (54)	12 (50)	8 (62)	0.6
· acute heart failure	7 (19)	5 (20)	2 (9)	
· trauma	5 (14)	4 (17)	1 (8)	
· other	5 (14)	3 (13)	2 (15)	
Days on MV (days)	6 (4, 10)	5 (4, 10)	6 (4, 11)	0.5
Heart Rate (bpm)	88 (74, 95)	90 (77, 95)	78 (71, 91)	**0.04**
Systolic BP (mmHg)	126 (113, 137)	125 (117, 137)	127 (109, 145)	0.9
MAP (mmHg)	80 (71, 89)	80 (76, 89)	80 (69, 88)	0.6
RR (bpm)	18 (17, 21)	18 (16, 21)	19 (17, 23)	0.1
PaO_2/FiO_2	262 (229, 341)	276 (240, 317)	243 (209, 380)	0.8
SpO_2 (%)	97 (95, 98)	97 (95, 98)	97 (95, 98)	0.2
Tidal volume (mL)	460 (390, 500)	467 (385, 500)	440 (400, 502)	0.7
PEEP (cmH_2O)	5 (5, 5)	5 (5, 5)	5 (5, 6)	0.2
FiO_2 (%)	30 (28, 35)	30 (30, 35)	30 (28, 32)	0.2
pH	7.48 (7.42, 7.49)	7.47 (7.41, 7.5)	7.48 (7.44, 7.5)	0.7
pCO_2 (torr)	35 (30, 39)	35 (29, 39)	36 (32, 40)	0.5
Base Deficit (mmol/L)	2.6 (-2.3, 5)	2.1 (-2.5, 5)	3.9 (-1.3, 5.4)	0.5
Hemoglobin (mg/dL)	9.1 (8.4, 10.1)	8.9 (8.3, 9.9)	9.2 (8.7, 11.4)	0.3
$ScvO_2$ (%)	65 (55, 71)	66 (51, 71)	61 (57, 76)	1

Data are presented as median values with interquartile ranges, unless otherwise indicated.
**p* value between weaning success and failure.
M, male; *F*, female; *COPD*, chronic obstructive pulmonary disease; *CHF*, chronic heart failure; *ARF*, acute respiratory failure; *MV*, mechanical ventilation; *BP*, blood pressure; *MAP*, mean arterial pressure; *RR*, respiratory rate; PaO_2, arterial partial oxygen pressure (torr); FiO_2, oxygen inspiratory fraction; SpO_2, oxygen saturation measured by pulse-oxymetry; *PEEP*, positive end-expiratory pressure; pCO_2, arterial carbon dioxide partial pressure (torr); $ScvO_2$, central venous oxygen saturation; StO_2, thenar oxygen saturation; *THI*, tissue hemoglobin index; DeO_2, deoxygenation slope; ReO_2, reoxygenation slope.

Table 2. Characteristics at baseline, and 30 minutes of Weaning Trial

	Weaning success (n=24)		Weaning failure (n=13)	
	baseline	**30 min**	**baseline**	**30 min (n=11)**
Heart Rate (bpm)	90 (77, 95)	95 (81, 100)§	78 (71, 91)*	91 (85, 98)§
Systolic BP (mmHg)	125 (117, 137)	127 (119, 141)	127 (109, 145)	120 (113, 157)
MAP (mmHg)	80 (76, 89)	81 (76, 89)	80 (69, 88)	83 (72, 94)
RR (bpm)	18 (16, 21)	24 (17, 27)§	19 (17, 23)	35 (28, 36)§
SpO_2 (%)	97 (95, 98)	96 (94, 98)	97 (95, 98)	95 (90, 96)
Tidal volume (mL)	467 (385, 500)	450 (370, 540)	440 (400, 502)	285 (237, 326)*§
pH	7.47 (7.41, 7.5)	7.45 (7.39, 7.48)	7.48 (7.44, 7.5)	7.45 (7.4, 7.47)
pCO_2 (torr)	35 (29, 39)	37 (30, 41)	36 (32, 40)	39 (34, 43)
Base Deficit (mmol/L)	2.1 (-2.5, 5)	1.1 (-1.5, 3.6)	3.9 (-1.3, 5.4)	3 (-2.1, 4.8)
StO_2 (%)	79 (75, 84)	81 (76, 84)	77 (73, 83)	75 (72, 88)
THI (U)	9.9 (8.1, 11.9)	10.5 (8.5, 12.9)§	10.1 (7.8, 11.1)	10.4 (7.7, 13)§
DeO_2 (%/min)	-12.4 (-16.4,-9.8)	-12.7 (-16.5, -10.5)	-11.2 (-16.9, -7)	-13.7 (-18.7, -7.9)*§
ReO_2 (%/min)	185 (144, 252)	205 (137, 293)	217 (181, 309)	261 (222, 365)
$nirVO_2$ (U)	109 (90, 158)	114 (66, 168)	92 (76, 146)	141 (93, 212)§
RR/Vt (bpm/L)		49 (33, 68)		**133 (85, 169)***
StO_2 ratio		1.0 (0.96, 1.05)		0.99 (0.97, 1.03)
DeO_2 ratio		1.03 (0.92, 1.22)		**1.27 (1.12, 1.49)***
ReO_2 ratio		1.06 (0.88, 1.25)		1.08 (0.92, 1.7)
THI ratio		1.05 (1.02, 1.19)		1.04 (0.98, 1.07)
$nirVO_2$ ratio		1.1 (0.8, 1.3)		**1.24 (1.21, 1.66)***

Data are presented as median values with interquartile ranges.
***p* < 0.05 *versus* weaning success at the same time point; §*p* < 0.05 vs baseline value.**
BP, blood pressure; *MAP*, mean arterial pressure; *RR*, respiratory rate; *SpO_2*, oxygen saturation measured by pulseoxymeter; *pCO_2*, arterial carbon dioxide partial pressure; *BD*, base deficit; *ScvO2*, central venous oxygen saturation; *StO_2*, thenar tissue oxygen saturation; *THI*, tissue hemoglobin index; *DeO_2*, deoxygenation slope; *ReO_2*, reoxygenation slope; *$nirVO_2$*, thenar muscle oxygen consumption ; *RR/Vt*, respiratory rate/ tidal volume index; *StO_2 ratio*, StO_2 time 30/StO_2 baseline; *DeO_2 ratio*, DeO_2 time 30/DeO_2 baseline; *ReO_2 ratio*, ReO_2 time 30/ReO_2 baseline; *THI ratio*, THI time 30/THI baseline; $nirVO_2$ *ratio*, $nirVO_2$ time 30/$nirVO_2$ baseline.
(Note that the failure group only has11 individuals at minute 30, as explained in figure 2.B).

Figure legends

Figure 1. Flow chart of patients recruited in the study.
WT, weaning trial. Patients who were extubated without reinstitution of mechanical ventilation (MV) within 24 hours were considered as "weaning success" (n = 23). Patients who failed either the WT or were extubated but required reinstitution of MV within 24 hours were considered as "*weaning failure*" (n = 7).

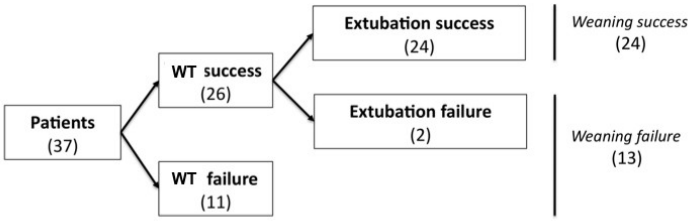
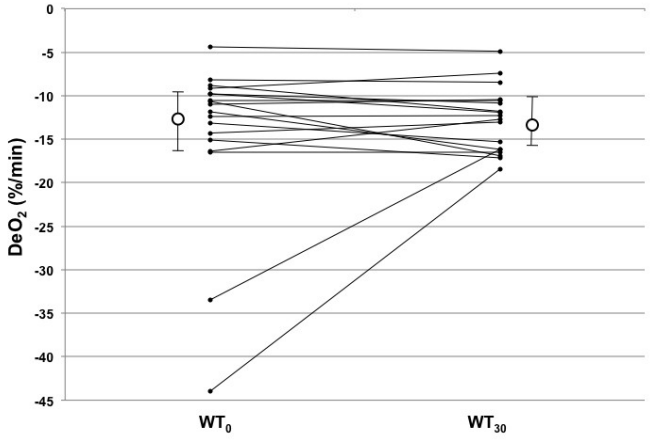


Figure 2. Deoxygenation slopes (DeO_2) at baseline (WT_0) and at minute 30 of WT (WT_{30}) for patients who succeed (A) and who failed (B) the overall weaning trial.
DeO_2 values for each patient (*closed circles*), and the median (IQR) value of DeO_2 at baseline and after 30 minutes of WT (*open circles*) are represented. Two patients in the weaning failure group (B) did not complete the WT, requiring reinstitution of MV, because of increased respiratory efforts, sweating and arterial oxygen desaturation.
*****$p < 0.05$, when comparing paired DeO_2_30 and DeO_2_0.



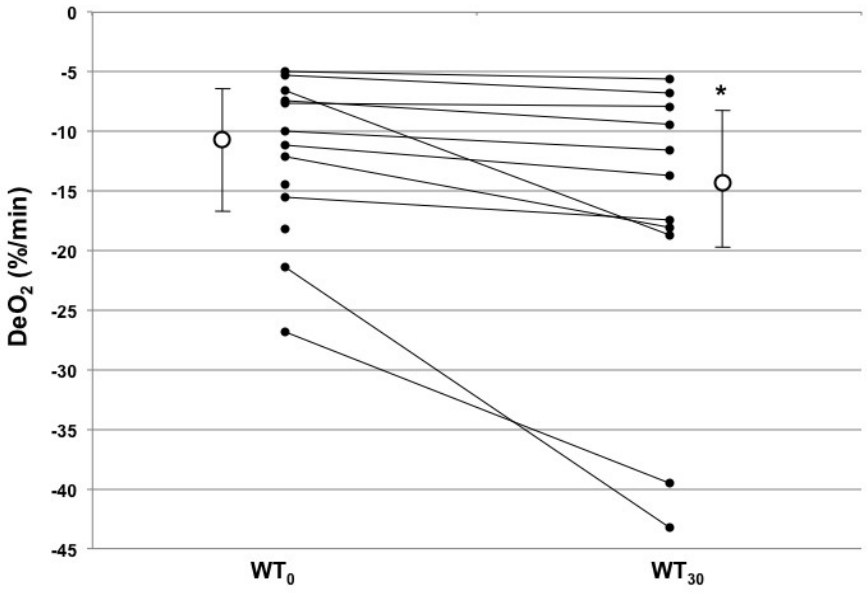


Figure 3. DeO_2 ratio for weaning success and failure.
DeO_2 ratios for weaning success group (*open circle*) and failure group (*closed circle)*, represented as median (IQR), were statistically different with a ***p* value < 0.01.