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Central Venous Oxygen Saturation as a Predictor of the Outcome of Weaning From Mechanical Ventilation

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Abstract

Weaning from mechanical ventilation represents a corner stone of management of critically ill patients. Successful weaning represents a great achievement in patient's critical course in the ICU. This makes the process of weaning one of the most difficult steps in ICU care, for those reason, such a study was done to create a new thinking about the predictors that facilitate patient weaning from mechanical ventilator. The aim of this study is to evaluate the central venous saturation as a predictor of the outcome of weaning from mechanical ventilation. Cohort, unicentric, clinical study research design was utilized in the current study. Sample consists of one hundred and twenty patients over a one year period, all patients passed the first SBT (spontaneous breathing trial) and weaned successfully from mechanical ventilation were extubated after undergoing a two-step weaning protocol (measurements of predictors followed by a T-tube trial). Extubation failure was defined as the need of re-intubation within 48 hrs. The weaning protocol evaluated hemodynamic, ventilation parameters, arterial and venous gases during mechanical ventilation (Immediately before T-tube trial), and at the 30th min of spontaneous breathing trial. Findings of this study show that re-intubation rate was 30%. Analysis by logistic regression revealed that central venous saturation was the only variable able to discriminate outcome of extubation. Reduction of central venous saturation by >5% was an independent predictor of re-intubation, with odds ratio of 52.6 (95% confidence interval =16.34–169.42), a sensitivity of 87%, and a specificity of 90%. Reduction of central venous saturation during spontaneous breathing trial was associated with extubation failure and could reflect the increase of respiratory muscles oxygen consumption. Results of the present study indicated that central venous saturation was an early and independent predictor of extubation failure and may be a valuable accurate parameter to be included in weaning protocols.

Keywords: Central Venous Saturation - Mechanical Ventilation - Extubation.

1. Introduction

Weaning from mechanical ventilation is an essential and universal element in the care of critically ill intubated patients receiving mechanical ventilation. Weaning covers the entire process of liberating the patient from mechanical support and from the endotracheal tube, including relevant aspects of terminal care (1). The first problem the clinician faces is how to determine when a patient is ready to resume ventilation on his or her own. Weaning procedures are usually started only after the underlying disease process that necessitated mechanical ventilation has significantly improved or is resolved (2-4). The patient should also have an adequate gas exchange, appropriate neurological and muscular status, and stable cardiovascular function (2). However, extubation failure (EF) occurs in approximately 14% to 32% of the patients meeting these criteria, indicating that the traditional two-step weaning protocol (evaluation of predictors followed by T-tube trial) does not adequately detect failure in patients weaned from mechanical ventilation (5-9).

Presence of cardiovascular dysfunction can contribute to weaning failure by increasing loads and reducing neuromuscular capacity. Although respiratory muscles do not develop fatigue, they perform a huge workload (16). Thus, they rely on efficient oxygen transport by the cardiovascular system (10). Jubran et al (11) examined the hemodynamics and mixed venous saturation (SvO_2) in patients during weaning trials. Patients who failed weaning also failed to increase oxygen delivery ($D\dot{}O_2$) to the tissues, in part due to elevated right and left ventricular afterloads. Central venous oxygen saturation ($ScvO_2$), although less accurate than SvO_2, has been successfully used as an adequate resuscitation goal in critical illness (10, 12). Earlier authors (13-15) had demonstrated adequate correlation between $ScvO_2$ and SvO_2, however, not in critically ill patients. As such, in the weaning process (recovery stage from critical disease), measurement of $ScvO_2$ could potentially be a reliable and convenient tool to warn rapidly about acute changes in the oxygen supply and demand of these patients. Given the hypothesis that changes in $ScvO_2$ during SBT could predict EF, a unicentric study was conducted to

evaluate the predictive value of measurements of $ScvO_2$ in weaning from mechanical ventilation. Patients submitted to a standard two step weaning protocol and extubated after successful SBT.

2. Methods

2.1. Design

This is a cohort, unicentric, clinical study performed in one medical-surgical intensive care unit, and approved by the Ethic Research Committee of the institution. The informed consent was obtained from all patients or next-of-kin.

2.2. Patients

Over a one year period, we studied prospectively all patients mechanically ventilated for >48 hrs. in the medical-surgical ICU in King Fahd general Hospital-Jeddah, Kingdom of Saudi Arabia. The minimal sample 120 patients with type I error α=5% and type II error β=1% by power of test 90%. All patients were ventilated with Evita-4 (Drager Medical AG, Lubeck, Germany). They were assessed daily for presence of the following readiness-to wean criteria: a) improvement in the underlying condition that leads to acute respiratory failure; b) adequate oxygenation, indicated by $PaO_2 \geq 60$ torr on $FIO_2 \leq 0.4$ and positive end-expiratory pressure $\leq$ 8 cm H_2O; c) cardiovascular stability (heart rate $\leq$ 130 beats/min and no or minimal pressors); d) afebrile; e) adequate hemoglobin ($\geq$8 g/dl); f) adequate mental status (arousal, Glasgow Coma Scale score of $\geq$ 13, and no continuous sedative infusions);g) effective cough; and (h) normal acid base and electrolytes (1). Exclusion criteria were: (a) tracheostomized patients; b) patients with no central venous catheter; c) negative for informed consent; d) intolerance to the first SBT; and e) dead before weaning trial (Fig. 1).

2.3. Weaning Protocol

Patients meeting these criteria were then weaned in a semirecumbent position, using a two-step weaning protocol (measurements of predictors followed by a T-tube trial during 30 min.). In spontaneous breathing, frequency to tidal volume index (f/VT) was calculated by the respiratory rate (RR) and VT ratio measured, using an electronic re-spirometer. Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were measured with a manometer and defined as the most negative and positive values, respectively, produced by three consecutive inspiratory and expiratory trials against a unidirectional valve during 20 sec.

Those with f/VT 105 were submitted to spontaneous breathing on the T piece for 30 min. (defined as SBT) with supplementary humidified oxygen (4–7L/min) to achieve arterial oxygen saturation $\geq$ 90% as measured by pulse oximetry. Patients with intolerance to SBT, defined by: RR $\geq$ 35 breaths/min, oxygen saturation by pulse oximetry (SpO_2) < 90%, heart rate $\geq$ 130 beats/min or changes $\geq$ 20%, change in mental status (drowsiness, coma, agitation, anxiety), worsened discomfort, diaphoresis or signs of increased work of breathing (use of accessory respiratory muscles or thoracoabdominal paradox) were returned to MV. At this point, patients were selected for entry in the study.

After successful completion of an SBT, patients were extubated, and followed for presence of post extubation respiratory distress during 48 hrs. EF was defined as need of re-intubation in 48 hrs. Noninvasive ventilation was used to prevent respiratory distress after extubation in all patients with chronic obstructive pulmonary disease (COPD).

3. Measurements

Measurements of ventilatory parameters were recorded at 1st min and at 30th min of SBT. Respiratory compliance, RR, oxygenation and pressure index (CROP) were measured immediately before SBT (during MV support) and calculated by the formula:

$[Cdyn \times MIP \times (PaO_2/PAO_2)]/RR$, where Cdyn stands for dynamic compliance, PAO_2 for alveolar oxygen pressure, and RR for respiratory rate. Arterial and venous blood samples were collected immediately before SBT (during MV support) and at 30th min of SBT. Hemodynamic variables (heart rate and arterial blood pressure), demographic data, Acute Physiology and Chronic Health Evaluation (APACHE II) score (17) at first 24 hrs. of ICU stay, ICU admission diagnosis, comorbidities, Glasgow Coma Scale score, days in ICU, MV days, were also registered. The $ScvO_2$ and arterial blood were sampled by central venous access (placed in the internal jugular or subclavian vein) and radial artery, respectively, and were analyzed immediately, using a blood gas analyzer. Oxygen extraction ratio (O_2ER) was calculated by the formula: $(SaO_2\text{-}ScvO_2)/SaO_2$.

3.1. Statistical Analysis

All data were expressed as mean ± standard deviation for continuous variables and percentages for categorical variables. Differences between the two groups at baseline were analyzed with the use of Student's t test or Mann-Whitney U test for continuous variable and chi-square test for categorical variable, including the Fisher test. Logistic regression was performed for multivariable analysis for all univariate relevant variables that discriminate EF for extubation success (ES) patients. The Pearson test and Spearman test were used to determine correlations of parametric and nonparametric variables, respectively. Incremental analysis of the area under the receiver operating characteristic curve was performed to quantify $ScvO_2$ differences between MV and the 30th min of SBT. Statistical analysis was performed by a statistician, using the commercially available software (Statistical Package for Social Science - SPSS 11.0, Chicago, IL). Statistical significance was set at $p<.05$.

3.2. Results

From December 2011 to November 2012 (12 months), 487 patients were submitted to MV in one study ICU of tertiary hospital: 39 died before weaning trial, 56 had been MV dependent for < 48 hrs. 38 declined consent, 17patients had no central venous catheter at the moment of weaning trial, and 116 were submitted to early tracheotomy. 221 consecutive MV patients were enrolled in the study (Fig. 1). The mean age of these patients was 54 ± 20 years; mean APACHE II score in first 24 hrs. of ICU stay was 16 ± 7, and 56.6% were male. The most frequent diagnosis at the time of ICU admission was sepsis (52.5%) and ICU sample mortality rate was 19%. All patients underwent a two-step weaning protocol, but the intubation rate was 30%. Patient characteristics, ventilator settings, ventilatory and hemodynamic parameters are shown in Table 1.

All Patients (Comparing MV and 30th Minute of SBT)

There was a significant lowering of Pao2, Sao2 and Scvo2 evaluated at 30th min. of SBT than at MV measurement (93 ± 7 mmHg vs. 113 ± 18 mmHg, p <.001; 95 ± 4% vs. 98 +- 1.9%, p < .001; 65 ± 9% vs. 70 ± 6%, p < .001, respectively) (Table 2). Heart rate increased significantly at the 30th min of SBT (93 ± 17 beats/min to 97± 20 beats/min, p = 0.02) and mean arterial pressure remained stable (91 ± 10 mmHg to 94 ± 10 mmHg, p= .35) when compared with MV measurement. Ventilatory parameters as well as other hemodynamic parameters and blood gas measurements were similar during MV and at 30th min of SBT.

Extubation Outcome (Comparing Extubation Failure and Extubation Success)

SaO_2, $ScvO_2$, and O_2ER at the 30thmin of SBT were associated with EF (Tables 1and 2). However, multivariate analysis demonstrated that only $ScvO_2$ (ES = 69 ± 7 vs. EF = 61 ± 7; p < .001) and O_2ER (ES = 28 ± 7 vs. EF = 35 ± 8, p < .001) at the 30th min of SBT could discriminate EF from ES. The PaO_2, SaO_2, $ScvO_2$, and O_2ER measurements between ES and EF from MV to 30th min of SBT are shown in Table 2.

A > 5% reduction of $ScvO_2$ was associated with greater risk for re-intubation (odds ratio = 52.6, 95% confidence interval= 16.3446–169.42, p <.0001). A receiver operating characteristic curve was obtained with this value and demonstrated 87% of sensitivity, 90% of specificity, positive predictive value of 0.78, and negative predictive value of 0.93 for EF (Fig 2). In our study, a reduction of 15% in $ScvO_2$ predicted 100% of EF. Mortality rate, ICU stay, and days on MV were significantly higher in the EF group than in the ES group (Table 4).

4. Discussion

According to the Fick principle, oxygen uptake ($V\dot{}O_2$) depends on $D\dot{}O_2$ and O_2ER (10, 25). The study by Jubran et al (11) looked at the mixed venous oxygen saturation (SVO_2) monitoring for assessing the hemodynamic performance and global tissue oxygenation in determining weaning outcome. He demonstrated that ventilator supported patients who failed a trial of spontaneous breathing developed a progressive decrease in SVO_2 caused by the combination of a relative decrease in O_2 transport and an increase in O_2 extraction by tissues. This was not found in the failure group. The combination of greater venous admixture and low SVO_2 can lead to rapid desaturation and a relative decrease of oxygen supply (24).

In our study a greater risk of re-intubation was associated with a > 5% reduction in $ScvO_2$ (87% sensitivity, 90% of specificity, positive predictive value of 0.78, and negative predictive value of 0.93), and with a higher calculated O_2ER in the re-intubated patients.

Use of Svo_2 during the weaning period have previously studied (10,19-23).Noll and Byes (25) showed correlation of SvO_2, vital signs, and arterial blood gases in 30 consecutive postoperative coronary artery bypass graft cases, but only SpO_2 and respiratory rate correlated with weaning failure.

Cassiano et al (18) studied the predictive value of $SCVO_2$ to predict for re-intubation in difficult to wean patients who were defined as failure to tolerate the first 2hrs T-tube trial , and found that a > 4.5% reduction in

$SCVO_2$ associated with a greater risk of re-intubation. Different from these studies, our study group was comprised predominantly of critical ill MV patients who succeeded and passed the first SBT and observed for 48 hours after extubation for the need of re-intubation, and our results demonstrated that $SCVO_2$ was an effective EF predictor even in patients who passed the first SBT successfully. The choice of $ScvO_2$ instead of SvO_2 was due to limited use of a pulmonary artery catheter during weaning period, reflecting our everyday clinical practice. Pulmonary artery catheterization is costly and has inherent risks. In comparison, $ScvO_2$ is part of the standard care of critically ill patients and is easier and safer.

Other investigators (13-15) had demonstrated adequate correlation between $ScvO_2$ and SvO_2, except in critically ill patients. Rivers et al (12) and Vallet et al (15) previously showed that early goal directed therapy based on $ScvO_2$ reduces mortality in patients with severe sepsis and septic shock. Measurement of $ScvO_2$ is a potentially reliable and convenient tool, which could rapidly warn about acute change in the oxygen supply and demand of critically ill patients. Our data showed that, during MV (immediately before SBT), $ScvO_2$ was not different between EF and ES patients, but that $ScvO_2$ reduction during T-tube trial was able to predict EF in 83% of the cases. $ScvO_2$ remained unchanged in the ES group.

Mortality rate, ICU stay, and days on MV were- significantly higher in the EF group than in the ES group, this is similar to the results obtained by Cassiano et al (18). Overall mortality was 19%, with a mean APACHE II score of 16—corroborating the findings of Knaus et al (17). This study's main limitation is the nonrandom design. In our patients, the success of SBT did not guarantee successful extubation. Therefore, we believe that measurements of $ScvO_2$ during T-tube trial could be considered as a new parameter for prediction of re-intubation in patients who passed the SBT.

5. References

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Fig. 1: Enrollment. MV:Mechanical Ventilation; SBT: Spontaneous Breathing Trial; CVL: Central Venous Line.

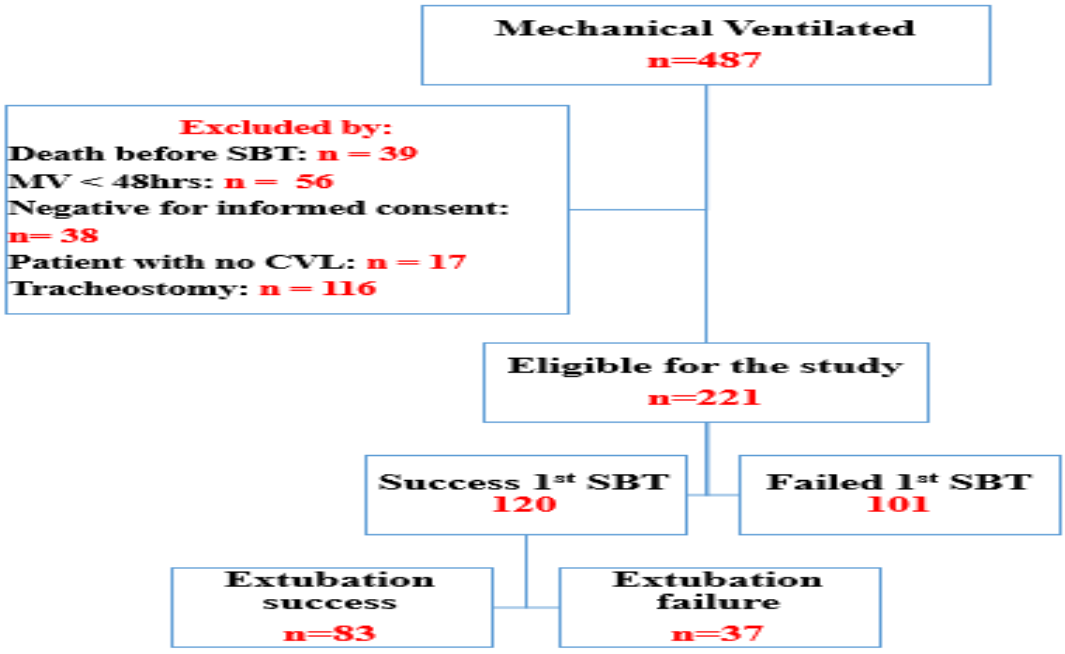

Table 1. Demographic Characteristics, Clinical Parameters & Ventilatory Settings

Variables	All patients (N=120)	Extubation Success (n=83)	Extubation Failure (n=37)	P
Age, yrs.	54±20	52±20	56±18	0.33
Male,%	68(56.6%)	42(50.6%)	26(7.27%)	0.05
Admission APACHE II	16.2 (3.4)	15.8 (2.8)	18.2(5)	0.170
GCS at extubation	14(3.3)	14.2(3)	12.8(4)	0.23.7
Hb concentration	9.8±1.6	10±1.7	9.6±1.5	0.63
ICU Admission, %				
Sepsis	63(53%)	43(51%)	20(45%)	0.42
Stroke	11(9%)	5(6%)	6(16%)	0.53
Postoperative	27(23%)	22(26.5%)	5(13.5%)	0.32
Exacerbation of asthma	4(3%)	4(4.8%)	0	N/A
Acute pulmonary edema	7(6%)	5(6%)	2(5.4%)	0.77
Exacerbation of COPD	8(7%)	4(4.8%)	4(10.8%)	0.63
Comorbidities %				
COPD	15(12%)	4(4.8%)	11(29%)	0.02
Heart disease	4(33%)	18(12%)	22(59%)	0.54
Ventilatory settings at weaning trials				
PEEP, CmH_2o	5±1	5±1	5±1	0.96
Inspiratory pressure, CmH_2O	17±4	18±5	19±4	0.71
VT (ml)	536± 143	547±136	526± 131	0.07
Cdyn (mL/cmH_2o)	52±25	53±17	50±23	0.45
Pao_2/Fio_2	288±101	299±92	289±109	0.67

APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: Intensive Care Unit; MV: Mechanical Ventilation; GCS: Glasgow Coma Scale; COPD: Chronic Obstructive Pulmonary Disease; PEEP: Positive End-Expiratory Pressure; VT: Tidal Volume; Cdyn: Dynamic Compliance; PaO_2/FIO_2: Arterial Pressure/Oxygen Fraction Ratio; NA: Not Analyzed. *A* Comparing extubation failure to extubation success.

Table 2: Ventilatory & Hemodynamic Parameters, Arterial & Central Venous Blood Gases Data During MV & at 30^{th} min of SBT

Variables	All patients (N=120)	Extubation Success (n=83)	Extubation Failure (n=37)	P
During Mechanical Ventilation				
ABG				
PH	7.39±1	7.37±0.9	7.4±0.6	.42
PCO_2	36±11	35±9	35±10	.20
PO_2	113±18	113±17	113±19	.44
aO_2%	98±1.9	98±2	97±2	.38
$SCVO_2$%	70±6	70±7	69±8	.46
O_2 ER	28.5±7	28.5±7	29±7	.1
Ventilatory Parameters measured at 1^{st} min of min				
F/VT breath/min/L	70±22	65±19	73±23	.65
RR breath/min	24±7	23±8	26±19	.27
MIP, cmH_2O	41±13	43±11	42±14	.36
MEP, cmH_2O	29±10	30±9	27±8	.49
Hemodynamics Parameter				
HR beat/min	93±17	94±12	96±8	.21
SAP mmHg	128±18	129±20	131±22	.39
DAP mmHg	74±13	73±12	70±17	.92
MAP mmHg	90±15	91±10	92±13	.81
At 30^{th} min SBT Blood gases				
PH	7.38±0.7	7.37±0.9	7.36±	0.8
$PaCo_2$ mmHg	36±12	35±8	39±9	0.9
PaO_2 mmHg	93±7	94±4	89±2	0.41
SaO_2%	95±4	96±3	94±4	0.02
$SCVO_2$%	65±9	69±7	61±7	.0001
O_2 ER%	31.5±8	28.1±7	35±8	.0001
Ventilatory Parameters				
f/vT breath/min/L	83±34	74±20	92±19	.52
RR breath /min	25±7	23±9	29±5	.14
MIP,cmH_2O	40±12	42±9	37±13	.15
MEP, cmH_2O	29±9	29±8	27±9	.16
Hemodynamic Parameters				
HR beat/min	97±20	92±10	103±10	.13
SAP mmHg	130±18	130±21	137±21	.15
DAP mmHg	75±12	75±13	76±16	.78
MAP mmHg	93±13	94±10	97±15	.32

MV: Mechanical Ventilation; SBT: Spontaneous Breathing Trial; $PaCO_2$: Carbon Dioxide Arterial Pressure; HCO3: Arterial Bicarbonate; PaO_2: Oxygen Arterial Pressure; SaO_2: Arterial Oxygen Saturation; $ScvO_2$: Central Venous Oxygen Saturation; O_2ER: Oxygen Extraction Rate; f/VT: Frequency To Tidal Volume Index; RR: Respiratory Rate; MIP: Maximal Inspiratory Pressure; MEP: Maximal Expiratory Pressure; HR: Heart Rate; SAP: Systolic Blood Pressure; DAP: Diastolic Blood Pressure; MAP: Mean Arterial Blood Pressure.

Table 3: Results of univariate and multivariate analyses for sample weaning predictors

Variable	Extubation Success (n=83)	Extubation Failure (n=37)	Univariate Analysis	Multivariate Analysis
Sao_2 at 30th min of SBT, %	96±3	94±4	0.02	0.41
$SCVo_2$ at 30th min of SBT, %	69±7	61±7	0.0001	0.008
O_2 ER at 30th min of SBT, %	28.1±7	35±8	0.0001	0.003

SaO_2 on SBT, arterial oxygen saturation measured at 30th min of spontaneous breathing trial; $ScvO_2$, central venous oxygen saturation measured at 30th min of spontaneous breathing trial; O_2ER, oxygen extraction rate measured at 30th min of spontaneous breathing trial.

Table 4: Outcomes

Variable	Extubation Success (n=83)	Extubation Failure (n=37)	P
ICU Days	14±12	26±16	<0.0001
MV days	7±5	9±6	0.02
Mortality in ICU %	2(2)	15(40)	<0.0001

ICU: Intensive Care Unit; MV: Mechanical Ventilation

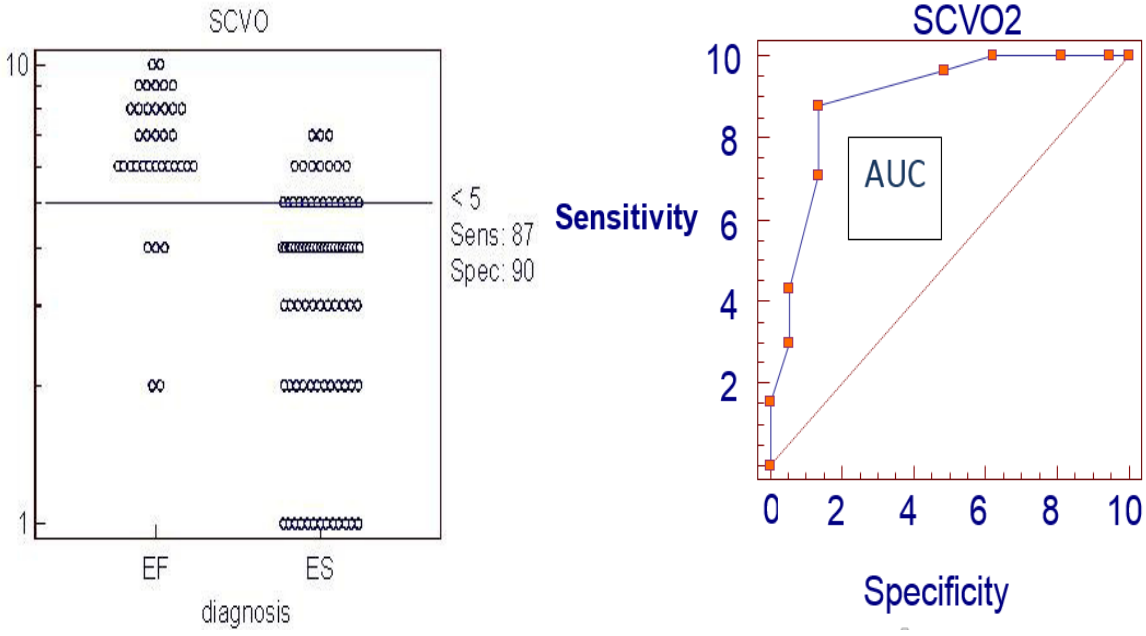

Fig.2. Receiver operating characteristic curve for $ScvO_2$ variations (30th min of SBT measured _ MV measured). A > 5% reduction of $ScvO_2$ was associated with greater risk of re-intubation (odds ratio _ 52.62, 95% confidence interval [CI[_ 16.3446–169.42, p > .0001). ROC curve demonstrated 87% of sensitivity, 90% of specificity, PPV of 0.78, and NPV of 0.93 for EF. *AUC*, area under the curve; *Scv*O_2, central venous oxygen saturation; EF, extubation failure; ES, extubation success *SBT*, spontaneous breathing trial; *MV*, mechanical ventilation; *PPV*, positive predictive value; *NPV*, negative predictive value.