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ORIGINAL ARTICLE

Quantitative evaluation proposal of a ultrasonographic protocol for weaning from mechanical ventilation

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Abstract

Introduction*: Mechanical ventilation is a therapy for vital support used in a significant proportion of critically ill patients. The right time to successfully discontinue this therapy is a challenge for the intensive care specialist. For this reason it is still a subject for research. The echocardiographic evaluation of the diastolic dysfunction, the diaphragm, and the lung have become an invaluable tool for weaning from mechanical ventilation protocols, especially in patients with difficult or prolonged weaning from mechanical ventilation. There is still a need to validate, in controlled trials, the efficacy of an ultrasound protocol for weaning from mechanical ventilation that integrates the three modalities in a single protocol.* **Methods:** *Based on current literature, we developed a score justified by a mathematical model based on inequations. When* $\chi \Rightarrow 5$ *the risk of failure in the weaning process rises, the weaning process should be suspended; when* $\chi \Rightarrow 1$ *the risk of failure is low, the weaning process should be continued.* **Conclusions.** *The use of math models for decision-making is of great importance, as it sets an objective parameter within the existing evaluations. We proposed the use of inequations to set intervals of solution with the three points of care for ultrasound-guided weaning from mechanical ventilation. With this, the inequations proposed generate an area of certainty within the proposed values and the solution intervals.* (Gac Med Mex. 2016;152:273-80)

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Introduction

Mechanical ventilation (MV) is a vital support modality used in a large proportion of seriously ill patients admitted to the Intensive Care Unit (ICU). Most of these patients can be extubated without complications; however, 20% of patients on MV will fail to the first weaning attempt, and more than 40% of the time a patient remains on MV will be invested on the MV weaning process[1,2].

Prolonged MV is associated with the presence of complications, with ventilation-associated pneumonia (VAP), ventilator-induced lung injury (VILI), digestive hemorrhage and deep venous thrombosis, among others, standing out. On the other hand extubation failure with subsequent reintubation is an independent risk factor for morbidity and mortality increase[3]. In view of the above,

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deciding the adequate moment to discontinue MV remains a challenge and, for this reason, new decision-making procedures and protocols continue to be developed.

Ultrasonography (USG) has been implemented in the routine assessment of seriously ill patients for diagnostic approach and follow-up. In this sense, ultrasound-guided ventilation weaning protocols assess, in contrast with merely mechanical protocols, alveolar aeration and collapse, real-time cardiac and diaphragmatic function, which facilitates follow-up, thus helping to predict the success of the weaning technique or indicating the clinician to stop the maneuver and to continue with the MV.

Causes of failure in weaning from MV

There are different entities that can cause for weaning from MV to fail, which are summarized in table 1. Early recognition and treatment of these causes helps to reduce the risk for weaning from MV failure.

Weaning from IMV

Once the decision to start weaning of MV has been made, the patient must be thoroughly assessed, the cause that led to intubation and MV has to have been controlled, as well as the integrity of the cardio-respiratory system, the function of respiratory muscles, especially the diaphragm, thoraco-pulmonary distensibility and metabolic stability.

In addition to the above, several indices have been developed to aid the decision to start the weaning from MV based on the resulting score. As an example, the following stand out:

- Peak inspiratory pressure, Initiative Weaning Index (IWI), CROUP index, which, according to the score obtained, serve as predictive indices for a successful weaning from MV[4,5].
- Rapid shallow breathing index (frequency/tidal volume), developed by Yang and Tobin[6], with 96% sensitivity and 64% specificity to predict weaning from MV failure or success.

Based on the development of ITU bedside ultrasonographic protocols, different methods have been proposed to assess and timely make the decision with regard to weaning from MV[7.8].

Ultrasound-guided MV weaning protocol

For this protocol, 3 bedside ultrasonographic assessments are carried out: cardiac, diaphragmatic and pulmonary functions.

Cardiac and hemodynamic function assessment

Hemodynamic alterations and cardiac dysfunction play a critical role in weaning from ventilation[9]. After discontinuing ventilation with positive pressure, intra-thoracic negative pressure and sympathetic overstimulation[10] increase venous return, cardiac workload[11], afterload, and left ventricle (LV) distensibility[12,13]; these changes can induce myocardial ischemia, LV diastolic dysfunction, pulmonary congestion and hypertension and right ventricle (RV) dysfunction[14-17]. This phenomenon, together with an increased venous return, increases LV filling pressures and generates acute pulmonary edema.

Different Doppler echo indices have to be obtained to assess the LV diastolic function. The different types of diastolic function and indices for their echocardiographic diagnosis, which are useful in the assessment of weaning from MV, are shown in table 2.A study conducted by Papanikolau[17] found that in the echocardiographic indices for diastolic dysfunction obtained prior to the spontaneous breathing trial (SBT), an E/Ea ratio higher than 7.8 has prognostic value to predict weaning from MV failure. Tissue Doppler of the lateral wall had an area under the curve of 0.86 with 100% specificity and 100% positive predictive value. This study suggests that diastolic dysfunction and increased LV filling pressures are associated with weaning from MV failure pathophysiology[18,19]. The presence of grade 2 or 3 diastolic dysfunction during SBT is associated with failure of the procedure.

Moschietto[20] found that the E/Ea ratio was higher in the group where weaning from MV failed in comparison with those with successful withdrawal. The cutoff point in this trial was 14.5 with 75% sensitivity and 95.8% specificity. No significant difference was found between groups with regard to LV ejection fraction.

Diastolic function deterioration during SBT is also associated with weaning from MV failure. In the study conducted by Lamia[21], the correlation between the E/A and E/Ea ratios with the pulmonary artery occlusion pressure (PAOP) was reported, with an E/A ratio > 0.95 and an E/Ea ratio > 8.5 during the SBT being found to predict a weaning from MV-induced PAOP elevation to over 18 mmHg, with 91% specificity and 82% sensitivity.An elevated percentage of weaning from MV failure is due to diastolic dysfunction and increased LV filling pressures. By means of USG, cardiac function modifications during the SBT can be assessed in real time, and in case any occurs, to start appropriate and opportune treatment with the best therapeutic decision to guarantee a successful weaning from MV.

Table 1. Causes of failure in weaning from mechanical ventilation

Pathophysiology	Consider	USG
Respiratory failure	1. Increased work of breathing: inappropriate ventilator settings 2. Reduced compliance: pneumonia (ventilator-acquired), cardiogenic or non-cardiogenic edema, pulmonary fibrosis, pulmonary hemorrhage, diffuse pulmonary infiltrates 3. Airway bronchoconstriction 4. Increased resistive load: during spontaneous breathing trial through the endotracheal tube. Post-extubation, glottic edema, increased secretions, sputum retention	Pulmonary ultrasound assessment with presence of alveolar-interstitial pattern, absence of pleural sliding due to dynamic hyperinflation, presence of pneumothorax. Loss of alveolar units by means of B-lines increase or presence of a new consolidation zone
Cardiac failure	1. Cardiac dysfunction prior to critical illness 2. Increased cardiac workload due to myocardial dysfunction, dynamic hyperinflation, increased metabolic demand, unresolved sepsis	Diastolic function echocardiographic assessment, right ventricle dysfunction, hyperdynamia
Neuromuscular	1.Depressed central drive, metabolic alkalosis, mechanical ventilation, hypnotic/sedative medications 2. Central ventilatory command, failure of the neuromuscular respiratory system (including respiratory muscles such as the diaphragm) 3. Peripheral dysfunction, primary causes of neuromuscular weakness, critical illness neuromuscular abnormalities	USG assessment of diaphragm, diaphragmatic excursion and diaphragmatic thickness delta
Neuropsychological	1. Delirium 2. Anxiety and depression	Clinical
Metabolic	1. Electrolytic alterations 2. Steroids 3. Hyperglycemia	Laboratory
Nutrition	1. Overweight 2. Malnutrition 3. Ventilator-induced diaphragm dysfunction	USG assessment of the diaphragmatic function, anemia causes diastolic dysfunction
Anemia	1. Anemia	

Table 2. Left ventricular filling patterns classification

	Normal	Impaired relaxation	Pseudonormalization	Restrictive
E/A ratio	1-1.5	< 1	1-1.5	> 2
DT msec	160-240	> 240	160-240	< 150
IVRT msec	60-100	> 110	60-100	< 60
PV S/D ratio	1	> 1	< 1	< < 1
PV Ar duration	< A	> A	> A	> A
PV Ar velocity	< 20	< 35	> 35	> 25
Ea cm/sec	< 8	> 8	> 8	> 8
pV cm/sec	> 45	< 45	< 45	< 45

E/A ratio: mitral; DT: deceleration time; IVRT: isovolumetric relaxation time; PV S/D: pulmonary vein systolic/diastolic wave ratio; PV Ar: pulmonary vein reverse atrial wave; Ea: early longitudinal mitral annulus tissue velocity; Vp: transmitral flow propagation velocity.

Modified according to the studies on weaning from mechanical ventilation considering that an E/e ratio greater than 8 is related to a pulmonary artery occlusion pressure greater than 18.

Diaphragmatic assessment

The diaphragm is the main respiratory muscle and its dysfunction in the critically ill patient favors the development of respiratory complications and prolongation of the time on MV[22].

In patients on controlled MV, there is serious diaphragmatic dysfunction and atrophy and, for this reason, attempts should be made for the patient to early initiate with spontaneous breathings, adjusting the work of breathing. This ventilation-induced diaphragmatic dysfunction has been demonstrated in animal models and clinical trials[23].

On the other hand, the ventilator setting should, in theory, look for an adequate work of breathing level. Most assisted MV modalities have been studied for their ability to reduce the work of breathing during the weaning process from both invasive and non-invasive MV[23].

Since diaphragmatic movement and thickening play a fundamental role during spontaneous breathing, evaluation of this muscle is essential in the weaning from MV assessment.

For some time, the tools used for diaphragmatic assessment were limited by the need to mobiliza the patient and exposure to radiation (fluoroscopy, computed tomography) or by its complexity, with very specialized equipment and an expert operator being required (trans-diaphragmatic pressure measurement by electromyography, magnetic resonance imaging with phrenic nerve stimulation).

Ultrasound has found its place as an excellent tool for anatomical and functional assessment of the diaphragm in patients to be started on a MV weaning potocol[24].

Diaphragm assessment by ultrasound has become a necessary tool for the evaluation of critical patients in situations that impair their mobility such as phrenic nerve injury, neuromuscular conditions and in patients on MV. Ultrasound-based diaphragmatic excursion determination can help to identify patients with diaphragmatic dysfunction during weaning from MV, as well as for direct visualization of diaphragm thickness. Measurement of this muscle's thickness has been described since 1989[26] and has been used to assess diaphragmatic contraction in healthy subjects and in the diagnosis of diaphragmatic paralysis.

For diaphragm assessment, two indices are primarily to be used. The first is diaphragmatic excursion, which consists in measuring diaphragm mobility at inspiration and expiration by M-mode ultrasound during a spontaneous IMV mode or during SBT. The other index is known as Delta thickness of diaphragm (Δtdi), which corresponds to the percentage of diaphragmatic thickening, using a sandwich technique, at inspiration and expiration.

Diaphragmatic excursion

Diaphragmatic ultrasound is carried out with a 3.5 to 5 MHz transducer. It should be placed beneath the right or left costal margin at the collar bone midline or at the right or left anterior axillary line and directed in the medial, cephalic and dorsal direction, in order for the transducer mark to perpendicularly reach the hemi-diaphragm posterior third. The best image of the exploration line is obtained with the bi-dimensional mode (2D); subsequently, the M-mode is used to visualize the movement of anatomical structures within the selected line. In the M-mode, the diaphragmatic excursion (displacement in cm), diaphragmatic contraction velocity, inspiratory time and cycle duration can be measured[22].

In patients on MV, diaphragmatic excursion measurement during SBT helps to visualize the patient´s spontaneous breathing efforts. Diaphragmatic excursion normal values in healthy individuals have been reported to range from 1.8 ± 0.3 to 2.9 ± 0.6 in males and from 1.6 ± 0.3 to 2.6 ± 0.5 in females[25].

For the weaning from IMV, Jiang[26] assessed the diaphragmatic movements by measuring liver and spleen displacement during the SBT. The use of a cutoff value of 1.1 cm for hepatic and splenic displacement was shown to be a good outcome predictor for weaning from IMV with 84.4% sensitivity and 82.6% specificity, outperforming routinely used parameters such as the rapid shallow breathing index and Pimax. Patients with adequate tidal volume during SBT who showed a decreased diaphragmatic excursion were more likely to experience weaning failure than those with adequate tidal volume and a good diaphragmatic excursion. This can be explained by the fact that tidal volume in spontaneous breathing is represented by a combination of respiratory muscles with no diaphragm contribution being recognized, whereas the diaphragmatic excursion represents the final result of the strength of the muscle itself in combination with intra-thoracic and intra-abdominal pressure.

Kim[27] conducted a study investigating diaphragmatic dysfunction with M-mode ultrasound in 88 ITUs and found a prevalence of 29% (by diaphragmatic excursion < 1 cm or diaphragm paradoxical movements). The patients with diaphragmatic dysfunction had an increase in the number of MV weaning attempts, as well as in the number of days on MV. These results suggest that diaphragm ultrasonographic assessment is useful to identify patients at risk of difficult or prolonged weaning, as well as a predictor of weaning from MV failure.

Δtdi

This index is another measurement that has been validated for the assessment of the diaphragmatic function.

For this measurement, a 10-15 MHz lineal transducer and the ultrasound bi-dimensional mode are used. The transducer is placed the same way than for the diaphragmatic excursion measurement, and measurements are taken of diaphragmatic thickness at inspiration and expiration. The percentage is calculated with the following formula:

End-inspiration thickness –
end-expiration thickness /end-expiration thickness

Diaphragmatic thickening normal values in healthy individuals are in accordance to their functional residual capacity (FRC), with ranges from 1.8 to 3 mm. As the lung increases the residual volume (RV) of total lung capacity (TLC) with Δtdi, which ranges from 42 to 78%[28,29].

DiNino[30] assessed Δtdi as a predictor of success in weaning from IMV, and found a Δtdi > 30% to have 88% sensitivity, 71% specificity, 91% positive predictive value and 63% negative predictive value, with an area under the curve of 0.79.

The combined use of both these diaphragmatic function assessment methods during SBT is a useful tool for the determination of patients at risk for weaning from MV failure.

Pulmonary ultrasound

Finally, pulmonary volume should be evaluated during SBT. Ever since Lichtenstein[31] described the pulmonary ultrasound devices in the Blue protocol, where he reported that the presence of aligned B-lines, which he named pulmonary rockets, is pathological and represents the presence of an alveolar-interstitial syndrome and then he subsequently described in the FALLS protocol[32] that the presence or augmentation of these lines are related to the presence of acute pulmonary edema during fluid resuscitation of patients in shock, both these findings have been the guideline for the performance of multiple studies on this ultrasound-driven phenomenon[33]. The presence of these lines or artifacts is associated, among other things, with pulmonary aeration. The presence of A-lines, which are horizontal to the pleural line, characterize a normally aerated lung. The presence of multiple B-lines (comet lines), which are well defined and spaced lines, corresponds to lung aeration moderate loss resulting from the presence of an alveolar-interstitial syndrome[34]. The presence of coalescent B-lines less than 3 mm apart corresponds to aeration severe loss, which results from alveolar spaces partial filling due to pulmonary edema. Finally, pulmonary consolidation is observed with the presence of hyper-echogenic spots with inspiratory reinforcement and dynamic bronchograms, which corresponds to lung aeration complete loss with persistent bronchiole distal aeration. Based on this, Bouhemad[35] created an aeration score for patients with acute respiratory distress syndrome. Using this score, we performed the same assessment for patients on IMV taking the aeration loss score as a prognostic factor for weaning from IMV failure. The study by Soummer[36], where the aeration loss index was used, found that those patients with a score higher than 19 had an increased risk for the development of post-extubation distress, with an area under the curve of 0.86 and hence the author concluded that scores lower than 13 predict weaning success, whereas scores higher than 17 predict the presence of post-extubation distress.

The purpose of the present work is to propose mathematical inequations in order to qualitatively and objectively assess USG-based weaning from MV.

Based on the above, a literature review was undertaken with the following search terms: ultrasound, weaning from ventilation, diaphragm, echocardiogram and pulmonary, with the purpose to identify and assess the most widely used established ultrasonographic parameters in weaning from MV.

An inequation-based mathematical model was developed, analyzing the tendencies and parameters used in the three large categories of the critically ill patient, pulmonary, cardiac and diaphragmatic, in the assessment of weaning from MV. The results show that, when $\chi \Rightarrow 5$, the risk for weaning failure increases, and the weaning from MV procedure should not be continued, and when $\chi \Rightarrow 1$, the risk of failure decreases and the weaning from MV procedure should be continued (Table 3).

Solution intervals with regard to the established weighing were constructed, where by echocardiogram (cardiac): C = 1 means absence of diastolic dysfunction; C = 3, presence of grade I or II diastolic dysfunction or presence of a change from normal to grade I diastolic dysfunction, or grade I to grade II diastolic dysfunction; and C = 5, presence of grade III diastolic dysfunction or presence of a change from normal function to grade II or III diastolic dysfunction, or from grade I to grade III diastolic dysfunction.

For the pulmonary category: P = 1 is normal (N), P = 3 from N to B1 or from B1 to B2, P = 5, presence of consolidation (C) or from N to B2, or B1 to C, or N to C.

In the case of the diaphragm: D = 1 means excursion larger than 1.5 cm and Δdti higher than 30%, D = 3 excursion smaller than 1.5 cm with Δdti higher than 30% or excursion larger than 1.5 cm with Δdti lower than 30%, and D = 5 excursion smaller than 1.5 cm with Δdti lower than 30%.

With the above described, the solution interval at all three statuses is closed on both sides [$1 \leq \chi \leq 5$], and in the same way, the interval that will determine the weaning is closed on the right and open on the left [$1 \leq \chi < 3$]; this condition means that a score equal to 5 at any category indicates no weaning from MV and a score from 1 to 3 means that the weaning from MV procedure should be continued; when the value of $\chi \Rightarrow 3$ for any category, the specific cause that made for this score to be obtained should be assessed, this way, weaning safety is warranted (Figs. 1 and 2) (Table 4).

Table 3. Weaning from mechanical ventilation score (GMEMI score)

USG	Description	Score
Pulmonary	N-C	5
	N-B2	
	B1-C	
	N-B1	3
	B1-B2	
	No change	1
Echocardiogram	Presence of grade III diastolic dysfunction OR N-DII or DIII OR DI-DIII	5
	Presence of grade II diastolic dysfunction OR N-DI DI-DII	3
	No change	1
Diaphragm	$E < 1.5 + \Delta D < 30\%$	5
	$E > 1.5 + \Delta D < 30\%$	3
	$E < 1.5 + \Delta D > 30\%$	
	$E > 1.5 + \Delta D > 30\%$	1

Pulmonary: 7-mm, well defined, regularly spaced B-lines (moderate aeration loss); B2: multiple coalescent B-lines (severe aeration loss); C: pulmonary consolidation; N: normal pattern (normal lung aeration). Cardiac; N: normal; DI: type I diastolic dysfunction; DII: type II diastolic dysfunction; DIII: type IIII diastolic dysfunction. Diaphragm: E: excursion; ΔD: diaphragmatic thickness delta; GMEMI *(Grupo Mexicano Para el Estudio de la Medicina Intensiva)*: Mexican Group for the Study of Intensive Medicine.

Conclusions

The search for new procedures for the weaning of MV that offer more safety in decision making is an essential part of the intensivist's tasks. With regard to works published so far on the use of ultrasound for weaning from MV, they have assessed individual parameters with an important rate of success and reported high sensitivity and specificity for each one of the assessed categories and, therefore, we propose their integration into a MV weaning protocol, where bedside assessments of the cardiac function,

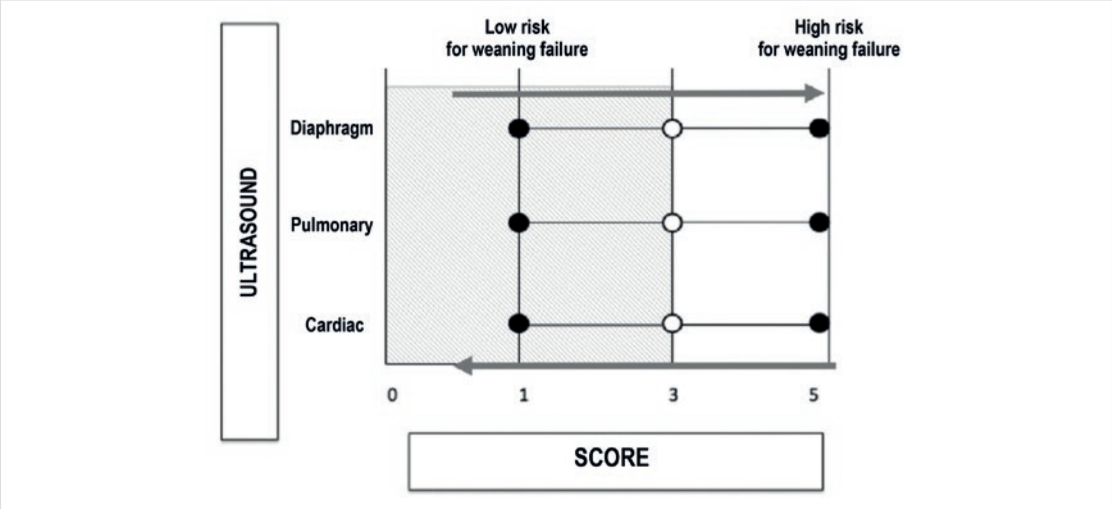

Figure 1. *The solution interval at all 3 statuses is observed to be [$1 \leq \chi \leq 5$], the same way the interval that will determine the weaning is [$1 \leq \chi < 3$], this condition means that a score equal to 5 for any category indicates no weaning from IMV and a score from 1 to 3 means that the procedure of weaning from IMV should be continued. When the value is $\Rightarrow 3$ for any category, the specific cause that made for this score to be obtained should be assessed and, this way, IMV can be safely weaned without compromising the subject's life.*

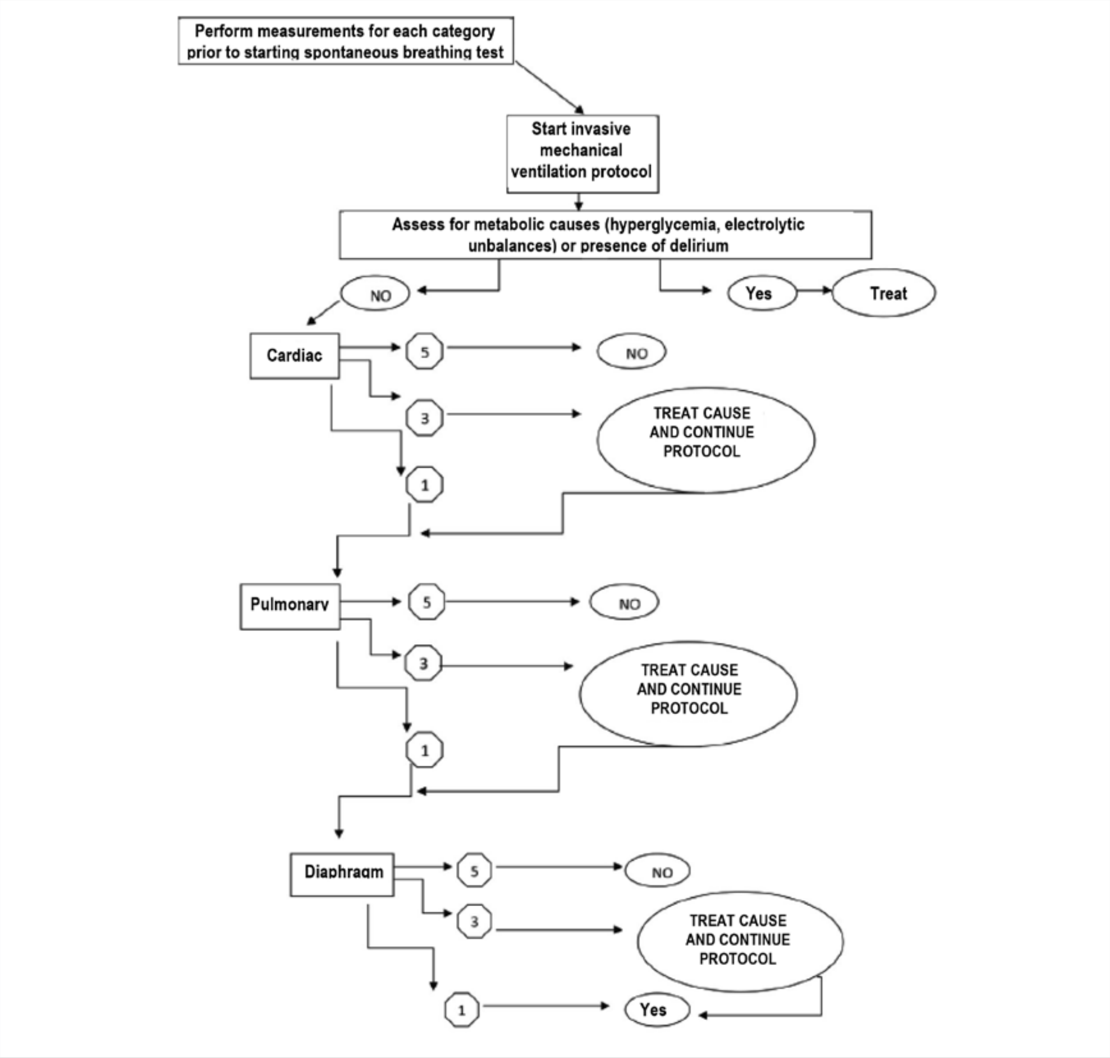

Figure 2. *Decision-making algorithm for ultrasound-guided weaning from mechanical ventilation based on the GMEMI score.*

Table 4. Table of decision per ultrasonographic protocol

Cardiac	Pulmonary	Diaphragm	Decision		
5	5	5	No	5C+5P+5D	$\chi \Rightarrow 5$
5	5	1	No	5C+5P+1D	
5	1	1	No	5C+1P+1D	
3	5	1	No	3C+5P+1D	
3	1	5	No	3C+1P+5D	
1	5	5	No	1C+5P+5D	
3	3	3	Yes	3C+3P+3D	$\chi \Rightarrow 3$
3	1	1	Yes	3C+1P+1D	
3	3	1	Yes	3C+3P+1D	
3	1	3	Yes	3C+1P+3D	
1	1	1	Yes	1C+1P+1D	$\chi \Rightarrow 1$

Global interval [$1 \le \chi < 3$]; score on any box from 3 to 1, weaning from IMV; if any score is 5 [$1 \le \chi \le 5$], weaning from IMV is not continued.

pulmonary function and muscular function will be carried out to aid decision making.

We know that the causes of failure in weaning from MV are multifactorial, and the capability to observe and quantify any dysfunction within this process can only be offered by ultrasonographic assessment with a high cost-benefit ratio since it is a non-invasive procedure with a short learning curve.

It is important mentioning that the use of mathematical models for decision making is of vital importance, since they establish an objectivity parameter with regard to the existing assessments. In the present work, the use of inequations is proposed with the purpose to establish solution intervals within the three large categories that are taken into account for decision making on weaning from MV; this way, the proposed inequations generate an area of certainty with regard to the proposed values and solution intervals of the present work.

With the advent of visual medicine, the use of biomarkers such as BNP and the SvO_2 delta for assessment of heart failure associated with weaning from MV, or P_{max} for assessment of neuromuscular integrity and gasometric changes for the loss of functional alveolar units, could be substituted by a comprehensive ultrasonographic assessment, as proposed in this work, or be yet another tool in the decision making process.

To assess the efficacy of this proposal, the Mexican Group for the Study of Intensive Medicine (GMEMI – *Grupo Mexicano para el Estudio de la Medicina Intensiva*) is designing a validation trial for this scores, with regard to currently established MV weaning protocols in patients with prolonged ventilation (more than 3 days on MV) as a non-inferiority trial. In our center, we have generated experience with ultrasonographic assessment in patients on weaning protocol with a high percentage of successful weaning from MV.

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