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ICU outcomes can be predicted by non invasive muscle evaluation: a meta-analysis.

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Abstract

Background The relationship between muscle function in critically ill patients assessed using bedside techniques and clinical outcomes has not been systematically described. We aimed to evaluate the association between muscle weakness assessed by bedside evaluation and mortality or weaning from mechanical ventilation, and the capacity of each evaluation tool to predict outcomes.

Methods Five databases (PubMed, EMBASE, CINAHL, Cochrane library, Science Direct) were searched from January 2000 to December 2018. Data were extracted and random effects meta-analyses were performed.

Results Sixty studies were analysed, including 4382 patients. ICU-related muscle weakness was associated with an increase in overall mortality with odds ratios ranging from 1.2 [95% CI 0.60 to 2.40] to 4.48 [95% CI 1.49 to 13.42]. Transdiaphragmatic twitch pressure had the highest predictive capacity for overall mortality, with a sensitivity of 0.87 [95%CI 0.76 to 0.93] and a specificity of 0.36 [95%CI 0.27-0.43]. The area under the curve (AUC) was 0.74 [95%CI 0.70 to 0.78]. Muscle weakness was associated with an increase in mechanical ventilation weaning failure rate with an odds ratio ranging from 2.64 [95% CI 0.72 to 9.64] to 19.07 [95% CI 9.35 to 38.9]. Diaphragm thickening fraction had the highest predictive capacity for weaning failure with a sensitivity of 0.76 [95%CI 0.67 to 0.83] and a specificity of 0.86 [95%CI 0.78 to 0.92]. The AUC was 0.86 [95%CI 0.83 to 0.89].

Conclusion ICU-related muscle weakness detected by bedside techniques is a serious issue associated with a high risk of death or prolonged mechanical ventilation. Evaluating diaphragm function should be a clinical priority in the ICU.

Systematic Review Registration: PROSPERO 2019 [CRD42019122081]

Keywords: Intensive care Unit, Muscles weakness, Mechanical Ventilation

Introduction

ICU-acquired weakness (ICU-Aw) is a frequent complication of hospitalisation in intensive care. It includes limb muscle weakness[1, 2], diaphragm dysfunction[3], and global respiratory muscle weakness. Muscle weakness is multifactorial with sepsis, multi-organ failure, mechanical ventilation and pre-admission status being the main risk factors.[4, 5] Muscle weakness is currently diagnosed by a clinical examination involving a voluntary manual muscle strength test graded, for example, by the Medical Research Council (MRC) Scale.[6, 7]

Muscle weakness is often associated with a poor prognosis: dysfunction of the diaphragm or respiratory muscle weakness can both prolong the duration of mechanical ventilation and cause a failure to be weaned from it.[3] Furthermore, limb muscle weakness reduces physical capacity, functional ability, and autonomy, [8] and for that reason early identification of muscle weakness is essential.[9] This is challenging, however, since voluntary muscle strength can currently only be tested in patients who are both awake and cooperative. One study, for example, showed that only 25% of eligible patients could be evaluated with the MRC scale; the others could not because of their neurological status.[7] Several authors have highlighted the need for better bedside-tools for the identification of muscle weakness.[4, 9, 10] Non-invasive methods that evaluate diaphragm contractility and function have been proposed, such as magnetic phrenic nerve stimulation,[11] neuromuscular or diaphragm ultrasonography.[12, 13] Although such tools show promise, issues remain that need resolution before they can be routinely used. Firstly, their clinical relevance has not been validated; data regarding the relationships between muscle function and critical outcomes are needed for each test. Secondly, their routine clinical use is limited since no evaluation of

diagnostic capacity has yet been undertaken in a large representative sample of critically ill patients.

Thirdly, we do not know which of these tests is the most applicable for predicting patient outcomes.

The first aim of this systematic review and meta-analysis, therefore, was to identify and determine the clinical relevance of currently available, non-invasive, bedside muscle weakness evaluation tools by analysing the relationship between these methods and critical outcomes such as mortality and ventilator weaning failure. The second aim was to determine the capacity of each evaluation tool to predict the critical outcomes.

Method

The systematic review was carried out in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [14] and our protocol registered in PROSPERO [CRD42019122081]. In January 2019 the following five databases were searched for publications in either English, French or Spanish dating between January 2000 and December 2018: PubMed, EMBASE, CINAHL, the Cochrane Library, and Science Direct; the reference lists of all included articles were also searched for possible articles.

The search strategy involved combining keywords from the three domains: the condition studied (i.e. muscle weakness), the evaluation tool used, and the outcome(s) measured. MeSh search terms for condition were: "critically ill patient" or "ICU-acquired weakness" or "diaphragm dysfunction" or "respiratory weakness", MeSh search terms for the evaluation tool were: "diaphragmatic ultrasound" or "transdiaphragmatic twitch pressure" or "phrenic nerve stimulation" or "maximal inspiratory pressure" or "handgrip dynamometer" or "handheld dynamometer" or "medical research council score" or "neuromuscular ultrasound"

and MeSh search terms for outcomes were: "mortality" or "mechanical ventilation weaning" or "extubation" or "mechanical ventilation".

Screening and study selection

The aim of the review was to evaluate the impact of muscle weakness on one or more of the following "critical outcomes": total mortality, mortality in ICU, mortality in hospital, weaning from mechanical ventilation, duration of mechanical ventilation and/or insertion of a tracheostomy. The capacity of each evaluation tool to predict each of the critical outcomes was also evaluated. A student physiotherapist (NA) supervised by a senior physiotherapist (CM) screened titles and abstracts for potential eligibility. A second senior physiotherapist (YC) also screened the studies (independently from NA and CM). Finally, CM and YC compared their results to determine which studies should be included or excluded. Any disagreements were resolved following discussion with a third senior reviewer (GP).

Observational cohort studies that compared the impact of limb and/or respiratory muscle weakness on critical outcomes in patients with and without weakness were included. Studies were excluded if patient strength was evaluated after discharge from ICU or if a prior intervention had been undertaken that might have influenced muscle weakness or critical outcomes or if muscle weakness was assessed by electromyography. As a result, letters were included but randomised control studies, retrospective analyses and conference abstracts were all excluded.

Data extraction

Two independent reviewers (CM and YC) extracted the data from each study using a standardized extraction form that included the patients' conditions, clinical outcomes, the evaluation tool and how it was used to evaluate muscle strength (Table 1). All data were

checked for accuracy by NA supervised by GP. Any missing data were requested from article authors by email and, if there was no reply, another email was sent each month for three months. Of the 26 authors contacted, 13 provided additional essential information; they have been included as "contributors".[5, 8, 11, 13, 15–23]

If several evaluation tools were used in the same article, then data were extracted for each tool individually.[3, 5, 15–17, 21, 24–29] When two articles reported the same cases [5, 13] care was taken to avoid double-counting (e.g. Ptrstim). In these cases, clarity was sought from the authors. Groups of patients that did not match the review question were excluded from the analysis [18].

The definitions provided in each article for the diagnosis of muscle weakness and "weaning failure" from mechanical ventilation (i.e. where either extubation or spontaneous breathing failed) were used. If raw data was received from an author for a tool that had not been fully described in the original article (e.g. cut-off values were missing) we determined the cut-off value based on values in the literature. This was only required for maximal inspiratory pressure (MIP) and MRC scores (respectively 25cmH₂O and 48/60).

Risk of bias assessment

Two reviewers (CM and YC) independently assessed the risk of bias for each study included in the meta-analyses in two stages: 1) bias was assessed for each outcome using the Quality in Prognosis Studies tool (QUIPS) [30] and 2) bias relating to the predictive capacity of each tool for mortality and weaning failure using the Quality Assessment of Diagnostic Accuracy Studies criteria (QUADAS-2).[31] Any disagreements were resolved following discussion with a third senior reviewer (GP).

Meta-Analysis

To analyse the association between each of the tests used to diagnose muscle weakness, random effects meta-analyses were performed using the DerSimonian & Laird method for binary outcomes, with odds ratios and their corresponding 95% confidence intervals calculated using the Hartung-Knapp-Sidik Jonkman method.[32] Standardized mean differences (Hedges' g) were calculated using a random effects model and the REML estimation method for the continuous outcomes. To assess heterogeneity, we used I^2 to express the amount of variability in the effect-estimates that is due to the differences between studies (above chance), H^2 to express the relative excess in Q over its degree of freedom; and τ^2 for the variance of the effect sizes. To evaluate a small study effect, we used funnel plots to evaluate asymmetry, and Harbord's test in situations where at least ten studies were included in a meta-analysis (a modification of Egger's test) to assess the hypothesis that smaller studies tend to show larger effects. Sensitivity and specificity were calculated based on true positive, false positive, false negative and true negative values and are presented as a forest plot of sensitivity and specificity. A hierarchical summary receiver operating characteristic curve (HSROC) [33] was plotted and sensitivity and specificity were pooled in the bivariate model.[34] Because there were no covariates in the analysis, these two methods represent different parametrizations of the same model.[35]

Results

Characteristics of the studies included in the systematic review

The search generated 6713 records. After screening abstracts and titles, 87 potentially eligible papers were downloaded for full-text review. Of these, 46 were included (Figure 1).[3, 5, 8, 11, 13, 15–29, 36–61] Some of these 46 articles evaluated more than one diagnostic test, therefore the final analysis included evaluation data from 60 separate studies on a total of 4392 patients (Figure 1). The main characteristics of each of the 60 studies are shown in Table

1. Of the 60 studies, 23 evaluated respiratory muscle strength using diaphragm ultrasound (1390 patients),[3, 13, 15–18, 24, 26–28, 36–48] 6 used transdiaphragmatic twitch pressure (292 patients) [3, 5, 11, 13, 49, 50] and 13 used MIP (709 patients) [3, 15–17, 25–28, 51–55]. A further fourteen graded limb muscle strength using the MRC score (1656 patients) [5, 8, 15, 19–21, 25, 29, 56–61] and 4 used the handgrip test (335 patients).[21–23, 29]

The majority of studies were European (52%), but several studies were from North America (20%), North-Africa (13%), Asia and South America (15%). The mean age of all the patients included was 61.8 ± 5.5 years with a male/female ratio of 60/40. In this worldwide population, the prevalence of patients with muscle weakness was 47%. 41% had diaphragm weakness, 49% had a global respiratory muscle weakness and 50% had limb muscle weakness.

Risk of bias analysis

QUIPS

Of the 6 domains of the QUIPS, the "study confounding" domain included the highest number of studies with a high "risk of bias": 39% had a risk of bias for mortality or ventilator weaning (53%) Only 51% of the studies specifically reported that they evaluated the impact of muscle weakness on mortality and 53% evaluated the impact on weaning. The figures for the bias analyses are available in the supplemental data (Figures E1, E2, E3, E4, E5).

QUADAS-2

The majority of studies had a low "risk of bias" according to the QUADAS-2 tool. The "flow and timing" component contained a high number of "unclears" because the time that elapsed between the measurements and patient death was infrequently specified.

The "patient selection" domain in the "applicability" section contained a higher number of studies classified with a "high" risk of bias for mortality and weaning because of several that focused on specific pathologies such as chronic obstructive pulmonary disease or difficult-to-wean patients. Details of the bias for each evaluation and the figures for the bias analysis for the predictive capacity of each tool itself are available in the supplemental data (Figure E6 and Figure E7).

Small study bias

For overall mortality with versus without diagnosed weakness, the analysis for the MRC Score showed funnel plot asymmetry but no statistical evidence of a small study effect (p value from Harbord's test p=0.7454). Too few studies were available to evaluate this bias for the other outcomes (Figure E8).

For weaning failure with versus without diagnosed weakness, the outcomes "Diaphragm ultrasound, Diaphragm excursion", "Diaphragm ultrasound, Diaphragm thickening fraction", and "Maximal Inspiratory Pressure" showed funnel plot asymmetries but no statistical evidence of a small study effect (p values from Harbord's tests p=0.22, p=0.77, p=0.56). Too few studies were available to evaluate small study effects for the other tests (Figure E9).

For intensive care unit mortality, the meta-analysis for the MRC Score showed funnel plot asymmetry but no statistical evidence of a small study effect (p value from Harbord's test p=0.83). Too few studies were available for the other outcomes to test small study effects (Figure E10).

For hospital mortality, too few studies were available for each test to formally evaluate small study effects (Figure E11).

Impact of muscle weakness on mortality and predictive capacity

Thirty-three studies (2974 patients) evaluated mortality [3, 5, 8, 11, 13, 15–21, 23, 29, 38, 39, 41, 47, 50, 55, 56, 58–61]: muscles weakness was strongly associated with an increase in overall mortality with odds ratios ranging from 1.2 [95% CI 0.60 to 2.40] using diaphragm ultrasound (decrease in diaphragm thickness) to 4.48 [95% CI 1.49 to 13.42] using maximal inspiratory pressure. Heterogeneity (I²) ranged from 18% to 55%. The results are shown in Figure 2. Muscle weakness evaluated by daphragm thickening fraction, Transdiaphragmatic twitch pressure, MRC and Handgrip tools was associated with an increase in mortality in patients both in ICU and in hospital. MIP was not statistically associated with ICU mortality (Figure E12 and Figure E13).

The sensitivity, specificity and area under the curve (AUC) for the predictive capacity of each tool are presented in Table 2. Studies were grouped according to the tool used and the measurement carried out. It was not possible to evaluate the sensitivity, specificity or AUC of diaphragm thickness,[18] or force measured by the handgrip test because the minimum required number of evaluations (at least four) was not met. Overall, the predictive capacities of transdiaphragmatic twitch pressure, diaphragm thickneing fraction and MIP were higher than those of MRC score or diaphragm excursion. Transdiaphragmatic twitch pressure had the highest predictive capacity for overall mortality, with a sensitivity of 0.87 [95%CI 0.76-0.93], a specificity of 0.36 [95%CI 0.27-0.43] and an AUC of 0.74 [95%CI 0.70-0.78]. The Receiver Operating Characteristics (ROC) curves and the predictive capacity of mortality in ICU and in the hospital are presented in the supplemental data (Figure E14, E15, E16, E17). Individual sensitivity and specificity values for each study are shown in the in the supplemental data (Figure E18).

Impact of muscle weakness on mechanical ventilation weaning and predictive capacity

The 41 studies that evaluated the impact of muscle weakness on mechanical ventilation weaning and the capacity of muscle weakness to predict difficult weaning or failure to wean included a total of 2514 patients.[3, 5, 15–18, 22–24, 26–28, 36–40, 42–46, 48, 51–55, 59, 60, 62] Muscle weakness was strongly associated with an increase in mechanical ventilation weaning failure rate with an odds ratio ranging from 2.64 (95% CI 0.72 to 9.64) using MRC score to 19.07 (95% CI 9.35 to 38.9) using diaphragm thickening fraction (Figure 3). Heterogeneity (I^2) ranged from 2% to 75%.

The sensitivity, specificity and area under the curve (AUC) of the prediction of weaning failure are presented in Table 2. Only diaphragm thickening fraction, diaphragm excursion and MIP could be analysed. Diaphragm thickening fraction had the highest predictive capacity for weaning failure with a sensitivity of 0.76 [95%CI 0.67-0.83], a specificity of 0.86 [95%CI 0.78-0.92] and an AUC of 0.86 [95%CI 0.83-0.89]. The sensitivity and specificity for each study are shown in the supplemental data (Figure E19).

Impact of muscle weakness on other outcomes.

As can be seen in Figure E20 and Figure E21, muscle weakness was often associated with a longer duration of mechanical ventilation (range of standardised mean difference across studies from -0.18 to 3.47) and a longer ICU length of stay (range of standardised mean difference across studies from -0.34 to 2.6), however there was substantial heterogeneity. Weakness was only associated with the incidence of tracheostomy using the Handgrip test.

Discussion

This systematic review included the largest sample of patients with ICU-Aw to date and evaluated all currently available non-invasive "bedside" tests. The results of this study have allowed the following conclusions to be drawn:

- Respiratory or limb muscle weakness was associated with an increase in the rate of mortality, a failure to wean from artificial ventilation as well as an increased duration of both mechanical ventilation and length of stay in ICU.
- 2. Short term outcomes (mortality in ICU or weaning failure) were better predicted by tools that specifically evaluated diaphragm function than other tools.
- 3. The capacity to predict long-term outcomes was lower than for short-term outcomes.
- There was significant heterogeneity among the measurement protocols and cut-off scores used.

The results of this meta-analysis showed that diaphragm function evaluated during a spontaneous breathing trial is a good indicator for the prediction of mortality in ICU and weaning failure. Poor diaphragm function (measured using transdiaphragmatic twitch pressure or ultrasound) was more strongly associated with an increased risk of mortality in ICU and failure to wean from mechanical ventilation than manual muscle testing. These results therefore suggest that in the initial stages of care, whilst the patient is in ICU and ventilated, evaluations of muscle strength should focus on the respiratory muscles in order to predict such critical outcomes. We suggest that diaphragm function should be closely monitored to detect patients with a high risk of poor clinical outcomes. The advantage of tools that evaluate respiratory muscle function is that they do not always require patient cooperation if the measurement is not maximal and can therefore be performed early, facilitating a faster diagnosis and commencement of treatment.

Phrenic magnetic stimulation is uncommon and difficult to use in routine clinical practice at the bedside, due to the equipment required, however diaphragm ultrasound and MIP are readily carried out and rapidly provide similar information for clinicians. Nevertheless, it is important to note that phrenic magnetic stimulation can be performed on admission to ICU, independently from the mode of ventilation, in contrast with diaphragm thickening fraction which is greatly influenced by the type of ventilation. Dubé et al. reported that the diaphragm thickening fraction was well correlated with magnetic stimulation of the phrenic nerves at the time of transfer to pressure support ventilation. However, it was not correlated during assisted, controlled ventilation, possibly due to passive lung inflation and the reduction in respiratory effort.[13] Even if the relationship between MIP and diaphragm function is weaker, we suggest that patients with a low MIP should also be closely monitored since MIP had an AUC>0.70 for all the critical mortality and weaning failure outcomes investigated.[63]

In our analysis, it was not possible to pool the sensitivity and specificity of the MRC scale and the handgrip test in order to predict weaning failure. Nevertheless, individual results suggested that weaning failure could not be accurately predicted by those tools and that the capacity of the MRC scale to predict ICU mortality was low. However, for longer-term mortality, the predictive capacity of the MRC scale was similar to that of the diaphragm thickening fraction and MIP. The MRC scale, which requires no equipment but involves patient cooperation could be more relevant and easier to evaluate later, following transfer to the general ward to evaluate limb muscle function and to determine appropriate rehabilitation strategies[64, 65].

At this time, therefore, systematic screening for muscle weakness appears pertinent and useful to optimise the treatment of critically ill patients. Moreover, our results highlight the need for the urgent consideration of any therapeutic or preventive interventions aiming at mitigating the effects of ICU-aw and respiratory muscle dysfunction. Although risk factors for the development of muscle weakness have been established,[5] few preventative strategies or cures currently exist. One strategy is to maintain spontaneous ventilation as far as possible under mechanical ventilation, such as has been demonstrated in animal studies with applying

a diaphragm protective ventilation.[66–68] Sedation can be concomitantly adapted in order to permit intensive early rehabilitation in ICU.[69, 70] However, several recent studies demonstrated that intensive rehabilitation in critically ill patients did not produce better results than standard, moderate intensity rehabilitation.[71-74] Another study found that active mobilising exercises did not reduce patient mortality, despite increased muscle strength and walking ability.[75] Similar results were found in studies of inspiratory muscle training (IMT) in ventilated patients [76, 77]: IMT improves MIP and reduces weaning duration in ventilated patients but does not appear to modify the total duration of mechanical ventilation and does not influence mortality. The modalities of application of this treatment and the effects on clinical outcomes remain to be specified.[78] Nevertheless, it should be noted that none of the aforementioned research evaluated rehabilitation in patients with ICU-Aw. An important finding of this study is that respiratory and limb muscle weakness is an international-wide health issue for patients in ICU, with a global prevalence of 47% meaning that one in two patients have an increased risk of mortality. Moreover, an increased rate of mechanical ventilation weaning failure, increased duration of mechanical ventilation and longer ICU stays as a result of ICU-Aw considerably increase the cost of care per patient (+30%).[8] Results from this meta-analysis support the need for an urgent evaluation of rehabilitation for both respiratory and limb muscle weakness in patients with ICU-Aw.

To our knowledge, this is the first study to evaluate the clinical relevance of all data published within the last decade that described non-invasive, bedside tests for use in ICU. The only currently available tool that could not be evaluated was neuromuscular ultrasound as no studies were found, either published or unpublished, that evaluated its clinical use. The pooled sample set of these articles resulted in analysis of the largest sample of patients with ICU-Aw studied to date. The review included research drawn from international sources, and missing

data were recovered from the authors. From these data, several key outcomes were evaluated, and the risk of bias was analysed for each outcome.

We consider the limitations of this review to be the following: firstly, evaluation of the impact of muscle weakness on mortality was not always the main aim of all articles, which may have led to confounding factors in the observations. Secondly, although it was not explicitly studied here, it is supposed that the relationship between muscle function evaluation and patient mortality is also likely to be influenced by the time since diagnosis, as well as the care pathway followed by the patient following discharge from ICU.[79, 80] Moreover, little is currently known about the development or the reversibility of muscle weakness. Thirdly, due to limited data it was impossible to undertake a pooled analysis of sensitivity and specificity since the studies used different cut-offs for the same outcome. Thus, in order to increase the external validity of our results, standardization of the timing and modalities of muscle evaluation in ICU is needed. Fourthly, the number of studies of the handgrip test was insufficient for analysis of its predictive capacity. Fifthly, there is currently a lack of information regarding the increase in diaphragm thickness as reported by Goligher et al, which represents a type of diaphragm injury. Finally, we were unfortunately unable to analyse all existing data for MIP, a test that is frequently reported in the literature. Despite efforts to obtain extra data for clarification from authors, only 3 [15-17] provided individual MIP values.

Conclusion

The results of this study allow firm conclusions to be drawn regarding the clinical relevance and utility of tools for the early diagnosis of muscle weakness. Muscle weakness during ICU is a serious issue associated with high rates of mortality and so we suggest that respiratory muscle function should be evaluated as a priority in ICU, preferably via the measurement of diaphragm thickening fraction using ultrasound. Patients found to have muscle weakness should then be closely monitored. Further studies are urgently needed to evaluate if rehabilitation could reduce mortality rate specifically in patients with ICU-Aw.

Acknowledgment

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Study concept and design: Medrinal, Combret, Prieur, Contal, Lamia

Acquisition of data: All authors

Analysis and interpretation of pooled data: Medrinal, Combret, Hlifiker, Prieur, Gravier, Bonnevie, Contal, Lamia

Drafting of the manuscript: Medrinal, Combret, Hilfiker, Prieur

Critical revision of the manuscript for important intellectual content: All authors

Statistical analysis of pooled data: Hilfiker

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Data Access, Responsibility, and analysis: Clément Medrinal had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data

analysis.

Data sharing: The study specific summary data included in the meta-analysis can be obtained

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Figures legend

Figure 1 Flowchart for study identification and selection

Figure 2 Odds ratios for overall mortality with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation; Q2=Study attrition; Q3=Pronostic factor measurment; Q4=Outcome measurment; Q5=Study confounding; Q6=Statistical analysis and reporting

Figure 3 Odds ratios for weaning failure with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation; Q2=Study attrition; Q3=Pronostic factor measurment; Q4=Outcome measurment; Q5=Study confounding; Q6=Statistical analysis and reporting



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Study	Cut-off	Q1	Q2	Q3	Q4	Q5	Q6				Yes	No	Yes	No	wit	h 95%	CI	(%)
Diaphragm ultrasound, Diaphrag	n excursion																	
Carrie 2017	>27 mm	low	low	low	high	high	mod		-		2	24	3	38	1.06 [0.16,	6.79]	2.16
Kim 2011	<10mm	low	low	low	mod	high	high		-		6	18	17	41	0.80 [0.27,	2.37]	4.37
Mariani 2015	≤11mm	mod	mod	low	low	high	mod			<u> </u>	4	9	1	20	8.89 [0.87,	91.20]	1.51
Spadaro 2016	>14 mm	low	lwo	low	high	mod	mod				8	20	1	22	8.80 [1.01,	76.71]	1.70
Heterogeneity: $\tau^2 = 1.02$, $I^2 = 55.55$	%, H ² = 2.25							-							2.25 [0.59,	8.61]	
Test of $\theta_i = \theta_j$: Q(3) = 6.21, p = 0.10																		
Diaphragm ultrasound, Diaphrag	n thickening	fractior	ı															
Ali 2016	<20%	low	high	low	mod	high	high	_	-		4	23	2	31	2.70 [0.45,	16.00]	2.31
Dubé 2017	<29%	low	low	low	low	low	low		-	-	19	42	2	36	8.14 [1.77,	37.36]	2.89
Lu 2016	<20%	mod	mod	low	mod	high	mod	_		-	2	12	0	27	11.00 [0.49,	246.41]	0.91
Tenza-Lozano 2018	>24%	low	low	low	mod	high	high		-		4	11	7	47	2.44 [0.61,	9.83]	3.26
Heterogeneity: $\tau^2 = 0.18$, $I^2 = 17.669$	%, H ² = 1.21									•					4.17 [1.59,	10.94]	
Test of $\theta_i = \theta_j$: Q(3) = 1.91, p = 0.59																		
Diaphragm ultrasound, decrease	in diaphragm	thickn	ess															
Goligher 2018 ≥10% decrea	se in DTh	low	low	low	low	low	low	-	-		28	50	21	45	1.20 [0.60,	2.40]	6.31
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, H^2	=.														1.20 [0.60,	2.40]	
Test of $\theta_i = \theta_j$: Q(0) = 0.00, p = .																		
Transdiaphragmatic twich pressu	ire																	
Demoule 2013	<11 cmH2O	low	low	mod	low	low	low				29	25	8	23	3.33 [1.27,	8.76]	4.89
Dres 2017	<11 cmH2O	low	low	low	low	low	low		-		11	37	1	27	8.03 [0.98,	65.97]	1.78
Dubé 2017	<11 cmH2O	low	low	low	low	low	low				10	17	1	4	2.35 [0.23,	24.10]	1.51
Jung 2015	<11 cmH2O	hiah	low	low	mod	mod	mod		-		11	21	2	6	1.57 [0.27,	9.12]	2.35
Supinski 2013	<10 cmH2O	mod	hiah	low	hiah	mod	mod				17	18	1	13	12.28 [1.45,	104.27]	1.74
Heterogeneity: $\tau^2 = 0.26 \ l^2 = 25.20^{\circ}$	$H^2 = 1.34$	mou	ingi	1011	ingit	meu	mou								3.77 [1.56.	9,131	20000
Test of $\theta_i = \theta_j$: Q(4) = 2.83, p = 0.59																,		
Maximal Inspiratory Pressure											2010							50.0078M
Carrie 2016	<25 cmH2O	low	low	high	high	high	high				2	17	0	11	3.29 [0.14,	74.87]	0.90
Medrinal 2016	≤30 cmH2O	low	low	low	low	low	low				21	46	4	53	6.05 [1.93,	18.91]	4.14
Spadaro 2016	<25 cmH2O	low	low	low	high	mod	mod				- 8	14	1	28	16.00 [1.82,	140.92]	1.69
Tenza-Lozano 2018	<20 cmH2O	low	low	high	mod	high	high	1. The second	-		3	10	8	41	1.54 [0.34,	6.86]	2.96
Heterogeneity: $\tau^2 = 0.44$, $I^2 = 35.61$	%, H ² = 1.55														4.48 [1.49,	13.42]	
Test of $\theta_i = \theta_j$: Q(3) = 3.58, p = 0.31																		
MRC Score																		
Ali 2008	<48	mod	low	mod	low	low	low		-		11	47	6	64	2.50 [0.86,	7.23]	4.45
Brunello 2010	<35	high	mod	mod	low	high	mod				8	5	5	21	6.72 [1.52,	29.61]	3.00
Carrie 2017	<48	low	low	high	high	high	high			_	3	28	2	34	1.82 [0.28,	11.67]	2.17
Dinglas 2017	<48	high	low	low	low	low	low				29	31	24	72	2.81 [1.41,	5.57]	6.36
Dres 2017	<48	low	low	low	low	low	low		-	_	7	19	5	45	3.32 [0.93,	11.77]	3.66
Hermans 2014	<48	hiah	low	low	low	low	low		-		72	155	27	161	2.77 [1.69,	4.541	7.46
Lee 2012	<48	mod	low	low	mod	low	low				5	39	2	49	3,14 [0.58	17.071	2.49
Medrinal 2017	<48	low	low	low	low	high	mod				9	40	1	49	11.03 [1.34	90.731	1.78
Pablo Diaz Ballye 2017	<48	low	mod	low	mod	mod	mod		-		4	41	4	62	1.51	0.36	6.391	3.11
Sharehar 2009	<18	mod	low	low	low	low	low			_	23	52	4	36	3 98 [1 27	12 491	4 12
Wieske 2015	<40	low	low	mod	low	low	low				37	13	11	65	5.08 [2 34	11 041	5.86
Witewase 2013	~40	low	low	high	low	high	low				2	30	0	30	3 86 [0.18	83 /11	0.03
	<40 V U ² = 1.20	IOW	IOW	nign	low	nign	nign				2	55	0	50	3 27 [2.20	4 711	0.35
Test of $\theta_i = \theta_j$: Q(11) = 5.88, p = 0.8	%, H ⁻ = 1.30 В								•						3.27 [2.20,	4.71]	
Handgrip																		
Ali 2008	<11/7 Kg	mod	low	mod	low	low	low		-	-	13	35	4	76	7.06 [2.15,	23.20]	3.94
Hussein 2018	<11/7 Kg	high	high	mod	mod	high	high	_	-		10	16	1	7	4.38 [0.47,	41.07]	1.61
Lee 2012	<11/7 Kg	mod	low	low	mod	low	low	-	-	-	6	74	1	13	1.05 [0.12,	9.49]	1.66
Heterogeneity: $\tau^2 = 0.41$, $I^2 = 31.559$	%, H ² = 1.46								-						3.97 [1.14,	13.81]	
Test of $\theta_i = \theta_j$: Q(2) = 2.23, p = 0.33								1/8	1 8	3 64								
						1	More deat	h not weak	More	death wea	k							

Random-effects Sidik-Jonkman model

Study	Cut-off	01	02	03	04	05	06					١	Neak Yes	No	Not	Wea	k O	dds Ra	tio Cl	Weight
Diaphragm ultrasound. Diaph	ragm excursion	<u>יפ</u> י ו	92	40	44	40	0,0						105	140	103	140		113070		(70)
Abbas 2018	≤12 mm	mod	low	low	mod	high	mod			_		_	12	3	1	34	136.00 [12.88,	1435.93]	1.79
Carrie 2017	>27 mm	low	low	low	low	hiah	mod		_	- 7	-		13	13	9	32	3.56 [1.22.	10.331	3.07
Flevari 2016	≥10 mm	high	low	low	low	mod	mod			-			6	3	1	17	34.00 [2.94,	392.85]	1.72
Jiang 2004	≥11 mm	mod	mod	low	low	mod	mod			-			19	5	4	27	25.65 [6.08,	108.24]	2.67
Khan 2018	≤13 mm	high	high	high	low	high	high		-	- I			22	13	6	49	13.82 [4.65,	41.12]	3.05
Kim 2011	<10 mm	low	low	low	low	mod	mod						20	4	34	24	3.53 [1.07.	11.65]	2.94
Mariani 2015	≤11mm	mod	mod	low	hiah	mod	mod				_		2	11	0	21	9.35 [0.41.	211.62]	1.28
Saeed 2016	>11 mm	high	hiah	mod	hiah	hiah	hiah		_	_			7	3	1	19	44.33 [3.93.	500.271	1.73
Spadaro 2016	>14 mm	low	low	low	low	low	low		_	<u> </u>			15	13	2	21	12.12 [2.37.	61.80]	2.46
Theerawit 2018	<12.8 mm	low	low	low	low	low	mod		_	Ē			6	9	5	42	5.60 [1.40.	22.44]	2.72
Heterogeneity: $\tau^2 = 0.79$, $I^2 = 56$.35%, H ² = 2.29																11.93 [5.52.	25.781	
Test of $\theta_i = \theta_j$: Q(9) = 16.32, p =	0.06									•										
Diaphragm ultrasound, Diaph	ragm thickenin	g fracti	on																	
Ali 2016	<20%	low	high	low	low	high	high			-			15	2	3	26	65.00 [9.73,	434.02]	2.19
Baess 2016	<29%	high	high	high	low	high	high			-			5	7	2	16	5.71 [0.89,	36.89]	2.23
Blumhof 2016	≥20%	low	low	mod	mod	high	mod		-				20	4	6	22	18.33 [4.51,	74.54]	2.71
Dinino 2014	<30%	high	low	mod	mod	high	mod		-				10	6	4	43	17.92 [4.24,	75.63]	2.67
Dres 2018	<26%	low	low	low	low	low	mod		-	-			21	13	7	35	8.08 [2.78,	23.46]	3.07
Farghaly 2016	≥34%	mod	low	high	low	high	high			-			10	5	4	35	17.50 [3.94,	77.71]	2.61
Ferrari 2014	>36%	high	low	low	low	high	mod				-		15	5	2	24	36.00 [6.18,	209.70]	2.33
Jung 2016	<20%	high	low	low	low	mod	mod		-		-		14	7	1	11	22.00 [2.34,	206.48]	1.88
Osman 2017	≥28%	high	high	high	mod	high	mod						14	0	4	50	325.44 [16.54,	6404.25]	1.36
Tenza-Lozano 2018	>24%	low	low	low	mod	high	mod		-	-			12	3	13	41	12.62 [3.08,	51.70]	2.70
Heterogeneity: $\tau^2 = 0.59$, $I^2 = 47$.14%, H ² = 1.89									•							19.07 [9.35,	38.90]	
Test of $\theta_i = \theta_j$: Q(9) = 9.81, p = 0	0.37																			
Diaphragm ultrasound, decre	ase in diaphraç	m thic	iness																	
Goligher 2018 ≥10% o	decrease in DTh	low	low	low	low	low	low			-			12	66	3	63	3.82 [1.03,	14.17]	2.81
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .%$, H ² = .																3.82 [1.03,	14.17]	
Test of $\theta_i = \theta_j$: Q(0) = -0.00, p =																				
Transdiaphragmatic twich pre	essure									_										
Dres 2017	<11 cmH2O	low	low	low	low	low	mod		-	-			31	17	2	26	23.71 [5.01,	112.26]	2.54
Jung 2015	<11 cmH2O	high	low	low	low	mod	mod			-			18	14	2	6	3.86 [0.67,	22.11]	2.34
Heterogeneity: $\tau^2 = 0.88$, $I^2 = 55$ Test of $\theta_i = \theta_i$: Q(1) = 2.32, p = 0	0.42%, H ² = 2.24 0.13																10.02 [1.74,	57.58]	
Maximal Inspiratory Pressure	>11	hinh	hi ah	1		h i sh				-			00		-		07.00.0	0.50	445 771	0.07
Aivisi 2000	244 cmH2O	nign	nign	low	moa	nign	moa			_			23	4	5	24	27.60 [0.58,	115.77]	2.67
Bruton 2002	<20 cmH20	low	moa	nign	low	nign	nign						11	3	1	0 10	10.07	1.00,	120 241	1.09
Da Japaha 2007	<20 om H2O	high	low	mod	high	low	nign						17	26	7	10	1 20 1	0.45	2 6 21	2.10
De Jongne 2007	S30 cmH20	nign	low	mod	nign	low	low			-			17	30	1	19	1.20[0.45,	3.03]	3.10
lieng 2004	<20 011H20	mod	mod	hiab	low	mod	mod						11	2	2	30	14.00 [82.50 [10.33	650 151	2.02
Jiang 2004	<25 cmH20	moa	moa	nign	low	mod	mod						17	2	2	30	02.50[0.53,	44.541	2.02
Jung 2015	<20 cmH20	nign	low	low	mod	low	mod						14	53	4	53	2.43	1.09	11.31]	2.04
	S30 cmH20	IOW	IOW	IOW	moa	IOW	moa						14	55	4	10	3.50[0.80	28.001	2.90
Saeed 2016	<20 cmH20	nign	nign	nign	nign	nign	nign						4	5 10	5	10	4.00 [5.76 [1.61	20.90]	2.29
Spadaro 2016	<25 cmH2O	low	low	low	low .	low	low	_					12	10	5	24	5.76[1.61,	20.67]	2.84
de Seuze 2015	<20 cmH20	low	low	high	mod	high	mod		Τ.				2	11	20 7	29	0.26	0.05,	1.32]	2.48
de Souza 2015	<25 cmH20	IOW	mod	mod	mod	nigh	nigh						30	22	/	38	8.88 [3.38,	23.32]	3.18
Test of $\theta_i = \theta_j$: Q(11) = 37.02, p	/8%, H⁻ = 3.96 = 0.00																ə.82 (∠.43,	13.96]	
MRC Score																				
Carrie 2017	<48	low/	low	bigh	high	high	hiab						13	18	Q	27	2 17 1	0.77	6 1 21	3 10
Dree 2017	<18	low	low	low	low	low	mod						15	11	19	32	2 10 1	0.07	6 201	3.10
Medrinal 2017	<48	low	low	low	high	high	mod						12	37	10	50	33.671	1 02	586 761	1 / 2
Bable Diaz Ballus 2017	~40	low	iow	low	hiat	nign	hint						5	40	7	50	1.0=1	0.24	3 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	2.04
Heterogeneibu =2 = 4 04 12 = 34	~40 72% ⊔ ² = 2.00	IOW	mod	IOW	nigh	nign	nigh						3	40	'	29	1.00[0.31,	0.00]	2.91
Test of $\theta_i = \theta_j$: Q(3) = 4.94, p = 0).18																2.04 [0.72,	9.04]	
 Handgrip																				
Cottereau 2015	<11/7 Ka	low	low	low	high	low	low		_	_			18	8	22	37	3.78 [1.41.	10.141	3.16
Hussein 2018	<11/7 Ka	hiah	hiah	mod	high	hiah	hiah	_		_			6	20	1	7	2.10[0.21	20.641	1.85
Heterogeneity: $\tau^2 = 0.02$ $I^2 = 20$	04%, H ² = 1.02									•			-		,		3.44 [1.35	8.721	
Test of $\theta_i = \theta_j$: Q(1) = 0.22, p = 0).64																	- 1	· _,	
								1/16	12	64	2	2048								
					More w	/eaning	failure n	ot weak	Mo	re wean	nng fa	ulure v	veak							
Random-effects Sidik-Jonkma	in model																			

First Author (name and year)	Country	Ν	Population	Measurments and cut- off value	Time and condition of measure
Diaphragm Ultrasound					
Abbas 2018	Egypt	50	COPD under $MV > 48h$	EXdi (≤12mm)	During First SBT on a T-tube
Carrie 2017	France	67	Patients under MV > 48h	EXdi (>27 mm)	During first SBT : PS : 7/Pep :0 cmH ₂ O
Flevari 2016	Greece	27	Patients with difficult and prolonged weaning	EXdi (≥10mm)	During SBT on a T-tube
Jiang 2004	Taiwan	55	Patients under MV	EXdi (≥11 mm)	During SBT on a T-tube
Khan 2018	Pakistan	90	Patients under MV > 48h	EXdi (≤13 mm)	During SBT
Kim 2011	Korean	82	Patients under MV > 48h	EXdi (<10mm)	During SBT
Mariani 2015	France	34	Patients under MV > 7 days	EXdi (≤11mm)	During SBT on a T-tube
Saeed 2016	Egypt	30	COPD under MV	EXdi (>11 mm)	During SBT
Spadaro 2016	Italy	51	Patients under MV > 48h	EXdi (>14 mm)	During First SBT on a T-tube
Theerawit 2018	Thailand	62	Patients under MV	EXdi (<12,8mm)	At the end of SBT on a T-tube
Ali 2016	Egypt	60	Patients under MV > 72h	TFdi (<20%)	Not specified
Baess 2016	Egypt	30	Patients under MV	TFdi (<29%)	During SBT
Blumhof 2016	USA	52	Patients under MV > 24h	TFdi (≥20%)	During SBT by pressure support
Dinino 2014	USA	63	Patients under MV	TFdi (<30%)	Prior to the first SBT : PS : 5/Pep :5 cmH ₂ O
Dres 2018	France	76	Patients under MV > 24h	TFdi (<26%)	Prior to the first SBT
Dubé 2017	Canada	99	Patients under MV > 24h	TFdi (<29%)	During Pressure Support Ventilation
Farghaly 2016	Egypt	54	Patients with pulmonary disease under MV	TFdi (≥34%)	During SBT : PS : 8/Pep :0 cmH ₂ O
Ferrari 2014	Italy	46	Patients on PSV with a tracheostomy tube	TFdi (>36%)	During SBT without MV
Jung 2016	France	40	Patients with ICU-Aw under MV > 48h	TFdi (<20%)	During SBT (T-tube or PS : 7/Pep :0 cmH ₂ O
Lu 2016	China	41	Patients with difficult and prolonged weaning	TFdi (<20%)	During SBT : PS : 5/Pep :3 cmH ₂ O
Osman 2017	Egypt	68	Patients under MV	TFdi (≥28%)	During SBT without MV
Tenza-Lozano 2018	Spain	69	Patients under MV > 24h	TFdi (>24%)	During SBT
Colighor 2019	Canada	1//*	Patients under MV	>10% docrosco in DTh	Daily on wookdays until artubation
GUIIGHEI ZUIO	Callaua	T44		≤10% decrease in DIII	Daily off weekuays until extubation
Transdiaphragmatic tw	ich pressure				
Demoule 2013	France	85	Patients under MV > 48h	Ptrstim (<11 cmH20)	Within 24 hours of intubation

Table 1. Characteristics of studies included in the meta-analysis

Dres 2017	France	76	Patients under MV > 24h	Ptrstim (<11 cmH20)	Prior to the first SBT
Dubé 2017	Canada	32*	Patients under MV > 24h	Ptrstim (<11 cmH20)	During Pressure Support Ventilation
Hermans 2010	Netherlands	10	Patients under MV	TwPdi (<10 cmH20)	Not specified
Jung 2015	France	40	Patients with ICU-Aw under MV > 48h	Ptrstim (<11 cmH20)	During SBT (T-tube or PS : 7/Pep :0 cmH ₂ O
Supinski 2013	USA	49	Patients under MV > 24h	TwPdi (<10 cmH20)	Not specified
Maximal Inspiratory P	ressure				
Alvisi 2000	Italy	56	COPD patients	MIP (≥44 cmH2O)	During SBT on a T-tube
Bruton 2002	UK	19	Patients with ICU-Aw under MV > 48h	MIP (<20 cmH20)	Within 12 h before extubation
Carrie 2016	France	30	Patients under MV > 48h	MIP (<25 cmH20) ⁺	Not specified
De Jonghe 2007	France	79	Patients under MV > 7 days	MIP (≤30 cmH2O)	The day of awakening
De Souza 2015	Brazil	103	Patients under MV > 24h	MIP (<25 cmH20)	Prior SBT
Flevari 2016	Greece	27	Patients with difficult and prolonged weaning	MIP (<20 cmH20)	During SBT on a T-tube
Jiang 2004	Taiwan	55	Patients under MV	MIP (<25 cmH20)	During SBT on a T-tube
Jung 2015	France	40	Patients with ICU-Aw under MV > 48h	MIP (<25 cmH20)†	During SBT (T-tube or PS : 7/Pep :0 cmH ₂ O
Medrinal 2016	France	124	Patients under MV > 24h	MIP (≤30 cmH2O)	During SBT : PS : 7/Pep :0 cmH ₂ O
Saeed 2016	Egypt	30	COPD under MV	MIP (<20 cmH20)	During SBT
Spadaro 2016	Italy	51	Patients under MV > 48h	MIP (<25 cmH20)	During First SBT on a T-tube
Tenza-Lozano 2018	Spain	69	Patients under MV > 24h	MIP (<25 cmH20)†	Not specified
Tzanis 2011	Greece	33	ICU stay >7 days	MIP (<36 cmH2O)	48 h after the discontinuation of sedation
MRC Score					
Ali 2008	USA	128	Patients under MV > 5 days	MRC <48/60	When patients was awake and attentive
Brunello 2010	Switzerland	39	Patients under MV > 48h	MRC <35/60	Not specified
Carrie 2017	France	30	Patients under MV > 48h	MRC <48/60	Prior to the first SBT
De Jonghe 2004	France	95	Patients under MV > 7 days	MRC <48/60	The day of awakening
Dinglas 2017	USA	156	ARDS patients	MRC <48/60	Prior to hospital discharge
Dres 2017	France	76	Patients under MV > 24h	MRC <48/60	Prior to the first SBT
Hermans 2014	Netherlands	415	ICU stay >8 days	MRC <48/60	When patients was awake and attentive
Lee 2012	USA	95	ICU stay >48h	MRC <48/60	When patients was awake and attentive
Medrinal 2017	France	99	Patients under MV > 24h	MRC <48/60	During SBT : PS : 7/Pep :0 cmH ₂ O
Pablo Diaz Ballve 2017	Argentina	111	Patients under MV > 24h	MRC <48/60	When patients was awake and attentive
Sharshar 2009	France	115	Patients under MV > 7 days	MRC <48/60	When patients was awake and attentive
Tzanis 2011	Greece	33	ICU stay >7 days	MRC <48/60	level of consciousness adequate for order
Wieske 2015	Netherlands	156	Patients under MV > 48h	MRC <48/60	as soon as patients were awake

Witeveen 2017	Netherlands	71	Patients under MV > 48h	MRC <48/60	as soon as patients were awake
Handgrip test					
Ali 2008	USA	128	Patients under MV > 5 days	11kg and 7Kg	When patients was awake and attentive
Cottereau 2015	France	85	Patients under MV > 48h	11kg and 7Kg	Prior to the SBT
Lee 2012	USA	95	ICU stay >48h	11kg and 7Kg	When patients was awake and attentive
Hussein 2018	Egypt	34	COPD under MV > 48h	11kg and 7Kg	24h after recovery from sedation

* Sample size differences between the original article and the analyse due to group of patient exclusion to avoid double-counting [13] or because it does not match the review question [18]. † Represent studies with undetermined cut-off value ; COPD, Chronic obstructive pulmonary disease ; MV, Mechanical ventilation ; EXdi, Diaphragm excursion ; PS, Pressure support ; Pep, positive expiratory pressure ; SBT, Spontaneous breathing trial ; TFdi, Diaphragm thickening fraction ; ICU-Aw, Intensive care unit acquired weakness ; DTh, Diaphragm thickeness ; Ptrstim, Transdiaphragmatic twich pressure (measured by tracheal pressure) ; TwPdi, Transdiaphragmatic twich pressure (measured by the substraction of abdominal pressure and oesophageal pressure) ; MIP, Maximal inspiratory pressure ; MRC, Medrical research council score ; ARDS, Acute respiratory distress syndrome.

	Number	Sensitivity	Specificity	Area under the curve	Likelihood ra	atio (95% CI)
Outcome and measurment	of				Positive	Negative
	studies	(95% CI)	(95% CI)	(55% CI)	FOSITIVE	
Overall Death						
Diaphragm excursion	4	0.59 [0.27 to 0.85]	0.62 [0.54 to 0.70]	0.64 [0.59 to 0.68]	1.60 [0.9 to 2.6]	0.65 [0.30 to 1.41]
Diaphragm thickening fraction	4	0.71 [0.41 to 0.90]	0.64 [0.49 to 0.77]	0.71 [0.67 to 0.75]	2.00 [1.50 to 2.70]	0.45 [0.21 to 0.97]
Transdiaphragmatic twich pressure	5	0.87 [0.76 to 0.93]	0.36 [0.27 to 0.43]	0.74 [0.70 to 0.78]	1.36 [1.15 to 1.61]	0.36 [0.19 to 0.68]
Maximal Inspiratory Pressure	4	0.79 [0.41 to 0.95]	0.61 [0.44 to 0.75]	0.71 [0.67 to 0.75]	2.01 [1.56 to 2.6]	0.34 [0.11 to 1.05]
MRC Score	12	0.70 [0.62 to 0.77]	0.57 [0.52 to 0.63]	0.68 [0.63 to 0.72]	1.64 [1.47 to 1.84]	0.52 [0.42 to 0.63]
ICU Death						
Transdiaphragmatic twich pressure	4	0.88 [0.76 to 0.94]	0.34 [0.23 to 0.48]	0.85 [0.82 to 0.88]	1.33 [1.08 to 1.64]	0.36 [0.16 to 0.77]
MRC Score	10	0.78 [0.65 to 0.87]	0.54 [0.48 to 0.59]	0.66 [0.61 to 0.70]	1.68 [1.48 to 1.91]	0.41 [0.26 to 0.64]
Hospital Death						
Diaphragm excursion	4	0.56 [0.21 to 0.86]	0.62 [0.54 to 0.69]	0.63 [0.58 to 0.67]	1.50 [0.80 to 2.80]	0.71 [0.30 to 1.65]
Diaphragm thickening fraction	4	0.71 [0.41 to 0.90]	0.64 [0.49 to 0.77]	0.71 [0.67 to 0.75]	2.00 [1.50 to 2.70]	0.45 [0.21 to 0.97]
Maximal Inspiratory Pressure	4	0.80 [0.40 to 0.96]	0.60 [0.42 to 0.75]	0.71 [0.67 to 0.75]	1.33 [1.08 to 1.64]	0.36 [0.16 to 0.77]
MRC Score	9	0.75 [0.67 to 0.82]	0.57 [0.51 to 0.63]	0.71 [0.67 to 0.75]	1.74 [1.52 to 2]	0.43 [0.32 to 0.57]
Weaning failure						
Diaphragm excursion	10	0.76 [0.61 to 0.87]	0.80 [0.73 to 0.85]	0.84 [0.81 to 0.87]	5.50 [3.40 to 9.00]	0.28 [0.20 to 0.38]
Diaphragm thickening fraction	10	0.76 [0.67 to 0.83]	0.86 [0.78 to 0.92]	0.86 [0.83 to 0.89]	3.70 [2.70 to 5.10]	0.30 [0.17 to 0.52]
Maximal Inspiratory Pressure	12	0.76 [0.61 to 0.86]	0.66 [0.54 to 0.77]	0.77 [0.73 to 0.80]	2.30 [1.6 to 3.3]	0.36 [0.21 to 0.62]

Table 2. Summary estimates of the performance bedsides methods for muscles weakness evaluation for predict critical outcomes

CI, Confidence interval ; MRC, Medical research council ; ICU, Intensive care unit.

Electronical Supplemental Figures Legend

Figure E1 Methodological quality assessment according to the QUIPS for overall mortality

Figure E2 Methodological quality assessment according to the QUIPS for mechanical ventilation weaning failure

Figure E3 Methodological quality assessment according to the QUIPS for mechanical ventilation duration

Figure E4 Methodological quality assessment according to the QUIPS for Intensive care unit length of stay

Figure E5 Methodological quality assessment according to the QUIPS for tracheostomy

Figure E6 Methodological quality assessment according to the QUADAS-2 for overall mortality

Figure E7 Methodological quality assessment according to the QUADAS-2 for mechanical ventilation weaning failure

Figure E8 Funnel plot of studies assessing overall mortality

Figure E9 Funnel plot of studies assessing weaning

Figure E10 Funnel plot of studies assessing ICU mortality

Figure E11 Funnel plot of studies assessing Hospital mortality

Figure E12 Odds ratios for intensive care unit mortality with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation; Q2=Study attrition; Q3=Pronostic factor measurment; Q4=Outcome measurment; Q5=Study confounding; Q6=Statistical analysis and reporting

Figure E13 Odds ratios for hospital mortality with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation; Q2=Study attrition; Q3=Pronostic factor measurment; Q4=Outcome measurment; Q5=Study confounding; Q6=Statistical analysis and reporting

Figure E14 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion, transdiaphragmatic twitch pressure, maximal inspiratory pressure and MRC score for overall mortality prediction and confidence ellipse around the optimal summary value

Figure E15 Hierarchical summary receiver operating characteristic (HSROC) curve of transdiaphragmatic twitch pressure and MRC score for ICU mortality prediction and confidence ellipse around the optimal summary value

Figure E16 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion, maximal inspiratory pressure and MRC

score for hospital mortality prediction and confidence ellipse around the optimal summary value

Figure E17 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion and maximal inspiratory pressure for mechanical ventilation weaning failure prediction and confidence ellipse around the optimal summary value

Figure E18 Forest plot of sensitivity and specificity in studies that measure overall mortality

Figure E19 Forest plot of sensitivity and specificity in studies that measure mechanical ventilation weaning failure

Figure E20 Standardized mean difference in mechanical ventilation duration (days) with and without weakness

Figure E21 Standardized mean difference in ICU length of stay (days) with and without weakness

Online Supplement

ICU outcomes can be predicted by non invasive muscle evaluation : a meta-analysis.

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Lamia^{1,8,9*}.





Figure E1 Methodological quality assessment according to the QUIPS for overall mortality

QUIPS mechanical ventilation weaning



Figure E2 Methodological quality assessment according to the QUIPS for mechanical ventilation weaning failure

QUIPS Mechanical ventilation duration



Figure E3 Methodological quality assessment according to the QUIPS for mechanical ventilation duration

QUIPS ICU duration



Figure E4 Methodological quality assessment according to the QUIPS for Intensive care unit length of stay

QUIPS Tracheostomy



Figure E5 Methodological quality assessment according to the QUIPS for tracheostomy



Figure E6 Methodological quality assessment according to the QUADAS-2 for overall mortality



Figure E7 Methodological quality assessment according to the QUADAS-2 for mechanical ventilation weaning failure

Quadas mechanical ventilation weaning



Figure E8 Funnel plot of studies assessing overall mortality



Figure E9 Funnel plot of studies assessing weaning



Figure E10 Funnel plot of studies assessing ICU mortality



Figure E11 Funnel plot of studies assessing Hospital mortality

Buby Coted Ot O O O O All Status No All Status No All Status No Carle 2017 127 mm box for key methods from a large mode 2 2 1 1.0 2.0 0.0 2.0 0.0 0.0 0.0 1.0 0.0 1.0 0.0 </th <th></th> <th>Weak</th> <th></th> <th>Not</th> <th>Weał</th> <th>k Od</th> <th>ds Rat</th> <th>tio</th> <th>Weight</th>													Weak		Not	Weał	k Od	ds Rat	tio	Weight				
Diphogeneitraceund, Diphogener excersion Game 2017 v 27 mm Kim 2011 v 10mm kov kov kov ngh ngh ngh ngh Nema 216 v 10 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10m kov kov ngh ngh ngh Nema 216 v 10 v 10m kov kov kov ngh Nema 216 v 10 v 10m kov	Study	Cut-off	Q1	Q2	Q3	Q4	Q5	Q6					Yes	No	Yes	No	with	n 95%	CI	(%)				
Carrie 2017 > 27 mm Nov how high age in end - 2 2 1 <td>Diaphragm ultrasound, Diaphragr</td> <td>n excursion</td> <td></td>	Diaphragm ultrasound, Diaphragr	n excursion																						
Kim 2011 Charm Even mod Now	Carrie 2017	>27 mm	low	low	low	high	high	mod			•	-	2	24	1	40	3.33 [0.29,	38.75]	2.47				
Martime 2015 Sittim mod	Kim 2011	<10mm	low	low	low	mod	high	high	-	_	_		4	20	12	46	0.77 [0.22,	2.67]	6.21				
Hearcognetic 7 ⁴ = 11.2, 1 ² = 24, 96, H ⁴ = 191 219 (0.3), 12.14 219 (0.4), 12.25 219 (0.4), 12	Mariani 2015	≤11 m m	mod	mod	low	low	high	mod		-			3	10	0	21	14.33 [0.68,	303.77]	1.71				
Tend of e = 0; QQ = 3.80, p = 0.16 Dephagoring utrace-out, Disparging thickening fraction Dephagoring 1: 03. I = 2.94%, H = 1.42 Torus.Locano 2016 - 24% E = 2.95%, H = 1.42 Tend 4 = -0; Q(1) = 1.15, p - 0.28 Dephagoring utrace-out, decrease in disparging theorem Dephagoring utrace-out, decrease in disparging theorem Derould 2013 - 0.01 = -5, H = -1 Tend 4 = -0; Q(1) = 1.05, p - 0.28 Dephagoring utrace-out, decrease in disparging theorem Derould 2013 - 0.01 = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(1) = -0.01, = -5, H = -1 Tend 4 = -0; Q(2) = -1.9 Heatrogrammity, t = -0.01, = -5, H = -1 Tend 4 = -0; Q(2) = -1.9 Heatrogrammity, t = -0.04, H = -1, H	Heterogeneity: τ ² = 1.12, I ² = 47.69%	6, H ² = 1.91								-							2.19 [0.39,	12.14]					
Dipbergamultraceound, Dipbergamultickening fraction 0.06 2017 <101 km c - 0.00 km c - 0.00 km c - 0.00 km mod high high high high high high high - 0.00 km mod high high high - 0.00 km mod high high high - 0.00 km mod high high high - 0.00 km mod high high high - 0.00 km mod high high high high high high high hig	Test of $\theta_i = \theta_j$: Q(2) = 3.60, p = 0.16																							
Dube 2017	Diaphragm ultrasound, Diaphragr	n thickening f	raction																					
Tarazt-zaraz 218 >241 Bow low low low mod high high low	Dubé 2017	<29%	low	low	low	low	OW	low					16	45	1	37	13.16 [1.67,	103.90]	3.23				
Heterogramity: *= 0.30, *= 2.54%, if *= 1.42 5.68 [1.21, 26.63] Disphragm ultrascund, decrease in disphragm thickness Golgier 2018 EV0% Generase in 10Th Isw Iow I	Tenza-Lozano 2018	>24%	low	low	low	mod	high	high		_			3	12	4	50	3.13 [0.62,	15.86]	4.54				
Tet d (= 0, C(1) = 1.15, p = 0.28 Diphragm ultrascurd, decrease in disphragm thickness Golghar 2018 = 10% 66 crosse in OTN is two low low low low low low low low low l	Heterogeneity: τ ² = 0.38, I ² = 29.549	6, H ² = 1.42								-							5.69 [1.21,	26.63]					
Dipplem ultrassund, decrease in displragm lickness Golgher 2018 105 doresease in displragm lickness 19 59 12 54 1.45[0.64, 3.26] 6.92 Teat of e, e, Q(0) = -0.00, p Tand liphragmatic twich pressure 1.45[0.64, 3.26] 6.92 Denoide 2017 -11 cmH20 two	Test of $\theta_i = \theta_j$: Q(1) = 1.15, p = 0.28																							
Cardger AD16 = 2000 = 5.000, 0 =	Diaphragm ultrasound, decrease	in diaphragm	thickn	ess										-	10									
The decompany: f = 0.00, 1 = 20, 0, 1 = . Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0.00, 0 = 0, 0, - Test of 4 = 0, 0, 0, 0 = 0, 0 = 0, 0	Goligher 2018 ≥10% decreas	sein DTh	low	low	low	lo₩	low	low			-		19	59	12	54	1.45	0.64,	3.26]	8.92				
Teat of et al. (20) = 4.00, p = - Transditphragmatic twich pressure Densition 213 <pre></pre>	Heterogeneity: τ = 0.00, Γ = .%, H	=.															1.45[0.64,	3.26]					
Transfliptragnatic twich pressure Demode 2013 2 8 4 8 4 2 8 4 2 8 2 8 4 2 8 4 2 6 4 2 6 1 <th 1<="" <="" colspan="4" td=""><td>Test of $\theta_i = \theta_j$: Q(0) = -0.00, p = .</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th>	<td>Test of $\theta_i = \theta_j$: Q(0) = -0.00, p = .</td> <td></td>				Test of $\theta_i = \theta_j$: Q(0) = -0.00, p = .																			
Lamba 2013 - 11 cm120 low	Transdiaphragmatic twich pressu	re									_		00	0.5	_									
Dres 2017	Demoule 2013	<11 cmH2O	low	low	mod	low	ow	low		-			26	28	5	26	4.83 [1.61,	14.45]	7.06				
Dubě 2017	Dres 2017	<11 cmH2O	low	lo₩	low	low	ow	low					8	40	0	28	11.96 [0.66,	215.72]	1.88				
Jung 2015 <11 cm120	Dubé 2017	<11 cmH2O	low	low	low	low	low	low					10	17	1	4	2.35 [0.23,	24.10]	2.69				
Heterogeneity: t ⁻ = 0.24, l ⁻ = 21.10%, H ⁺ = 1.27 Test of 0, e; 0; Q(3) = 1.32, p = 0.59 Maximal Inspiratory Pressure Carrie 2016 <25 cmH2O low	Jung 2015	<11 cmH2O	high	low	low	mod	mod	mod			-		11	21	2	6	1.57 [0.27,	9.12]	4.08				
Test of \$\$\$ = \$\$, C(2) = 1.32, p = 0.59 Maximal hspiratory Pressure Carrie 2016 <25 cmH2O low	Heterogeneity: $\tau^2 = 0.24$, $I^2 = 21.10$ %	6, H ² = 1.27								1							3.58 [1.31,	9.78]					
Maximal Inspiratory Pressure	Test of $\theta_i = \theta_j$: Q(3) = 1.92, p = 0.59																							
Carrie 2016 425 cmH2O low	Maximal Inspiratory Pressure																							
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Carrie 2016	<25 cmH2O	low	low	high	high	high	high				_	1	18	0	11	1.86 [0.07,	49.77]	1.50				
Tenza-Lozano 2018 <20 cmH2O	Medrinal 2016	≤30 cmH2O	low	low	low	low	ow	low		-	-	_	10	57	1	56	9.82 [1.22,	79.31]	3.18				
Heterogenetity: $r^2 = 1.04$, $l^2 = 39.72\%$, $l^3 = 1.66$ Test of $\theta_1 = 0$; $Q(2) = 3.29$, $p = 0.19$ MRC Score All 2008 < 48 mod low mod low high high nod Brunello 2010 < 35 high mod mod low high high high Dres 2017 < 48 low low low low low low low low Hermans 2014 < 48 high low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low low Medrinal 2017 < 48 low low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low low Medrinal 2017 < 48 low low low low low low low Measke 2015 < 48 low low low low low low low low low Migh high high high Heterogenetity: $r^2 = 0.25$, $l^2 = 2.592\%$, $l^2 = 1.35$ Test of $\theta_1 = 0$; $Q(1) = 0.02$, $p = 0.90$ Test of $\theta_1 = 0$; $Q(1) = 0.02$, $p = 0.90$ Test of $\theta_1 = 0$; $Q(1) = 0.02$, $p = 0.90$ Test of $\theta_1 = 0$; $Q(1) = 0.02$, $p = 0.90$	Tenza-Lozano 2018	<20 cmH2O	low	low	high	mod	high	high		-			1	12	6	43	0.60 [0.07,	5.45]	2.92				
Test of $0_{1} = 0$; $O(2) = 3.29$, $p = 0.19$ MRC Score Ali 2008 < <48 mod low mod low high mod Garrie 2017 < <48 low	Heterogeneity: $\tau^2 = 1.04$, $I^2 = 39.72$ %	6, H ² = 1.66								-							2.36 [0.38,	14.65]					
MRC Score Ali 2008 <48	Test of $\theta_i = \theta_j$: Q(2) = 3.29, p = 0.19																							
Ali 2008 c48 mod low mod low	MRC Score																							
Brunello 2010 <35	Ali 2008	<48	mod	low	mod	low	ow	low		-	-		5	53	4	66	1.56 [0.40,	6.09]	5.63				
Carrie 2017	Brunello 2010	<35	high	mod	mod	low	high	mod		-	-	_	3	10	1	25	7.50 [0.69,	80.96]	2.60				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Carrie 2017	<48	low	low	high	high	high	high	-				2	29	1	35	2.41 [0.21,	27.98]	2.48				
Hermans 2014 < <8 high low low low high mod Medrinal 2017 < <8 low low low low high mod Pablo Diaz Ballve 2017 < <48 low mod low mod mod mod Sharshar 2009 < <48 mod low	Dres 2017	<48	low	low	low	low	low	low		+	-		5	21	3	47	3.73 [0.82,	17.07]	4.94				
Medrinal 2017 <48 low	Hermans 2014	<48	high	low	low	low	high	mod		-			18	209	5	183	3.15 [1.15,	8.66]	7.58				
Pablo Diaz Ballve 2017 <48 low mod low mod low low <thl< td=""><td>Medrinal 2017</td><td><48</td><td>low</td><td>low</td><td>low</td><td>low</td><td>high</td><td>mod</td><td></td><td>+</td><td></td><td></td><td>6</td><td>43</td><td>0</td><td>50</td><td>15.09 [</td><td>0.83,</td><td>275.62]</td><td>1.86</td></thl<>	Medrinal 2017	<48	low	low	low	low	high	mod		+			6	43	0	50	15.09 [0.83,	275.62]	1.86				
Sharshar 2009 <48	Pablo Diaz Ballve 2017	<48	low	mod	low	mod	mod	mod		-	-		4	41	4	62	1.51 [0.36,	6.39]	5.28				
Wieske 2015 <48 low	Sharshar 2009	<48	mod	low	low	low	low	low		-			17	58	1	39	11.43 [1.46,	89.44]	3.26				
Witeveen 2017 < <8 low high low high low high high high high high high high hig	Wieske 2015	<48	low	low	mod	low	low	low			_		20	60	3	73	8.11 [3	2.30,	28.61]	6.14				
Heterogeneity: $\tau^2 = 0.25$, $t^2 = 25.92\%$, $H^2 = 1.35$ Test of $\theta_i = \theta_i$: Q(9) = 7.12, p = 0.62 Handgrip Ali 2008 <11/7 Kg mod low mod low low low low Hussein 2018 <11/7 Kg high high mod mod high high Heterogeneity: $\tau^2 = 0.00$, $t^2 = 0.01\%$, $H^2 = 1.00$ Test of $\theta_i = \theta_i$: Q(1) = 0.02, p = 0.90 Test of $\theta_i = \theta_i$: Q(1) = 0.02, p = 0.90 Test of $\theta_i = \theta_i$: Q(1) = 0.02, p = 0.90	Witeveen 2017	<48	low	low	high	low	high	high	-		•		2	39	0	30	3.86 [0.18,	83.41]	1.69				
Handgrip Ali 2008 <11/7 Kg mod low mod low	Heterogeneity: $\tau^2 = 0.25$, $I^2 = 25.929$ Test of $\theta_i = \theta_j$: Q(9) = 7.12, p = 0.62	6, H ² = 1.35									•						3.76 [3	2.02,	7.01]					
Ali 2008 < 11/7 Kg mod low mod low	Handgrip																							
Hussein 2018 <11/7 Kg high high mod mod high high Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.01\%$, $H^2 = 1.00$ Test of $\theta_1 = \theta_2$: Q(1) = 0.02, p = 0.90 More death not weak More death weak	Ali 2008	<11/7 Kg	mod	low	mod	low	low	low		+			6	42	3	77	3.67 [0.87,	15.41]	5.30				
Heterogeneity: $\tau^2 = 0.00$, $t^2 = 0.01\%$, $H^2 = 1.00$ Test of $\theta_1 = \theta_2$: Q(1) = 0.02, p = 0.90 More death not weak More death weak More death weak	Hussein 2018	<11/7 Kg	high	high	mod	mod	high	high			-	-	10	16	1	7	4.38 [0.47,	41.07]	2.86				
Test of $\theta_i = \theta_i$: Q(1) = 0.02, p = 0.90 1/8 More death not weak More death weak	Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.01\%$	H ² = 1.00								-							3.86 [1.15,	12.93]					
1/8 1 8 64 More death not weak More death weak	Test of $\theta_i = \theta_j$: Q(1) = 0.02, p = 0.90																							
More death not weak More death weak									1/8	1	8	64												
								More	death not	weak	More d	eath wea	ik											

Figure E12 Odds ratios for intensive care unit mortality with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation ; Q2=Study attrition ; Q3=Pronostic factor measurment ; Q4=Outcome measurment ; Q5=Study confounding ;Q6=Statistical analysis and reporting

											Weak		Not	Weak	Odds Radio Codds Radio Codds Radio Codds Radio Codd	atio	Weight
Study	Cut-off	Q1	Q2	Q3	Q4	Q5	Q6				Yes	No	Yes	No	with 95%	6 CI	(%)
Diaphragm ultrasound, Diaphragm	excursion																
Carrie 2017	>27 mm	low	low	low	high	high	mod				0	26	2	39	0.30 0.01,	6.46]	1.32
Kim 2011	<10mm	low	lwo	low	mod	hiah	hiah		-		6	18	17	41	0.80 [0.27.	2.371	5.53
Mariani 2015	≤11mm	mod	mod	low	low	high	mod				4	9	1	20	8.891 0.87.	91,201	2.10
Spadaro 2016	>14 mm	low	low	low	high	mod	mod				8	20	1	22	8 80 [1 01	76 71	2.35
Heterogeneity: $\tau^2 = 1.74$ $I^2 = 62.62\%$	$H^2 = 2.68$	1011	1011	1011	ingri	mou	mou		-			20			2111 0.40	11 181	LIGO
Test of $\theta = \theta \cdot O(3) = 7.14$, $\theta = 0.07$, 11 = 2.00														2.111 0.40,	11.10	
Diaphragm ultrasound, Diaphragm	thickening f	raction															
Ali 2016	<20%	low	hiah	low.	mod	high	high		_		4	23	2	31	2 70 1 0 45	16.001	3 13
Dubé 2017	~20%	low	low	low	low	low	low				10	12	2	36	8141 1 77	37 361	3.94
1 2016	~2070	mod	mod	low	mod	high	mod			1	- 2	12	0	27	11 00 [0.40	246 411	1 20
Tanza Lazana 2019	~2070	mou	mou	1044	mou	nign	mou				4	14	7	47	2441.0.61	0.921	4.37
Hotorogonolity $x^2 = 0.19$ $1^2 = 17.66\%$	$u^2 = 1.21$										12		,	47	4 17 1 1 50	10.041	4.27
Test of $0 = 0$; $O(2) = 1.01$ $p = 0.50$,11 - 1.21														4.17 [1.55,	10.54]	
Test of $\theta_i = \theta_j$. Q(3) = 1.91, p = 0.59																	
Dianbragm ultrasound, decrease in	n dianhraam	thickne	Dee														
Colistor 2018 >10% decrease in DT	h low	low	low	low.	low	low					28	50	21	45	1 20 [0.60	2 401	7 53
Hotorogopoity: $r^2 = 0.00$ $l^2 = 0.01^2$	- 1044	1000	IUW	1044	IOW	10.44					20	50	21	45	1.20 0.00,	2.40]	1.55
Test of $0 = 0$; $O(0) = 0.00$, $1 = .76$, H =															1.20 [0.00,	2.40]	
Test or $\theta_i = \theta_j$: Q(0) = 0.00, p = .																	
Transdianbragmatic twich pressure																	
Demoulo 2012	e <11.emU20	low	low	mad	lour	law	low				20	25	0	00	2 2 2 1 1 27	0 761	6.00
Demoule 2013	<11 cmH20	low	low	Inou	low	low	low				29	23	4	23	0.001 0.00	65.071	0.09
Dres 2017	<11 cmH2O	woi	IOW	woi	IOW	IOW	IOW				11	37	1	21	8.03 [0.98,	104.001	2.45
Dube 2017	<11 cmH2O	IOW	IOW	IOW	IOW	IOW	IOW				10	17	0	5	6.60 [0.33,	131.83]	1.38
Heterogeneity: $\tau = 0.04$, $\Gamma = 3.89\%$,	H" = 1.04									-					4.13 [1.69,	10.08]	
Test of $\theta_i = \theta_i$: Q(2) = 0.66, p = 0.72																	
Manimal Incontrations Decome																	
Maximal Inspiratory Pressure	05 1150			1.15.15						_		4.0	0		4 00 1 0 07	40.771	
Carrie 2016	<25 cmH2O	low	low	high	high	high	high			-	1	18	0	11	1.86 0.07,	49.77	1.18
Medrinal 2016	≤30 cmH2O	low	low	low	low	low	low				12	55	2	55	6.00 [1.28,	28.07]	3.78
Spadaro 2016	<25 cmH2O	low	low	wo	high	mod	mod				8	14	1	28	16.00 [1.82,	140.92]	2.34
Tenza-Lozano 2018	<20 cmH2O	low	low	high	mod	high	high		-		3	10	8	41	1.54 [0.34,	6.86]	3.92
Heterogeneity: τ ² = 0.53, l ² = 35.43%	, H [*] = 1.55									-					4.08 [1.22,	13.66]	
Test of $\theta_i = \theta_j$: Q(3) = 3.60, p = 0.31																	
MRC Score										_							
Ali 2008	<48	mod	OW	mod	low	low	low				11	47	6	64	2.50 0.86,	7.23]	5.62
Brunello 2010	<35	high	mod	mod	low	high	mod				8	5	5	21	6.72 [1.52,	29.61]	3.96
Carrie 2017	<48	low	low	high	high	high	high			-	3	28	2	34	1.82 [0.28,	11.67]	2.95
Dres 2017	<48	low	low	low	low	low	low				7	19	5	45	3.32 [0.93,	11.77]	4.74
Hermans 2014	<48	high	low	low	low	low	low				46	181	12	176	3.73 [1.91,	7.27]	7.67
Lee 2012	<48	mod	low	low	mod	low	low		-	-	5	39	2	49	3.14 [0.58,	17.07]	3.35
Medrinal 2017	<48	low	low	low	low	high	mod				9	40	1	49	11.03 [1.34,	90.73]	2.45
Sharshar 2009	<48	mod	low	low	low	low	low				23	52	4	36	3.98 [1.27,	12.49]	5.26
Wieske 2015	<48	low	low	mod	low	low	low				33	47	7	69	6.92 [2.83,	16.95]	6.45
Heterogeneity: $\tau^2 = 0.09$, $I^2 = 20.79\%$, H ² = 1.26									•					4.08 [2.62,	6.37]	
Test of $\theta_{i} = \theta_{j}$: Q(8) = 4.44, p = 0.82																	
Handgrip																	
Ali 2008	<11/7 Kg	mod	low	mod	low	low	low				13	35	4	76	7.06 [2.15,	23.20]	5.06
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 =$	<u>.</u>									-					7.06 [2.15,	23.20]	
Test of $\theta_i = \theta_j$: Q(0) = 0.00, p = .								-			-						
								1/64	1/4	1464							
							More of	death not w	eak	More death w	eak						
Bandom-effects Sidik-Jonkman model	0																

Figure E13 Odds ratios for hospital mortality with versus without a diagnosed weakness. Q represents the different Quality in Prognosis Studies tool (QUIPS) items. Q1=Study participation; Q2=Study attrition; Q3=Pronostic factor measurment; Q4=Outcome measurment; Q5=Study confounding;Q6=Statistical analysis and reporting



Figure E14 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion, transdiaphragmatic twitch pressure, maximal inspiratory pressure and MRC score for overall mortality prediction and confidence ellipse around the optimal summary value



Figure E15 Hierarchical summary receiver operating characteristic (HSROC) curve of transdiaphragmatic twitch pressure and MRC score for ICU mortality prediction and confidence ellipse around the optimal summary value



Figure E16 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion, maximal inspiratory pressure and MRC score for hospital mortality prediction and confidence ellipse around the optimal summary value



Figure E17 Hierarchical summary receiver operating characteristic (HSROC) curve of diaphragm thickening fraction, diaphragm excursion and maximal inspiratory pressure for mechanical ventilation weaning failure prediction and confidence ellipse around the optimal summary value



Figure E19 Forest plot of sensitivity and specificity in studies that measure overall mortality



Figure E20 Forest plot of sensitivity and specificity in studies that measure mechanical ventilation weaning failure

												Treat	nent		Contro	I	Hedges'	sg	Weight
Study	Cut-off	Q1	Q2	Q3	Q4	Q5	Q6				1	I Mea	n SD	Ν	Mean	SD	with 95%	CI	(%)
Diaphragm ultrasound, Diaphragi	n excursion																		
Carrie 2017	>27 mm	low	low	low	high	hiah	mod				2	6 1	14	41	10.3	11.3	0.29 [-0.19	0.781	3.25
Kim 2011	<10 mm	low	low	low	mod	high	high					4 24	57	58	9.2	37	3 47 [2 76	4 181	2.84
	<1011111	1044	1011	1044	mou	nign	nign					0 40		24	10.4	6.4	0.02 0.00	0.741	2.04
Mariani 2015	≤11 mm	mod	mod	low	low	nign	mod	_	<u> </u>			3 IZ.	0.0	21	12.1	0.4	0.03 [-0.65	, 0.71	2.90
Spadaro 2016	>14 mm	low	low	low	high	mod	mod		-	-	2	8 6.	3 4.2	23	2.5	1.6	1.28 [0.69	, 1.88]	3.05
Heterogeneity: τ ² = 2.29, I ² = 95.979	%, H ² = 24.80																1.26 [-0.26	, 2.78]	
Test of $\theta_i = \theta_j$: Q(3) = 63.14, p = 0.00	0																		
Diaphragm ultrasound, Diaphragi	n thickening f	raction																	
Ali 2016	<20%	low	high	low	mod	high	high				2	7 2	5.7	33	14.5	3.7	2.41 [1.75	, 3.08]	2.93
Dubé 2017	<29%	low	low	low	low	low	low		-		6	1 9	7.7	38	6.1	5.7	0.47 [0.06	. 0.871	3.39
1 2016	<20%	mod	mod	low	mod	high	mod			_	1	4 12	81	27	6	47	101[034	1 671	2.91
	~2070	mou	mou	1044	mou	nign	mou								Ũ		1 39 [0.15	2 401	2.01
Heterogeneity: $\tau = 0.89$, $T = 91.30$	%, H = 11.50								\sim								1.20[0.13	, z.40j	
Test of $\theta_i = \theta_j$: Q(2) = 24.08, p = 0.00	0																		
Diaphragm ultrasound, decrease	in diaphragm	thickne	ess																
Goligher 2018 ≥10% decrea	se in DTh	low	low	low	low	low	low		•		7	8 12.	1 1.7	66	8.8	10.3	0.37 [0.04	, 0.70]	3.51
Heterogeneity: τ^2 = 0.00, I ² = .%, H ²	=.								•								0.37 [0.04	, 0.70]	
Test of $\theta_i = \theta_i$: Q(0) = 0.00, p = .																			
Transdiaphragmatic twich pressu	ire																		
Demoule 2013	<11 cmH2O	low	low	mod	low	low	low	-	-		ŧ	4 1	12	31	11	11	0.00 [-0.44	. 0.441	3.34
Dres 2017	<11 cmH2O	low	low	ION	low	low	low				4	8 8	5 7 5	28	5	6	0.50[0.03	0.961	3 29
Dies 2017	<11 cm120	10.44	low	1044	1017	10.44	1000					7 8	7 1	5	96	0	0.18[-1.12	0.751	2.41
Dube 2017	<11 cmH2O	IOW	low	IOW .	IOW	IOW	IOW							5	3.0	10	-0.10[-1.12	, 0.75]	2.41
Hermans 2010	<10 cmH2O	low	mod	mod	low	hig	high	_		-		6 14.) <u> </u>	4	8	10	0.63 [-0.55	, 1.80]	1.99
Heterogeneity: $\tau^2 = 0.06$, $I^2 = 35.93$	%, H [∠] = 1.56								•								0.22 [-0.19	, 0.62]	
Test of $\theta_i = \theta_j$: Q(3) = 3.48, p = 0.32																			
Maximal Inspiratory Pressure																			
Carrie 2016	<25 cmH2O	low	low	high	high	high	high				1	9 17.	2 17.8	11	5.6	2.7	0.79 [0.04	, 1.54]	2.76
De Jonghe 2007	≤30 cmH2O	high	low	mod	low	low	low				ŧ	3 11.	5 4.8	26	6.5	4.6	1.05 [0.55	, 1.54]	3.25
Medrinal 2016	≤30 cmH2O	low	low	ow	low	low	low		-		6	7	3 5	57	7	4	0.22 [-0.13	0.57	3.47
Spadaro 2016	<25 cmH2O	ION	low	ION N	bigh	mod	mod		Γ _	-	:	2 7	4.3	29	2.6	1.3	1.72 [1.08	2.361	2.97
	-20 cmi 120	hinh i	1011	1011	ling.r	hink	mod					<u>с</u> 1	14	10	2.0		0.71[0.03	1 401	2.07
	<36 cmH2O	nign	moa	IOW	IOW	nign	moa					5 1	/ 14	10	3	5	0.71[0.02	, 1.40]	2.07
Heterogeneity: $\tau^{2} = 0.23$, $\Gamma = 74.68$	%, H ⁼ = 3.95																0.87 [0.37	, 1.36]	
Test of $\theta_i = \theta_j$: Q(4) = 18.87, p = 0.00	0																		
MRC Score																			
Ali 2008	<48	mod	low	mod	low	low	mod				ŧ	8 9.	9.6	70	4.5	4.6	0.63 [0.27	, 0.98]	3.47
Brunello 2010	<35	high	mod	mod	low	high	mod		-	⊢	1	3 1	5.5	26	7	4.5	1.41[0.69	, 2.14]	2.81
Carrie 2017	<48	low	low	high	high	high	high		-		3	1 1	5 15	36	9	8	0.50 [0.02	, 0.99]	3.26
Dres 2017	<48	low	low	low	low	low/	low		-		2	6 9.	7.8	50	6.2	6.6	0.49 0.02	. 0.971	3.28
Hermone 2014	<18	high	low	ION N	low	low	low				22	72	21.5	188	11	15	0.53[0.33	0.731	3.66
	-40	nign	1014	1044	10W	1044	1.		_					E1	-	2.4	0.31 [0.00	0.721	2.40
	×40	niou	low	IOW	nign	1010	100		-			4 1.7·		51	.5	2.4	0.51[-0.08	, 0.72]	0.00
Medrinal 2017	<48	low	low	low	low	mod	mod				2	9	9 4.5	50	6	3	0.78[0.37	, 1.19]	3.39
Pablo Diaz Ballve 2017	<48	low	mod	low	low	mod	mod		-		4	5	4.4	66	4	3.9	0.73 [0.34	, 1.11]	3.42
Tzanis 2011	<48	high	high	mod	low	high	mod			-	1	7 1:	2 14	16	2	3	0.95 [0.25	, 1.65]	2.85
Wieske 2015	<48	low	low	mod	low	low	low		-		8	0 1	5 1 1	76	6	4	1.07 [0.74	, 1.41]	3.50
Witeveen 2017	<48	low	low	high	low	high	mod				4	1 1	10.5	30	7	5	0.57 [0.10	, 1.05]	3.28
Heterogeneity: $\tau^2 = 0.05$, $I^2 = 57.28$	%. H ² = 2.34			-		-			•								0.69 0.50	, 0.87]	
Test of $\theta_1 = \theta_2$: $Q(10) = 16.63$, $p = 0.1$	08								· ·										
Handgrip																			
Ali 2008	<11/7 Km	mod	low	mod	low/	low	mod		-		4	8 9) 10	80	41	38	0.85 0 48	1.221	3.45
Cottorogu 2015	<11/7 K~	low	low	low	med	low	low					6 19	12.9	50	10	10.2	0.751 0.29	1 221	3.28
	~11// Kg	IOW	IOW ELL	1044	mou	IOW .	iow blat					c	, 10.0		F 4	10.Z	0.471 0.20	1.001	3.20
Hussein 2018	<11// Kg	nign	nign	mod	moa	nign	nign	-			4	0 0.	, J	8	5.1	3.4	0.47 [-0.31	, 1.20	2.70
Lee 2012	<11/7 Kg	mod	low	low	high	low	low	-			8	0	3	14	.4	.35	0.21 [-0.35	, 0.78]	3.12
Heterogeneity: $\tau^2 = 0.04$, $I^2 = 36.20$?	%, H ² = 1.57								•								0.63 [0.31	, 0.95]	
Test of $\theta_i = \theta_j$: Q(3) = 3.73, p = 0.29																			
																			1
								-2	U	2	4								

Random-effects Sidik-Jonkman model

Figure E21 Standardized mean difference in mechanical ventilation duration (days) with and without weakness

Online Supplement

ICU outcomes can be predicted by non invasive muscle evaluation : a meta-analysis.

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Bonnevie^{1,6}, Olivier Contal^{7*}, Bouchra Lamia^{1,8,9*}.

Online table

Table E1. Excluded studies with reasons

Reason for exclusion	First author	Year of publication	Journal	Article Title					
	Baldwin CE	2014	Rhysical Therapy	Alterations in respiratory and limb muscle strength and size in patients					
	Daluwin CE	2014	Physical merapy	with sepsis who are mechanically ventilated.					
	Puschor	2015	Aposthosia and Intonsivo Caro	Assessment of diaphragmatic function with cervical magnetic					
	Buscher	2013	Allestilesia allu ilitelisive cale	stimulation in critically ill patients.					
	Cartwright MS	2013	Muscle Nerve	Quantitative neuromuscular ultrasound in the intensive care unit.					
	Cattanan SE	2002	Thorax	Can diaphragmatic contractility be assessed by airway twitch pressure					
	Cattapan SE	2005	THUTAX	in mechanically ventilated patients?					
Evaluation not	Chlan II	2015	Amorican Journal of Critical Caro	Peripheral muscle strength and correlates of muscle weakness in					
relevant		2015	American Journal of Critical Care	patients receiving mechanical ventilation.					
	Goligher FC	2015	American Journal of Respiratory	Diaphragm Thickness during Mechanical Ventilation. Impact of					
	Oungrief LC	2015	and Critical Care Medicine	Inspiratory Effort.					
	Hough Cl	2011	Critical Caro	Manual muscle strength testing of critically ill patients: feasibility and					
	Hough CL		Citical care	interobserver agreement.					
			American Journal of Respiratory	Rapidly progressive diaphragmatic weakness and injury during					
	Janel 2	2011	and Critical Care Medicine	mechanical ventilation in humans.					
Lerolle N 2009			Chest	Ultrasonographic diagnostic criterion for severe diaphragmatic					

				dysfunction after cardiac surgery.						
	Mills GH	2001	British Journal of Anesthesia	Tracheal tube pressure change during magnetic stimulation of the phrenic nerves as an indicator of diaphragm strength on the intensive care unit						
				Ultrasonography in the intensive care setting can be used to detect						
	Parry SM	2015	Journal of Critical Care	changes in the quality and quantity of muscle and is related to muscle strength and function.						
	Sánchez Solana L	2018	Enfermeria Intensiva	Acquired neuromuscular dysfunction in the intensive care unit.						
	Schepens T	2015	Critical Care	The course of diaphragm atrophy in ventilated patients assessed with ultrasound: a longitudinal cohort study.						
	Valette X	2015	Intensive Care Medicine	Diaphragmatic dysfunction at admission in intensive care unit: the value of diaphragmatic ultrasonography.						
	Watson AC	2001	Critical Care Medicine	Measurement of twitch transdiaphragmatic, esophageal, and endotracheal tube pressure with bilateral anterolateral magnetic phrenic nerve stimulation in patients in the intensive care unit.						
	Wieske L	2013	Intensive Care Medicine	Autonomic dysfunction in ICU-acquired weakness: a prospective observational pilot study.						
	Wieske L	2014	PloS One	Early prediction of intensive care unit-acquired weakness using easily available parameters: a prospective observational study.						
	Zambon M	2016	Critical Care Medicine	Mechanical Ventilation and Diaphragmatic Atrophy in Critically III Patients: An Ultrasound Study.						
	Bien UDS	2015	Journal of Physical Therapy Science	Maximum inspiratory pressure and rapid shallow breathing index as predictors of successful ventilator weaning.						
Insufficient	Connolly BA	2013	Critical Care	Clinical predictive value of manual muscle strength testing during critical illness: an observational cohort study.						
information despite	De Jonghe B 2002	2002	JAMA	Paresis acquired in the intensive care unit: a prospective multicenter study.						
contacting the authors	Luo L	2017	BMC Pulmonary Medicine	Different effects of cardiac and diaphragm function assessed by ultrasound on extubation outcomes in difficult-to-wean patients: a cohort study.						
	Pirompanich P 20	2018	Journal of Intensive Care Medicine	Use of diaphragm thickening fraction combined with rapid shallow breathing index for predicting success of weaning from mechanical						

				ventilator in medical patients.
	Qing Q	2018	Journal of Thoracic Disease	Using twitch tracheal airway pressure, negative inhale forced pressure, and Medical Research Council score to guide weaning from mechanical ventilation.
	Samanta S	2017	Journal of Intensive Care Medicine	Diaphragm thickening fraction to predict weaning-a prospective exploratory study.
	Supinski GS	2016	Critical Care	Correlation of maximal inspiratory pressure to transdiaphragmatic twitch pressure in intensive care unit patients.
	Savi A	2012	Journal of Critical Care	Weaning predictors do not predict extubation failure in simple-to-wean patients.
	Angel MJ	2007	Canadian Journal of Neurological Science	Neuromuscular function in survivors of the acute respiratory distress syndrome.
Use	Guarneri B	2008	Journal of Neurology Neuro surgery and Psychiatry	Long-term outcome in patients with critical illness myopathy or neuropathy: the Italian multicentre CRIMYNE study.
electromyography or other tool for	Jansen D	2018	Critical Care	Estimation of the diaphragm neuromuscular efficiency index in mechanically ventilated critically ill patients.
ICU-Aw diagnosis	Khan J	2006	Neurology	Early development of critical illness myopathy and neuropathy in patients with severe sepsis.
	Nordine T	2007	Revue Neurologique	The predominance of myopathy as a cause of intensive-care-unit- acquired paralysis: the diagnostic value of direct muscle stimulation
	Young GB	2004	Critical Care	A stronger approach to weakness in the intensive care unit.
Net ICH	Adler D	2014	American Journal of Respiratory and Critical Care Medicine	Does inspiratory muscle dysfunction predict readmission after intensive care unit discharge?
Population	Palkar A	2018	Lung	Serial Diaphragm Ultrasonography to Predict Successful Discontinuation of Mechanical Ventilation.
	Semmler A	2013	Journal of Neurology	Long-term neuromuscular sequelae of critical illness.
Study design	Herridge MS	2014	American Journal of Respiratory and Critical Care Medicine	ICU-acquired weakness, morbidity, and death.
	Liu Y-Y	2018	Experimental Biology and	Ventilator-induced diaphragm dysfunction in critical illness.

			Medicine	
	Schefold JC	2010	Journal of Cachexia and Sarcopenia Muscle	Intensive care unit-acquired weakness (ICUAW) and muscle wasting in critically ill patients with severe sepsis and septic shock.
				Patterns of diaphragm function in critically ill patients receiving
No original data	Demoule A	2016	Annals of Intensive Care	prolonged mechanical ventilation: a prospective longitudinal study.
Qualitative consideration concerning the publisher journal	Fayed	2016	Journal of American Science	Use of Ultrasound to Assess Diaphragmatic Thickness as a Weaning Parameter in Invasively Ventilated Chronic Obstructive Pulmonary Disease Patients