A Prospective Comparative study between the Tobin Index and Integrative Weaning Index to predict the outcome of trials of weaning from mechanical ventilation

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Abstract:

Weaning indices that are simple to derive and apply have been developed for predicting the likeliness of a patient to tolerate weaning. This study compared the Tobin Index and Integrative Weaning Index (IWI) to determine the better predictor for a successful weaning.

This was a prospective observational study done on 60 patients on mechanical ventilation meeting the defined criteria whose physicians considered clinically stable to be given a weaning trial. Pre-determined threshold values of the Tobin index and IWI for determining a successful or unsuccessful weaning were used. A daily assessment was made with calculation of the Tobin index in GroupTI for extubation when Tobin Index≤105 breaths/min/L and IWI in GroupIWI when IWI>25 ml/min/cm H2O, with each group having 30 patients. A spontaneous breathing trial of 2 hours was given. The variables compared between the two groups were the outcome of weaning, duration of mechanical ventilation, ICU stay and hospital stay in days, and mortality. Comparison was done using Chi square test / Fisher's exact test and Mann Whitney test.

There was no significant comparison in terms of weaning success or failure, durations of mechanical ventilation, hospital stay and mortality. The duration of ICU stay was less and of statistical significance in the IWI group. However, the percentage of successful weanings while using the indices, both considered separately, was higher than the failures.

Both the predictive indices studied did not successfully predict weaning outcomes in all the cases thus limiting their use in clinical practice.

Key words: *successful weaning, mechanical ventilation, weaning predictors, Tobin index, integrated weaning index*

Introduction:

The optimal timing for discontinuation of ventilatory support in mechanically ventilated patients based solely on clinical judgement is known to often be inaccurate *[1]*. For this purpose, predictive weaning indices that are simple to derive and apply have been developed for predicting the likeliness of a patient to tolerate weaning. Unnecessary prolongation of mechanical ventilation can potentiate the risk of complications like, VILI and pulmonary barotrauma, ventilator associated pneumonia, airway injury, lengthened ICU stay and hospital expenses. Successful weaning has been defined as successful spontaneous ventilation for ≥24 hours *[2]*. Weaning can be classified as simple, difficult, or prolonged *[3]*. Simple wean – Patients passing their first SBT is considered a simple wean. This category comprises approximately half to two-thirds of the patients in ICUs, leading to extubation for most of them. Difficult-to-wean – Those patients subjected to a SBT, failing the first and then needing a minimum of three SBTs or up to one week to pass it are included in difficult-to-wean category, which includes patients intubated in the initial weeks of acute ICU admission. Prolonged weaning – This category includes patients that fail SBTs thrice or need beyond a week to pass it. If weaning takes beyond a week, there is a higher risk for death and extubation failure. It has been found that weaning based solely on clinicians' judgement has been associated with complications due to premature discontinuation of support *[4]* or unnecessary delay in removal of support *[5]*.

Weaning indices, by identifying the ability of a patient for spontaneous breathing at the earliest and patients who might have a failed weaning trial, helps to avoid diaphragmatic atrophy and cardiorespiratory distress or collapse. They help to assess different physiologic functions that could suggest reasons for ventilator dependence *[5]*.

The initial indices included as predictors of weaning were vital capacity *[6]*, minute ventilation *[7]*, and maximal inspiratory pressure (MIP) *[6,7]*. However, Conti and colleagues in their study in 2004 showed that these have poor predictive power. The study also evaluated other indices like airway occlusion pressure ($P_{0.1}$), respiratory rate (f), f/VT ratio with VT being tidal volume, MIP, $P_{0.1}$ in association with MIP and f/VT, and concluded that these were not powerful enough to predict successful weaning. The reasons for this were attributed to the differences in the study population (the clinical characteristics and diagnosis), the requirement for restarting mechanical ventilation during the T-piece trial being based on clinical criteria, and the method used to take measurements *[8]*. Indices such as the Integrative Weaning Index (IWI), the CROP index, the Inspiratory Effort Quotient (IEQ) and the CORE index were formulated which were considered to be more accurate as predictors of weaning as they took into account several physiologically mediated parameters. This study was conducted with a view to compare the Tobin Index and IWI to determine the better predictor for a successful weaning that would help to assess the accurate timing of weaning, and to determine the differences in the effect of including a weaning predictor on the duration of mechanical ventilation (days) and length of ICU stay (days) between the two groups. The Tobin Index or the RSB, described as the ratio of frequency of respiration to tidal volume (f/VT) is a well-studied and widely accepted index to assess readiness for weaning *[9]*. The IWI on the other hand, is an integrative index which integrates the physiologic parameter of static

respiratory system compliance and hence might be considered a better predictor *[10]* and sufficient studies to prove the same are not available.

Materials and methods:

This study was carried out as a prospective observational study on 60 patients with an admission diagnosis of respiratory disease on mechanical ventilation for more than 24 hours whose physicians considered clinically stable to be given a weaning trial in which first 30 subjects were in the TI group and the next 30 in the IWI group, in the ICUs of tertiary care hospitals of KMC Mangalore. It was conducted from September 2018 to June 2020 after approval from the Institutional Ethics Committee. Written informed consent for participation in the study was obtained from the relatives. Patients less than 18 years of age and more than 75 years of age, and patients with raised intracranial tension, neuromuscular disorders, pregnancy, hemodynamically unstable patients, or on high dose vasopressor or inotropes with evidence of active myocardial ischaemia, and patients with survival less than 48 hours were excluded from the study. The threshold value of the indices for determining a successful weaning was taken as Tobin Index ≤105 breaths/min/L for successful, and>105 breaths/min/L for an unsuccessful weaning and IWI >25 ml/cmH_2O for successful, and <25 ml/cmH_2O for an unsuccessful weaning *[11]*. The patients' readiness for weaning was assessed based on the ABCD model which is a patient centered therapist driven protocol (TDP) *[12]*. It is based on signs of improvement of the underlying cause of respiratory failure, adequate oxygenation assessed in terms of PaO_2/FiO_2 ≥ 150-200 and pH ≥ 7.25, PEEP ≤ 5-8cm H_2O, FiO_2 ≤ 0.4-0.5, hemodynamic stability, that is, there should be no active myocardial ischemia or clinically significant hypotension (not on vasopressors or low dose vasopressors like dopamine or dobutamine at <5mg/kg/min), and the patients' ability to initiate inspiration.

A daily formal assessment was made with calculation of the Tobin Index in Group$_{\mathbf{TI}}$ for extubation when Tobin Index≤105 breaths/min/L and IWI in Group$_{\mathbf{IWI}}$ when IWI>25 ml/min/cm H_2O, with each group having 30 patients. IWI was calculated using the formula IWI= (C_{st} X SaO_2)/ (f/VT) where C_{st} =VT/ (plateau pressure –PEEP).

All the variables for the Tobin Index and IWI were obtained from the ventilator settings and arterial blood gas samples. The variables in the study that were considered were respiratory frequency(f), VT, plateau pressure, PEEP, SaO_2, and static compliance (C_{st}) which were recorded in the form of open-ended observational protocols in a proforma after attending to ethical issues. After assessment of the patient's readiness for weaning based on the patient centered therapist driven protocol discussed, the patient was given a 2 hour SBT using PSV or a T-piece if the index of the respective group was at or above the threshold value. Absence of clinical signs of cardiorespiratory distress was considered a successful SBT which was followed by extubation. Failed SBT or re-intubation within 24 hours of extubation was considered a failed weaning trial. The primary outcome was the difference in the weaning outcome and the number of days of mechanical ventilation between the groups. Additionally studied outcomes were the differences in the durations of ICU stay and hospital stay in days, and mortality. A purposive/judgement sampling method was used and the sample size for this study was calculated by the formula, n

$=Z_{\alpha}^{2} .S_{n} (1-S_{n}) / L^{2} .P$, where Z_{α} =1.56 at 95% confidence interval, S_{n} = Sensitivity (81%), L= allowable error (Precision), P= Prevalence, with 95% confidence interval and 90% power with respect to sensitivity =81%, which was 60. (Reference: N Engl J Med 1991; 324:1445-50) *[2]*. Data between groups was analysed and compared using Chi square test / Fisher's exact test and Mann Whitney test for association between categorical variables. A statistical package SPSS version 17.0 was used to do the analysis. P <0.05 was considered as significant.

Results:

The use of weaning predictors indicated a successful weaning outcome more than an unsuccessful one, with TI being better than IWI in the success outcome (76.7% vs. 73.3% respectively).However the comparison was statistically nonsignificant with a p value of 0.766 using the Chi square/Fisher's exact test. Also, the percentage of unsuccessful weaning was seen to be less in the $Group_{TI}$ when compared with the $Group_{IWI}$ (23.3% vs. 26.7% respectively) as shown in Table 1 and 2. Patient age was categorised and compared between the two groups using t test and p value was 0.853 which was not significant.Patient gender was compared by using the Chi square/Fisher's exact test and p value hence obtained was 0.426 which was not significant. Hence it can be said the patient groups compared are similar. Duration of mechanical ventilation, length of ICU stay and length of hospital stay were categorised and compared between the two groups using Chi square/Fisher's exact test and the same parameters were compared between the two groups based on an average (mean, SD, median and IQR) by Mann Whitney test because the data regarding the parameters was not normally distributed. It was seen that the mean duration of mechanical ventilation (days) was lesser in $Group_{IWI}$ than $Group_{TI}$ (3.55 vs 5.39 respectively) which was statistically nonsignificant with a p value of 0.185 and 0.056 with the respective statistical tests for comparison [Tables 2 and 3]. However, the percentage of the number of subjects whose duration of mechanical ventilation (days) was within 1-5 days was lesser in the $Group_{TI}$ as compared to the $Group_{IWI}$ with 69.6% and 86.4%respectively. Also, the percentage of the number of subjects whose length of ICU stay (days) was within 3-5 days was lesser in the $Group_{TI}$ when compared with $Group_{IWI}$ with 17.4% and 54.5% respectively [Table 1]. The reasons for these differences are not clear. The number of days of ICU stay was lesser in $Group_{IWI}$ compared to $Group_{TI}$ (5.86 vs. 9.96 respectively), which was of statistical significance with a p value of 0.013 (statistical significance p<0.05) using the Chi square/Fisher's test and was highly significant with a p value of 0.003 (statistical significance p<0.05) using the Mann-Whitney test. However, there was no significant difference in the duration of hospital stay (days) and mortality between the two groups as shown in Tables 2 and 3.

Table 1: Patient cohort, demographic data

	Group			
	GROUP TI		GROUP IWI	
	Count	Column N %	Count	Column N %

AGE	30 and below	2	6.7%	3	10.0%
	31 - 50	8	26.7%	6	20.0%
	51 - 70	17	56.7%	19	63.3%
	Above 70	3	10.0%	2	6.7%
	Total	30	100.0%	30	100.0%
GENDER	F	13	43.3%	10	33.3%
	M	17	56.7%	20	66.7%
	Total	30	100.0%	30	100.0%
OUTCOME	SUCCESSFUL	23	76.7%	22	73.3%
	UNSUCCESSFUL	7	23.3%	8	26.7%
	Total	30	100.0%	30	100.0%
DURATION OF MECHANICAL VENTILATION (days)	1 - 5	16	69.6%	19	86.4%
	6 - 10	4	17.4%	3	13.6%
	> 10	3	13.0%	0	.0%
	Total	23	100.0%	22	100.0%
LENGTH OF ICU STAY(days)	3 - 5	4	17.4%	12	54.5%
	6 - 10	10	43.5%	8	36.4%
	> 10	9	39.1%	2	9.1%
	Total	23	100.0%	22	100.0%
LENGTH OF HOSPITAL STAY(days)	3 - 5	2	8.7%	3	13.6%
	6 - 10	7	30.4%	10	45.5%
	10 - 20	10	43.5%	6	27.3%
	> 20	4	17.4%	3	13.6%
	Total	23	100.0%	22	100.0%
MORTALITY	Present	4	13.3%	5	16.7%
	Absent	26	86.7%	25	83.3%
	Total	30	100.0%	30	100.0%

Table 2: Significance of comparison between IWI and TI

Group with Following parameters	chi square/Fishers exact test p	
AGE	0.850	NS
GENDER	0.426	NS
OUTCOME	0.766	NS
DURATION OF MECHANICAL VENTILATION(days)	0.185	NS
LENGTH OF ICU STAY(days)	0.013	sig
LENGTH OF HOSPITAL STAY(days)	0.604	NS
MORTALITY	0.718	NS

NS-Nonsignificant, sig-significant

Table 3: Comparison of age with mean and standard deviation

AGE	N	Mean	Std. Deviation	t test p value	
GROUP TI	30	54.90	14.136	.853	NS
GROUP IWI	30	55.60	14.975		
Total	60	55.25	14.442		

None of the patients in the study had a subsequent failed extubation after passing the SBT. Any reintubation beyond 24 hours was considered to be due to relapse or worsening of underlying pathology and not extubation failure.

Discussion:

Weaning indices have been suggested to help in assessment of patients on mechanical ventilation for readiness for a successful weaning.

Based on the study done by Yang and Tobin *[2]* we used the threshold values of f/VT≤105 breaths/min/L and the study done by Nemer et al *[13]* for the threshold value of IWI >25 ml/cm of water breaths/min/L for considering the readiness for weaning.

In our study, it was found that there was no significant comparison between the two indices in terms of weaning success or failure using the Chi square test/Fisher's exact test and the Mann Whitney test. There was no significant difference in the outcomes of duration of mechanical ventilation, duration of hospital stay and mortality between the two groups. The duration of ICU stay was less and of statistical significance in the IWI group but the factors for the difference were not clear in the study. However, it can be said that the percentage of successful weanings while using the indices, both considered separately, has been considerably higher than the weaning failures.

Yang and Tobin in their study to compare the Tobin index with the CROP index in 1991 concluded that rapid shallow breathing indicated by the Tobin index accurately predicted failure, and its absence accurately predicted weaning success. The Tobin index was the best predictor of weaning success and failure.[2] Our study was in concordance with this study, and showed that the Tobin index is a good predictor of successful weaning, with lesser number of failed weaning, unlike another study by Tanios et al in 2006 where it was concluded that the use of f/VT prolonged weaning time and there was no reduction in incidence of extubation failure and that absence of its use did not change the mortality rate, requirement of tracheostomy, or unplanned extubation *[14]* and hence it was concluded that it should not be used routinely while making decisions. Lakshmi Kumar et al *[11]* in their study suggested that f/VT can assess the outcome of a successful weaning even if the patient has an increased workload of breathing, which is seen when the patients were given a spontaneous breathing trial especially those considered difficult -to-wean which is supported by our study also.

Our study showed that using these indices as a predictor of successful weaning was beneficial in preventing a failed extubation with a success outcome of 76.7% in the TI group and 73.3%

in the IWI group which showed that the Tobin index was more accurate than the IWI, though not statistically significant. It was also seen that the mean duration of mechanical ventilation (days), the number of days of ICU stay and hospital stay was lesser in the IWI group than the TI group. It was seen that the TI group had lesser number of mortalities than the IWI group (13.3% vs. 16.7% respectively), however, the difference was statistically nonsignificant. This was in concordance with the study done by El- Baradey et al it where it was shown that the use of IWI significantly reduced the number of days of mechanical ventilation and ICU stay. The group where IWI was used had significantly higher rate of weaning success, significantly lower rate of failure, and lower failure of SBT and failure of extubation *[10]* IWI strongly predicts both successful and failed weaning which was also seen in our study.

The outcome of weaning failure in our study, that is, 23.3% in the TI group and 26.7% in the IWI group, shows that weaning indices cannot be used as sole predictors of a successful weaning and the decision for weaning a patient from mechanical ventilation depends more importantly on the intensivists' decision based on his clinical judgement, along with individual functional parameters being in the normal physiologic range *[10]* and also the sustenance of spontaneous ventilation, However, since the use of the indices proved to have a better success rate than failure, it can be said that they should be used as an adjunct in the decision making process as they will help to avoid premature weaning that could result in respiratory and cardiovascular stress or unnecessary prolongation of mechanical ventilation, the Tobin index being better than the IWI in predicting successful weaning.

In a study done by Nemer et al *[13]* in 2009 in a patient population of 331, it was reported that IWI had a better predictive performance in comparison with f/VT which was already considered to be the most accurate predictor for weaning success or failure. The study concluded IWI was better in terms of accuracy than other weaning predictors including the Tobin index. However, their study did not assess the index over a range of fiO2 and the static compliance was measured with minimal interference using observation of the pressure-time inspiratory plateau curve, unlike our study where a range of fiO2 between 0.4-0.5 was used and the plateau pressure was a variable displayed on the ventilator .Our study did not presume f/VT as the most accurate predictor, hence bias was reduced.

Some of the factors that are known to affect the outcome of weaning and could be responsible for the limited predictive ability of weaning indices are the need for different cut-off values for different patient populations based on the reason for need of mechanical ventilation, the initial functional status of the patient and of the other organs, and the duration of sickness, and also the duration of mechanical ventilation and respiratory impedance and strength of the inspiratory muscles. The timing at which the physiologic variables are measured represent a static measure for calculation of the indices. However, the patient's clinical condition is subject to continuous change, thus making the weaning process dynamic. Other factors include differences in clinical practice in ICUs such as the ventilator management prior to attempted weaning, which could result in respiratory alkalosis, fluid excess, excessive sedation, or fatigue of respiratory muscle, inadequate nutritional status and electrolyte balance causing inadequate muscle mass and force for respiration and psychological factors such as stress, fear, or anxiety leading to rapid shallow breathing, tachycardia and hypertension *[15,16]*.

A study conducted by Gok et al *[17]* concluded that sonographic evaluations accompanied by an RSBI will increase extubation success in the weaning process. Weaning failure may be due

to underlying lung pathologies such as pulmonary fibrosis, pulmonary hemorrhage, and diffuse pulmonary infiltrate and also weaning-induced pulmonary edema as a result of heart-lung interactions which may be diagnosed by echocardiographic assessment. Ultrasound assessment of diaphragmatic function can be incorrect due to impedance of adjacent structures, abdominal compliance, PEEP, and ventilation support. Factors such as catheters, cables, and patients' positioning in the ICU also contribute. Since the breathing process is carried out by the diaphragm and auxiliary respiratory muscles, RSBI can be at desired values due to the auxiliary respiratory muscles, even if the diaphragm function is inadequate, so that RSBI values can be misleading in making the weaning decision. This is in accordance with our study which suggests that weaning indexes cannot be solely used as a method for successful extubation. However ultrasound assessment with echocardiographic investigation may be a better method for assessment of weaning readiness and can be performed by technically skilled personnel. Automated weaning systems with newer modes of ventilation such as Adaptive Support Ventilation, Neurally Adjusted Ventilatory Assist and several others appear to enable a more efficient weaning process than those that depend upon clinician-directed weaning protocols, as they provide greater adaptability of the ventilation support to each patient's requirements through continuous monitoring and real-time intervention. However, further trials are needed to demonstrate the clinical impact of fully-automated weaning in terms of length of ventilation, morbidity and costs. A detailed understanding of the impact of therapists' control of the system's settings and of human judgments about adequacy of the weaning strategy, timing for starting and reliability of results is also needed *[18,19]*.

Based on our study results we conclude that both the predictive indices studied did not accurately predict a successful extubation in all the cases thus limiting their use in clinical practice. Even the integrative weaning index which has been suggested by earlier studies to be a better predictor did not give a hundred percent outcome of successful weaning. Used along with ultrasound assessment for lung-heart and diaphragm adequacy and clinical judgement, they may have a better weaning outcome.

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