What is the Optimal Cutoff Point of Rapid Shallow Breathing Index Calculated by the Mechanical Ventilator Parameters? A Retrospective Observational Study

Mekanik Ventilatör Parametreleri ile Hesaplanan Hızlı-Yüzeyel Solunum İndeksinin En Uygun Cutoff Değeri Nedir? Retrospektif Gözlemsel Bir Çalışma

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ABSTRACT

Background: The discontinuance of mechanical ventilatory support (MVS) is identified as weaning and weaning process is started whenever escalating factor for respiratory failure resolves. Although all weaning criteria were fulfilled, 20% of weaning attempts were unsuccessful. The Rapid Shallow Breathing Index is one of the most studied indices. In this study, we aimed to find out the optimal cutoff point of the RSBI measured in MVS.
Methods: This retrospective, non-interventional cohort study was conducted at a tertiary care hospital in Ankara, Türkiye. After collecting all data, the study population was divided into two group according to weaning failure (WF). Statistical analysis included Mann Whitney U-test, Youden index, and ROC-curves to predict WF.
Results: 46 patients fulfilled the inclusion criteria, and nine patients could not tolerate extubation and required reintubation [WF (+)group, 19.5%] within 72 hours. Not only the RSBI but also the other parameters like Static compliance (Cstat) and PaO_2/FiO_2 differed among groups. In this study, the discriminative power which was appraised using the AUC was high enough with RSBI (AUC= 0.962).
Conclusion: MVS may decrease RSBI and lower predictive value in classical original cutoff point (105). However, the discriminative power with 40 as the threshold level was proven to be effective in our study.

Key Words: Rapid Shallow Breathing Index, weaning failure, cutoff point

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ÖZET

Amaç: Mekanik ventilasyon desteği (MVS)'nin kesilmesi "weaning" olarak tanımlanır ve solunum yetmezliğine sebep olan faktör ortadan kalkınca süreç başlatılır. Tüm weaning kriterleri yerine getirilse dahi weaning teşebbüslerinin yaklaşık% 20'si başarısız olmaktadır. Hızlı Yüzeyel Solunum İndeksi (RSBI) en çok çalışılan prediktif indekslerden biridir. Bu çalışmada, MVS'de ölçülen RSBI'nın en uygun cutoff değerini bulmayı amaçladık.
Yöntem: Bu retrospektif, girişimsel olmayan kohort çalışması, Ankara, Türkiye'de bir üçüncü basamak hastanesinde yapılmıştır. Tüm veriler toplandıktan sonra çalışma popülasyonu weaning başarısızlığına (WF) göre iki gruba ayrıldı. İstatistiksel analiz, Mann Whitney U-testi, WF'yi tahmin etmek için Youden indeksi ve ROC eğrilerini içeriyordu.
Bulgular: 46 hasta çalışma kriterlerini sağladı ve değerlendirmeye alındı ve dokuz hasta 72 saat içinde ekstübasyonu tolere edemedi ve tekrar entübasyon [WF (+) grubu% 19.5] gereksinimi oldu. Sadece RSBI değil aynı zamanda Statik kompliyans (Cstat) ve PaO_2 / FiO_2 gibi diğer parametreler açısından da gruplar arasında farklılık bulundu. Bu çalışmada, AUC kullanılarak değerlendirilen diskriminatif güç, RSBI (AUC= 0.962) ile yeterince yüksekti.
Sonuç: MVS, RSBI'yı düşürebilir ve klasik orijinal cutoff değerinde (105) RSBI'nın prediktif değerini azaltabilir. Bununla birlikte, çalışmamızda eşik seviyesi 40 olarak belirlendiğinde diskriminatif gücünün etkili olduğu kanıtlanmıştır.

Anahtar Sözcükler: Hızlı yüzeyel Solunum İndeksi, weaning başarısızlığı, cutoff değeri

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INTRODUCTION

Even though mechanical ventilatory support (MVS) is a foundation stone in intensive care practice, discontinuation of this support as soon as possible decreases not only the morbidity and mortality rates but also the hospitalization charges (1). The transfer process of the respiratory load to the patient's spontaneous breathing (the discontinuance of MVS) is identified as weaning and weaning process is started whenever the escalating factor for respiratory failure resolves (2). Actually, this tough and labor demanding process - weaning from mechanical ventilatory support (WMVS) - has been the primary target right after endotracheal intubation of the patient. Unless it occurs abruptly, WMVS is handled by intensivists in a gradual manner in the intensive care unit (ICU) practice. It is shown that relying on solely clinical expertise is generally incorrect so some indices and weaning criteria are utilized to increase weaning time accuracy (3,4). Major weaning criteria are summarized as resolution of the escalating condition for intubation, sufficient respiratory effort, and hemodynamic, neurologic and metabolic stability. However, previous studies about WMVS showed that approximately 20% of the weaning trials failed, even all the weaning criteria are fulfilled (3,5,6).

Redundant delays increase the rate of ventilatory induced pneumonia, hospital infections, and diaphragmatic dysfunction. In the meantime, matutinal WMVS leads to further tension on the cardiovascular and respiratory systems. Increased morbidity and mortality due to either matutinal or redundant delayed WMVS enforce intensivists to search objective indices to prognosticate weaning failure (WF) and appropriate weaning time (1,5,7). In the literature, there are many studies investigating a better index to predict weaning success or failure in the most accurate way, whereas the efficiency of these studied indices is not perfect in most cases (3,8). Among them, the ratio between respiratory rate and tidal volume (f/VT) or in another and well known word " the Rapid Shallow Breathing Index (RSBI)" is one of the most studied indices. It has become popular because of its simplicity and abstinence of complicated respiratory mechanic calculations (5,8,9).

RSBI was presented first by Yang and Tobin in 1991 and in this original study, the positive predictive value (PPV) for RSBI was claimed to be 0.85 with the cutoff point 105. In this study, RSBI was measured by a hand-held spirometer attached to the endotracheal tube (ET) while the patient breathed room air for 1-min without any ventilator assistance (10). Since that time, a number of studies suggest different alterations like serial measurements and varied cut off points to advance its PPV (8,11,12).

The spontaneous breathing trial (SBT) with a T-piece and the usage of low support pressure (LSP), in either continuous positive airway pressure (CPAP) or in spontaneous mode, are the most widelyused WMVS methods (4,13). LSP becomes important especially in patients with cardiac problems because they could not tolerate the extinction of supported positive pressure which decreases the preload and work of breathing (WOB). It was shown that the usage of LSP with positive end-expiratory pressure (PEEP) will reduce the WOB by 36% comparing to a T-piece (14,15). The mode of ventilation may affect equitable physiologic and respiratory measurements utilized to identify readiness for WMVS (4,11,16).

This positive pressure requirement and the advancements in technology lead researchers to new quests while numerous ventilator algorithms started to incorporate and to demonstrate RSBI as a parameter (17). Some researchers took advantage of this improvement and it has been shown that RSBI value calculated either from mechanical ventilator data or classical ventilometry is similar (4,8,11). But in some specific patient populations-like the ones with cardiac problems- the RSBI values were found smaller in CPAP than in T-piece SBTs (9,18,19).

In this study, we aimed to find out the optimal cutoff point of the RSBI measured in MVS –ventilator data- to predict WF and the relations between weaning outcomes.

MATERIALS and METHODS

This retrospective, non-interventional cohort study was conducted during the period between July 2017 and June 2018 at a tertiary care hospital in Ankara, Türkiye. It was approved by the ethics committee of the Turkey Advanced Specialty Education and Research Hospital (number 929/2018). Since our study was in the category of non-interventional clinical research with its retrospective structure, an extra formal consent other than the patients or relatives had given prior to hospitalization was not required.

In this study, the mechanical ventilator records of the patients who were clinically stable and decided to be ready for WMVS by their primary intensivists (other than the study authors) were appraised. The patients were either in CPAP or in spontaneous mode 30 minutes before extubation. To standardize the data and avoid any bias related to mechanical ventilator type, only the patients who were supported with the same mechanical ventilator type [(Hamilton Galileo, (Hamilton Medical AG, Bonaduz, Switzerland)] and with pressure support ranging from 10–15 cm H_2O were evaluated.

The patients who needed MVS> 72 hours for any reason –neurological, cardiovascular and respiratory reasons- and met the criteria for WMVS, classically used in the ICU routine, were included. These criteria were as follows: resolution of the escalating condition for intubation, sufficient respiratory effort and hemodynamic, neurologic and metabolic stability. In our ICU department, all intubated patients were appraised for WMVS daily as a routine procedure by using standard parameters. These parameters other than criteria mentioned above were including partial pressure of arterial oxygen (PaO_2)>60 mmHg with fractional inspired oxygen (FiO_2)<0.4, PEEP ≤ 5 cm H_2O. The patients who had not fulfilled these criteria were excluded from the study. Also, the patients with incomplete records, multiple weaning trials, the tracheostomized patients and self-extubated patients were excluded from the study. Additionally, only the first data set of patients with a history of multiple intubations was included in the data analysis.

Data acquisition

All clinical variables of patients were retrospectively collected from our institutional database. RSBI and the other ventilatory parameters which were determined by mechanical ventilator software were imported into a spreadsheet (Microsoft Excel 2013, Microsoft Corporation). Demographic data, diagnosis at admission, the reason for intubation, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score, length of stay (LOS) in the hospital and in ICU, duration of MVS before weaning, morbidity, and mortality were collected as well. After collecting all data, the study population was divided into two group according to WF and it was defined as the requirement for the reinstitution of MVS within 72 h after ET removal. To forestall the variability in the data collection, all values were reviewed by the authors of the study.

Statistical analysis

Statistical analysis was performed using SPSS version 20.0 for Windows (SPSS Inc.; Chicago, IL, USA)and MedCalc 15.8 software (MedCalc, Ostend, Belgium). Data were analyzed, and the continuous variables were reported as mean± standard deviation (SD), and nominal variables were reported as total number and percentages.

One-Sample Kolmogorov-Smirnov test was used to evaluate the normal distribution of the variables in order to select the type of statistical tests –parametric or non-parametric tests-. Asymp.sig. (2-tailed) levels were ≤ 0.05 so we had to choose non-parametric tests. The Spearman's rho test was used to evaluate the correlations between variables and the Mann-Whitney U test was chosen to appraise the categorical variables significance. Comparisons were two-tailed and a 'p' value < 0.05 was considered statistically significant in all analyses.

Other than these tests, the Hosmer-Lemeshow test was used to calculate the calibration of RSBI and receiver operating characteristic (ROC) curve to appraise the discrimination power of RSBI in WF cases. ROC-Area Under Curve (AUC) was determined to quantify the accurate prediction of RSBI model and the method designed by DeLong et al. (20) was used. Additionally, the Youden Index (*J*) which is one of the most used brief statistic method of the ROC curve with similar importance to sensitivity and specificity, was utilized to define the most accurate cutoff point. J value is between zero and one, while closeness to one indicates bigger efficacy for the test variable which is evaluated. AUC value more than 0.75 was appraised as satisfactory, AUC value more than 0.8 was appraised as well, and AUC value more than 0.9 was appraised as very good.

Ethics approval and consent to participate

This study was approved by the ethics committee of the Turkey Advanced Specialty Education and Research Hospital (number 929/2018). Since our study was in the category of non-interventional clinical research with its retrospective structure, an extra formal consent other than the patients or relatives had given prior to hospitalization was not required. It was a case-control medical record review.This study adhered to the principles in accordance with the Helsinki Declaration of 1975, as revised in 2008.

RESULTS

From July 2017 to June 2018, 86 patients weaned from MVS but only 46 of them fulfilled the inclusion criteria of our study (Figure 1).

10 patients were self-extubated, 5 patients were tracheostomized and 35 patients' data were either missing or discordant in the hospital database.

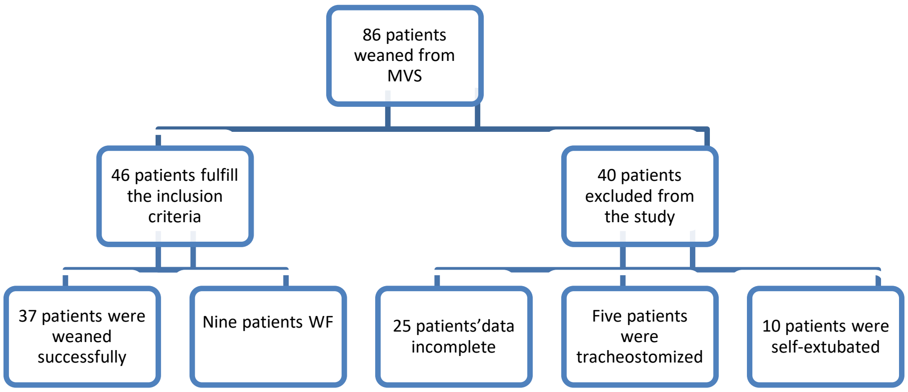

Figure 1: The flowchart that describes the study population.

Nine patients could not tolerate extubation and required reintubation [WF (+)group, 19.5%] within 72 hours. Of the 46 patients who were included in this study, 28 (60.9%) were male, and the mean age was 63.1 ±13 years (Table 1).

The reason for intubation in the majority of the cases was respiratory conditions like pneumonia or acute respiratory distress syndrome (47.8%). Demographic data were summarized in Table 1 and there was no significant difference between groups according to WF.

Table 1: Demographic data and medical history of the patients.

	WF (+) (n =9)	WF(-) (n= 37)	Total(n =46)	p*
Male gender	5 (55.6%)	23 (62.2%)	28(60.9%)	0.723
Age	62.2 ±11.6	63.3 ±13.5	63.1 ±13	0.638
Body mass index	26.2 ±2.6	25.4 ±2.5	25.5 ±2.5	0.514
Reason for intubation				0.157
Cardiac	3 (33.3%)	16 (43.2%)	19 (41.3%)	
Respiratory	6 (66.7%)	16 (43.2%)	22(47.8%)	
Neurological	0	5 (13.5%)	5 (10.9%)	
In-hospital mortality	4 (44.4%)	6 (16.2%)	10 (21.7%)	0.068
Medical history				0.685
None	2 (22.2%)	7 (18.9%)	9 (19.6%)	
Cardiac	5 (55.6%)	20 (54.1%)	25 (54.3%)	
Respiratory	2 (22.2%)	7 (18.9%)	9 (19.6%)	
Renal	0	3 (8.1%)	3 (6.5%)	

p-values calculated for comparison of the WF (+) group versus WF (-) group by statistical analysis.
Data are mean ±SD or n (%)
*Determined by Mann-Whitney U test or Spearman's rho test.
Abbreviations: WF, weaning failure

The mean duration of LOS in the hospital was 37.8 ±27.2 days, whereas LOS in ICU was 28.7 ±23 days. As it is summarized in Table 2, the outcomes and clinical variables between the two groups were similar and no significant difference was detected statistically.

Table 2: The clinical outcomes and clinical variables between the two groups.

	WF (+) (n =9)	WF(-) (n= 37)	Total(n =46)	p*
APACHE II score	13.2 ±6.3	12.5± 6.5	12.6± 6.4	0.697
Mean arterial pressure- mmHg	68.5 ±7.8	70 ±9.8	69.7 ±9.4	0.989
Heart rate beats/min	92 ±117	94.6 ±12.1	94.1 ±11.9	0.488
LOS hospital (days)	39.2 ±25.4	37.5 ±27.9	37.8 ±27.2	0.688
LOS ICU (days)	32.9 ±23.8	27.7 ±23.1	28.7 ±23	0.471
MVS duration before weaning (days)	9.3 ±4.6	6.5± 3.1	7 ±3,6	0.079

p-values calculated for comparison of the WF (+) group versus WF (-) group by statistical analysis.
Data are mean ±SD
*Determined by Mann-Whitney U test.
Abbreviations: WF, weaning failure; APACHE-II, Acute Physiology and Chronic Health Evaluation; LOS, length of stay; ICU, intensive care unit; MVS, mechanical ventilatory support

The data and the calculations derived from mechanical ventilator parameters were reported in Table 3. Not only the RSBI but also the other parameters like Static compliance (Cstat) and PaO_2/FiO_2 had differed among groups.

Peak pressure variable between groups was significantly different whereas the difference regarding the support pressure was not significant statistically.

Table 3: Mechanical ventilator data and calculated parameters

	WF (+) (n =9)	WF(-) (n= 37)	Total(n =46)	p*
Frequency	26.6± 6.2	17.8 ±4.9	19.5 ±6.2	0.001
Tidal volume, ml	394 ±121	565 ±132	532.2 ±146	0.002
Expiratory minute volume, ml	9.9 ±2.9	10 ±2	10 ±2.2	0.489
PaO_2/FiO_2, mmHg	228± 49.4	270 ±32	262.2 ±39.3	0.025
Cstat	37.4 ±8	58.3 ±14.7	54.2 ±15.9	<0.001
RSBI, breaths/min/L	78.4 ±19.7	34.1 ±15.1	42.8 ±23.8	<0.001
Support pressure, cmH_2O	13.8 ±1.9	13.7 ±1.6	13.7 ±1.6	0.695
Peak pressure, cmH_2O	21.9 ±4.3	18.8 ±2.2	19.4 ±2.9	0.046

p-values calculated for comparison of the WF (+) group versus WF (-) group by statistical analysis.
Data are mean ±SD
*Determined by Mann-Whitney U test.
Abbreviations: WF, weaning failure; Cstat, Static compliance; RSBI, Rapid Shallow Breathing Index; PaO_2/FiO_2, partial pressure of arterial oxygen/ fractional inspired oxygen

The Hosmer–Lemeshow goodness-of-fit test revealed a good calibration for the RSBI as shown in Table 4 and Table 5 with sig.level 0.994 and overall percentage 91.3.

Table 4: Hosmer and Lemeshow Test for RSBI

Step	Chi-square	df	Sig.
1	1.45	7	0.994

Table 5: Classification table and overall correct percentage value with RSBI

Observed			Predicted WF		Percentage Correct
			1	0	
Step 1	WF	1	6	3	66.7
		0	1	36	97.3
	Overall Percentage				91.3

Abbreviations: WF, weaning failure; RSBI, Rapid Shallow Breathing Index

In this study, the discriminative power which was appraised using the AUC was high enough with RSBI (AUC 0.962) while confidence interval (0,860 to 0,996) and specificity (78.38%) were high enough for cutoff point 40 (Figure 2 and Table 6).

Table 6 also demonstrates that the cutoff point 40 was the optimal cutoff point with maximum sensitivity and 78.38 specificity.

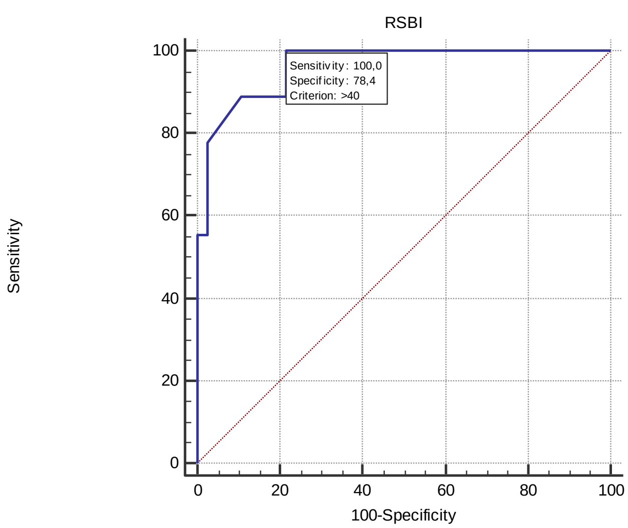

Figure 2: Receiver operating characteristic (ROC) curves of RSBI with WF as a dependent factor
Abbreviations: WF, weaning failure; RSBI, Rapid Shallow Breathing Index

Table 6: Area Under the Curve levels with RSBI and Youden index

	Value	95% Confidence interval	z statistic	Associated criterion
AUC	0.962	0.860 to 0.996	16.713	
Youden index	0.7838	0.6216 to 0.8649		>40

Abbreviations: AUC, Area Under the Curve; RSBI, Rapid Shallow Breathing Index

The other possible cutoff points are summarized in Table 7 and it is clearly shown that 40 is the optimal cutoff point with maximum efficiency.

Table 7: The comparison of Criterion values and coordinates of the Receiver operating characteristic curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
>12	100.00	66.4 - 100,0	2.70	0.07 – 14.2	1.03	0.00
>25	100.00	66.4 – 100.0	32.43	18.0 – 49.8	1.48	0.00
>40	100.00	66.4 – 100.0	78.38	61.8 – 90.2	4.62	0.00
>44	88.89	51.8 – 99.7	78.38	61.8 – 90.2	4.11	0.14
>53	88.89	51.8 – 99.7	86.49	71.2 – 95.5	6.58	0.13
>60	77.78	40.0 – 97.2	97.30	85.8 – 99.9	28.78	0.23
>77	55.56	21.2 – 86.3	100.00	90.5 – 100.0		0.44

Abbreviations: CI, Confidence interval; LR, likelihood ratio

The calculated AUCs for different indices, like Cstat and Expired minute volume which are the other most used weaning indexes, were smaller than RSBI (0,929 and 0.575) and these indices are compared to RSBI in Table 8 and Figure 3.

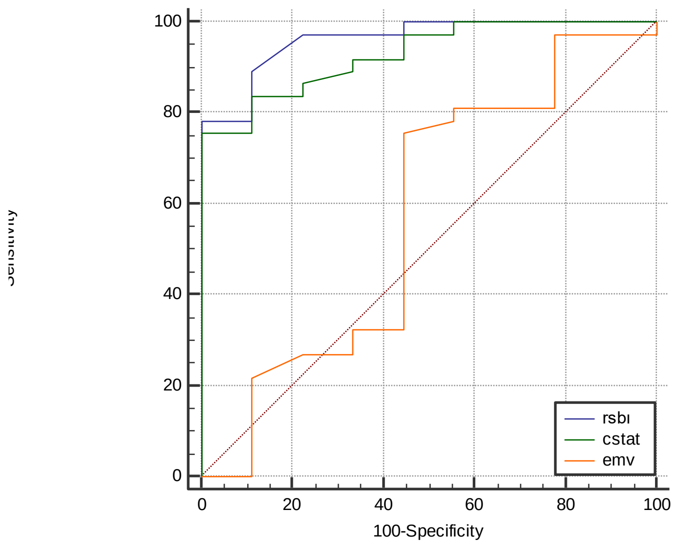

Figure 3: Comparison of ROC curves with different weaning indices according to WF
Abbreviations: ROC, Receiver operating characteristic; WF, weaning failure; RSBI, Rapid Shallow Breathing Index; Cstat, Static compliance; EMV, Expired minute volume

Table 8: Comparison of AUC with different weaning indices according to WF

Variable	AUC	SE	95% CI
RSBI	0,962	0,0277	0,860 to 0,996
Cstat	0,929	0,0383	0,814 to 0,984
EMV	0,575	0,128	0,421 to 0,719

Abbreviations: RSBI, Rapid Shallow Breathing Index; Cstat, Static compliance; EMV, Expired minute volume; CI, Confidence interval; AUC, Area Under the Curve

DISCUSSION

The timing for WMVS is crucial to avoid morbidity related to matutinal or late extubation whereas widely used indices that prognosticate WF in ICU practice are imperfect. WF is related to poor outcomes and each reintubation episode increases the mortality rates unrelated to underlying disease seriousness (21). In our study, the WF rate was smaller than that was reported in the literature (19.5% vs 30%), probably due to the relatively younger age population in the study group (5). Corbellini et al. (22) concluded that aging >80 increased the WF rate (27.8% vs 22.1%) in their study and the mean age of our study group was 63.1 ±13 years while no significant difference was detected regarding age variable.

Weaning readiness tests like SBT or LSP and indices like RSBI are utilized before discontinuance of MVS to assist judgment (4,5). The usage of LSP is required as a protective option especially in cardiac patients because SBT may increase cardiopulmonary distress and O_2 demand with a rise in cardiac failure risk (13,16,23).

RSBI was appraised by at least 25 different studies with different cutoff points and measurement techniques (11,17,24,25). Different ventilation modes, different support pressures and mechanical ventilatory data utilizing to determine RSBI cutoff point rather than classical hand-held spirometer are the reasons for this rearrangement necessity. It is stated that the LSP decreases the WOB and may influence the intensivists' decision by lowering the RSBI (15). Nevertheless, Shingala et al. (26) claimed that RSBI had better predictive power with less cardiovascular stress when it was calculated on LSP rather than T-piece.

The RSBI measured in the original manner had a sensitivity of 97% in predicting weaning success defined as both successful SBT and not requiring re-intubation within 24 h. However, 105 which was described by Yang et al. (10) as cutoff point was observed in none of the patients in our study.

The mean RSBI value in WF (+) group was 78.4 ±19.7 cycles/min/L whereas it was 34.1 ±15.1cycles/min/L in WF (-) group. There was a significant difference between groups statistically and this was in line with the literature (8,25). Youssef et al. (27) proposed cutoff point of 51 with AUC 0.609 while Frutos et al. (28) recommended 57 as a threshold value. In our study, it is computed that an RSBI cutoff point of 40 had sensitivity and specificity with maximal efficacy (100 and 78.38 respectively) compared to other threshold values.

The AUC value (0.962) was appraised very good and the overall correct percentage was 91.3. This finding was similar or even better than the study of Goncalves et al. (4). In this study 78 was claimed as the best cutoff point, but for RSBI with LSP 50- as a cutoff point- had better accuracy compared to 78 (61 vs 48).

Hosseini et al. (29) claimed that the APACHE II score could be used as a prognostic index to estimate WF whereas in our study (the mean APACHE II score was 12.6± 6.4) no relation was detected with WF.

Being retrospective, observational and non-interventional study is the major limitation of our study. Due to the nature of this study, a specific protocol for WMVS could not be provided. However, to overcome this protocol bias data were searched thoroughly and approximately half of the cases were excluded from the study (Figure 1). This situation resulted in the second limitation as small sample size which was not suitable for parametric tests. The third limitation was using only mechanical ventilator data to calculate RSBI and other respiratory parameters, not respirometer as in the original study. The final limitation was that our study findings could not be generalized due to retrospective nature.

CONCLUSION

MVS –even in low-pressure support and PEEP- may decrease RSBI and lower predictive value in classical original cutoff point which was 105. However, the discriminative power with 40 as a threshold level was proven to be effective in our study. This relation should be reinforced and validated with prospective studies.

Conflict of interest
No conflict of interest was declared by the authors.

List of abbreviations
MVS, Mechanical Ventilatory Support;
WMVS, Weaning From Mechanical Ventilatory Support;
ICU, Intensive Care Unit;
WF, weaning failure;
f/VT, the ratio between respiratory rate and tidal volume;
RSBI, Rapid Shallow Breathing Index;
PPV, positive predictive value;
ET, endotracheal tube;
SBT, spontaneous breathing trial;
LSP, low support pressure;
CPAP, continuous positive airway pressure;
WOB, work of breathing;
PEEP, positive end-expiratory pressure;
PaO2, partial pressure of arterial oxygen;
FiO2, fractional inspired oxygen;
APACHE, Acute Physiology and Chronic Health Evaluation;
LOS, length of stay;
SD, standard deviation;
ROC, receiver operating characteristic;
AUC, Area Under Curve;
J, Youden Index;
Cstat, Static compliance

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