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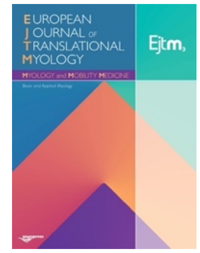

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Diaphragm muscle parameters as a predictive tool for weaning critically ill patients from mechanical ventilation: a systematic review and meta-analysis study

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Abstract

Diaphragmatic ultrasound, valued for its portability and safety, assesses both structural and functional aspects of the diaphragm. While some studies support its predictive value, others conflict. This meta-analysis aims to clarify diaphragmatic ultrasound's role in predicting successful liberation from mechanical ventilation in intensive care settings. A systematic search was performed on Web of Science, Scopus, and PubMed up to March, 2024. The search strategy included a combination of relevant medical subject heading (MeSH) terms and relevant keywords. We defined our eligibility criteria based on the PICO framework. Two authors performed the data extraction using a standardized sheet. The pooled mean difference was calculated using random effects model and Hedges' g along with SD estimation. R and RStudio were used for the statistical analysis and creating forest and funnel plots. The pooled mean difference was 7.25 (95% CI: 4.20, 10.21) for DE among the two groups. We found a statistically significant difference among the two groups indicating that those with successful weaning from intubation had higher means of DE compared to those with failed weaning attempt (p-value<0.01). The mean difference of DTF was also higher among those with successful weaning from intubation compared to those with failed weaning attempt with the pooled mean difference of 14.52 (95% CI: 10.51, 18.54, p-value<0.01). The mean difference of RSBI was lower among those with successful weaning from intubation compared to those with failed weaning attempt with the pooled mean difference of -28.86 (95% CI: -41.82, -15.91, p-value<0.01). Our results suggest that evaluating diaphragmatic excursion and thickening fraction can reliably anticipate successful liberation from mechanical ventilation. However, significant heterogeneity was present among the included studies. High-quality research, particularly randomized clinical trials, is required to further elucidate the role of diaphragmatic ultrasound in predicting weaning from mechanical ventilation.

Key words: ultrasound, ultrasonography, diaphragm, thickening fraction, excursion.

Weaning patients off mechanical ventilation in the ICU poses a significant challenge. It's crucial for the multidisciplinary team to determine the ideal timing for this process. Premature weaning can result in weaning failure, leading to higher risks of hospital-acquired infections, increased healthcare costs, prolonged ICU and hospital stays, and potential diaphragmatic dysfunction.[1,2] Existing guidelines suggest using various bedside indices to anticipate successful weaning from mechanical ventilation. However, these indices have not demonstrated absolute effectiveness, likely because critically ill patients exhibit diverse characteristics, which can impede the predictive accuracy of these indices across different patient groups. While a Spontaneous Breathing Trial (SBT) is a suitable method to ready the patient for extubation, failure rates and the need for subsequent reintubation can surpass 20% in patients at the highest risk.[3-5]

Patients undergoing mechanical ventilation may experience a complex decline in diaphragmatic function, which can contribute to weaning difficulties and prolonged dependence on invasive mechanical ventilation. Therefore, evaluating diaphragmatic function could aid in predicting the patient's capacity to sustain spontaneous breathing over an extended period.[6-8] The application of diaphragmatic ultrasound in the intensive care setting has garnered increasing interest due to its portability, rapidity, and safety. This technique enables assessment of both the structural and functional aspects of the diaphragm, offering insights into the likelihood of successful weaning from mechanical ventilation. While certain studies have highlighted the utility of ultrasound in predicting weaning success, others have presented conflicting findings, prompting ongoing investigation into its efficacy.[6-11] This systematic review and meta-analysis aim to assess the role of diaphragmatic ultrasound in predicting successful liberation from mechanical ventilation.

Methods and Materials

The present study was conducted based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline 2020.[12]

Search strategy

A systematic search was performed on electronic databases such as Web of Science, Scopus, and PubMed from the beginning until March, 2024. The search strategy included a combination of relevant medical subject heading (MeSH) terms and relevant keywords for ("ultrasonography" OR "ultrasound" OR "US") AND ("diaphragm excursion" OR "diaphragm thickening fraction" OR "rapid shallow breathing index") AND ("extubating" OR "weaning" OR "extubation").

Eligibility criteria

We defined our eligibility criteria based on the PICO framework: (P) Population: critically ill patients. (I) Intervention: mechanical ventilation. (C) Comparison: diaphragm parameters. (O) Outcome: weaning succus. The exclusion criteria were defined as: absence of diaphragm parameters, not reporting weaning outcome, lack of individual data, and non-English language.

Data extraction and outcome measures

Two independent authors performed the data extraction using a standardized sheet. Any disagreement was resolved through a discussion with a third party. The standardized sheet included: authors' name, year of publication, total number of participants, male to female ratio, mean and SD of diaphragm excursion, mean and SD of diaphragm thickening fraction, mean and SD of rapid shallow breathing index. The aforementioned variables were extracted in two groups: the weaning succus and weaning failure.

Statistical analysis and data synthesis

The pooled mean difference was calculated using random effects model and Hedges' g along with SD estimation. For assessing the heterogeneity of the included studies, the I^2 (I square) test was used. The Mantel-Haenszel method and random effects model was used for pooling the effect sizes and SD was consequently calculated. For testing the overall significance of the random model, *z*-test was performed Potential publication bias was graphically assessed by creating funnel plots for each of the aforementioned groups. R (R Foundation for Statistical Computing, Vienna, Austria) and RStudio (RStudio, Inc., Boston, MA) were used for the statistical analysis and creating forest and funnel plots.

Results

Our initial search retrieved 2444 articles from PubMed, Scopus, and Web of Science, from which 942 duplicates were removed. After screening the title and abstract of 1502 records, 91 full texts were retrieved, among which 16[10,11,13-26] studies were included based on our eligibility criteria (Figure 1). More detail regarding the study characteristics of the included studies is summarized in Table 1.

Based on the random effects model for pooling the mean difference of DE among those with/without successful weaning from intubation, the pooled mean difference was 7.25 (95% CI: 4.20, 10.21). We found a statistically significant difference among the two groups indicating that those with successful weaning from intubation had higher means of DE compared to those with failed weaning attempt (p-value<0.01). Figure 2 and 3 show the forest and funnel plots for the pooled mean difference of DE among the two groups. Table 1 summarizes the characteristics of the included studies for DE.

The mean difference of DTF was also higher among those with successful weaning from intubation compared to those with failed weaning attempt with the pooled mean difference of 14.52 (95% CI: 10.51, 18.54) based on the random effects model (p-value<0.01). Figure 4 and 5 show the funnel and forest plots for pooled DTF among the two groups. Table 2 summarizes the characteristics of the included studies for DTF.

The mean difference of RSBI was lower among those with successful weaning from intubation compared to those with failed weaning attempt with the pooled mean difference of -28.86 (95% CI: -41.82, -15.91) based on the random effects model (p-value<0.01). Figure 6 and 7 show the funnel and forest plots for pooled RSBI among the two groups. Table 3 summarizes the characteristics of the included studies for RSBI.

Discussion

Based on the results of our systematic review and meta-analysis, DE and DTF showed significant difference among those with successful weaning from intubation and those with failed attempt of weaning. These results can indicate that DE and DTF and be used as non-invasive methods for prediction of the outcome of weaning from mechanical ventilation among critically ill patients.

In recent years, several systematic reviews and meta-analyses have examined the utility of diaphragmatic ultrasound in predicting weaning success or failure in mechanically ventilated patients.[27-34] Our findings align with the conclusions drawn in most of these previously published studies. For instance, one study reported satisfactory diagnostic accuracy in predicting extubation outcomes, while another concluded that diaphragmatic thickening fraction alone modestly predicts weaning outcomes.[35-37] Additionally, recent research has linked ultrasound-detected diaphragm dysfunction with an elevated risk of extubation failure. Moreover, findings from another study indicate that reduced diaphragmatic excursion and thickening fraction values are associated with a heightened risk of extubation failure, exhibiting moderate to high specificity.[20,38,39]

In clinical practice, patients experiencing respiratory failure often rely on mechanical ventilation for assistance in breathing. This form of respiratory support is widely utilized and effectively facilitates the transition from shallow, rapid breathing to normal breathing, without imposing additional strain on the respiratory system.[40,42] This improves overall alveolar ventilation. However, the mechanical stimulation associated with mechanical ventilation can trigger a heightened inflammatory response in the patient's body. Prolonged use of mechanical ventilation may also contribute to progressive organ damage and subsequent multi-organ failure, thereby increasing the risk of mortality. As such, it is crucial to withdraw mechanical ventilation promptly once the underlying causes of respiratory distress have been adequately addressed. While weaning from mechanical ventilation is typically successful, there are cases where patients fail spontaneous breathing trials or require reintubation shortly after extubation. Thus, successfully weaning patients from mechanical ventilation remains a significant clinical challenge in the management of respiratory failure.[19,34,43,44]

Bedside ultrasound technology has gained widespread acceptance and is often referred to as a visual "stethoscope" due to its rapid, non-invasive, reproducible, and intuitive nature. In the context of weaning from invasive mechanical ventilation, bedside ultrasound plays a crucial role by facilitating diaphragm function monitoring, lung ultrasound, volume responsiveness assessment, and cardiac ultrasound indicators.[45-47] Its utility extends to assessing the pathophysiological status of patients and identifying the underlying causes of weaning failure. One key parameter used to evaluate diaphragm function is the diaphragm thickening fraction.[15,48-50]

Several limitations should be acknowledged in this study. First, potential biases may exist in each of the included studies as randomized trials were not incorporated. Additionally, the absence of a standardized reference value for diaphragmatic thickening and excursion fraction could introduce measurement inaccuracies. Furthermore, subgroup analysis based on sex and the duration of mechanical ventilation prior to the spontaneous breathing trial and ultrasound assessment was not conducted, which could potentially influence the ultrasound outcomes.

Contrary to the outcomes of this meta-analysis, two referenced studies did not discover any correlation between diaphragmatic excursion and thickening fraction values below the designated cutoff point measured via ultrasound and the outcome of weaning from mechanical ventilation. A recent study characterized extubation failure as the necessity for intubation within 72 hours post-extubation, while another study defined it as the requirement for intubation or death within seven days post-extubation.[27,34] This contrasts with our investigation, as the studies included in this meta-analysis assessed extubation success within 48 hours following mechanical ventilator weaning.[51,54]

Even minor differences in measurement among observers could impact the results and introduce heterogeneity; indeed, it is a technique dependent on the observer. Nevertheless, several studies have determined that diaphragmatic ultrasound measurements are replicable. The findings of this study hold significance for clinical application, indicating that diaphragmatic ultrasound is a viable tool in the intensive care unit during spontaneous breathing trials to objectively anticipate successful weaning from mechanical ventilation. It is a convenient, swift, noninvasive, straightforward, and safe technique that does not expose healthcare workers to ionizing radiation.[27-34] However, given the observed high heterogeneity, which is common in diagnostic test meta-analyses, the aggregated measurements should be cautiously interpreted, especially across various subgroups of critically ill patients, to ensure personalized determination of the optimal outcome.[13,55-59]

Conclusions

The findings of this systematic review and meta-analysis indicate that assessing diaphragmatic excursion and diaphragmatic thickening fraction can effectively predict the likelihood of successful weaning from mechanical ventilation. However, notable heterogeneity was observed across the various studies included in the analysis. There is a need for high-quality studies with robust methodologies, particularly randomized clinical trials, to further assess the utility of diaphragmatic ultrasound as a predictor of weaning from mechanical ventilation.

List of abbreviations:

MeSH, Medical Subject Heading

ICU, Intensive Care Unit

PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses

SBT, Spontaneous Breathing Trial

DE, Diaphragmatic Excursion

DTF, Diaphragm Thickening Fraction

RSBI, Rapid Shallow Breathing Index

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Table 1. Characteristics of the included studies for DE.

Author	Year	Country	Population	M/F	DE Succuss mean	DE Succuss SD	DE Succuss n	DE Failure mean	DE Failure SD	DE Failure n
Alam et al. (14)	2022	Bangladesh	31	19/12	12.41	2.38	18	9.2	1.87	13
Elshazly et al. (15)	2020	Egypt	62	NR	21.81	7.04	34	9.28	3.9	28
Eltrabili et al. (16)	2019	Egypt	35	16/19	18.37	7.27	17	7.78	4.15	13
Farghaly et al. (17)	2017	Egypt	54	31/23	15.07	5.07	40	10.23	2.63	14
Fossat et al. (19)	2022	France	100	NR	23.8	9.2	91	25.9	10.5	9
Kaur et al. (20)	2022	India	50	NR	37.5	9	31	21.2	6.7	19
Li et al. (21)	2021	China	101	42/59	15.93	5.14	69	8.03	4.57	32
Osman et al. (23)	2017	Egypt	68	NR	24.17	4.23	50	9.29	5.48	18
Palker et al. (24)	2018	USA	73	37/36	22	9	53	16.6	8	20
Sabetian et al. (25)	2024	Iran	50	39/11	12.50	4.78	26	10.22	3.15	24
Theerawit et al. (10)	2018	Thailand	52	38/14	13.5	5.3	51	12.8	9.6	11
Yoo et al. (26)	2018	Korea	60	42/18	15.93	5.20	47	8.03	4.90	13

Table 2. Characteristics of the included studies for DTF

Author	Year	Country	Population	M/F	DTF Succuss mean	SD	n	Failure mean	SD	n
Abdelwahed et al. (13)	2019	Egypt	65	40/25	49.48	12.5	51	27.83	9.95	14
Alam et al. (14)	2022	Bangladesh	31	19/12	22.34	2.73	18	14.74	6.89	13
Elshazly et al. (15)	2020	Egypt	62	NR	33.52	14.51	34	18.57	9.37	28
Eltrabili et al. (16)	2019	Egypt	35	16/19	43.43	7.35	17	22.31	13.37	13
Farghaly et al. (17)	2017	Egypt	54	31/23	60.49	35.60	40	47.43	51.64	14
Ferrari et al. (18)	2014	Italy	46	34/12	52.43	20.27	29	26	6.46	17
Kaur et al. (20)	2022	India	50	NR	36.57	8.22	31	19.26	3.49	19
Li et al. (21)	2021	China	101	42/59	49.48	12.5	69	27.83	9.95	32
Lin et al. (22)	2024	China	79	69/10	35	7.8	57	28.7	8.1	22
Osman et al. (23)	2017	Egypt	68	NR	33.50	1.56	50	23.11	4.11	18
Sabetian et al. (25)	2024	Iran	50	39/11	51.99	21.33	26	48.33	11.55	24
Theerawit et al. (10)	2018	Thailand	52	38/14	37	14	51	28	13	11

Yoo et al. (26)	2018	Korea	60	42/18	40.40	28.44	47	24.06	25.49	13

Table 3. Characteristics of the included studies for RSBI

Author	Year	Country	Population	M/F	RSBI					
					Succuss			Failure		
					mean	SD	n	mean	SD	n
Abdelwahed et al. (13)	2019	Egypt	65	40/25	79.58	20	51	102	17.07	14
Alam et al. (14)	2022	Bangladesh	31	19/12	100.46	2.84	18	99	3.71	13
Elshazly et al. (15)	2020	Egypt	62	NR	43.95	14	34	54	25.48	28
Eltrabili et al. (16)	2019	Egypt	35	16/19	39	18	17	77	30	13
Farghaly et al. (17)	2017	Egypt	54	31/23	58.59	26	40	51	20.59	14
Ferrari et al. (18)	2014	Italy	46	34/12	70	20	29	126	30.71	17
Fossat et al. (19)	2022	France	100	NR	56	26	91	56	28.3	9
Kaur et al. (20)	2022	India	50	NR	46.61	18.	31	105	7.93	19
Li et al. (21)	2021	China	101	42/59	75.68	18.	69	105	16.07	32
Lin et al. (22)	2024	China	79	69/10	44.57	6.	57	73	16.85	22
Osman et al. (23)	2017	Egypt	68	NR	72.18	10	50	114	5.48	18

Palker et al. (24)	2018	USA	73	37/36	45.9	19	53	75.5	57.4	20
Sabetian et al. (25)	2024	Iran	50	39/11	38.24	7	26	120	16.86	24
Tenza-Lozano et al. (11)	2018	Spain	69	43/26	31.35	17	44	40	18.86	25
Theerawit et al. (10)	2018	Thailand	52	38/14	55.11	25	51	83	53.11	11

Figure 1. The PRISMA flow chart of the included studies

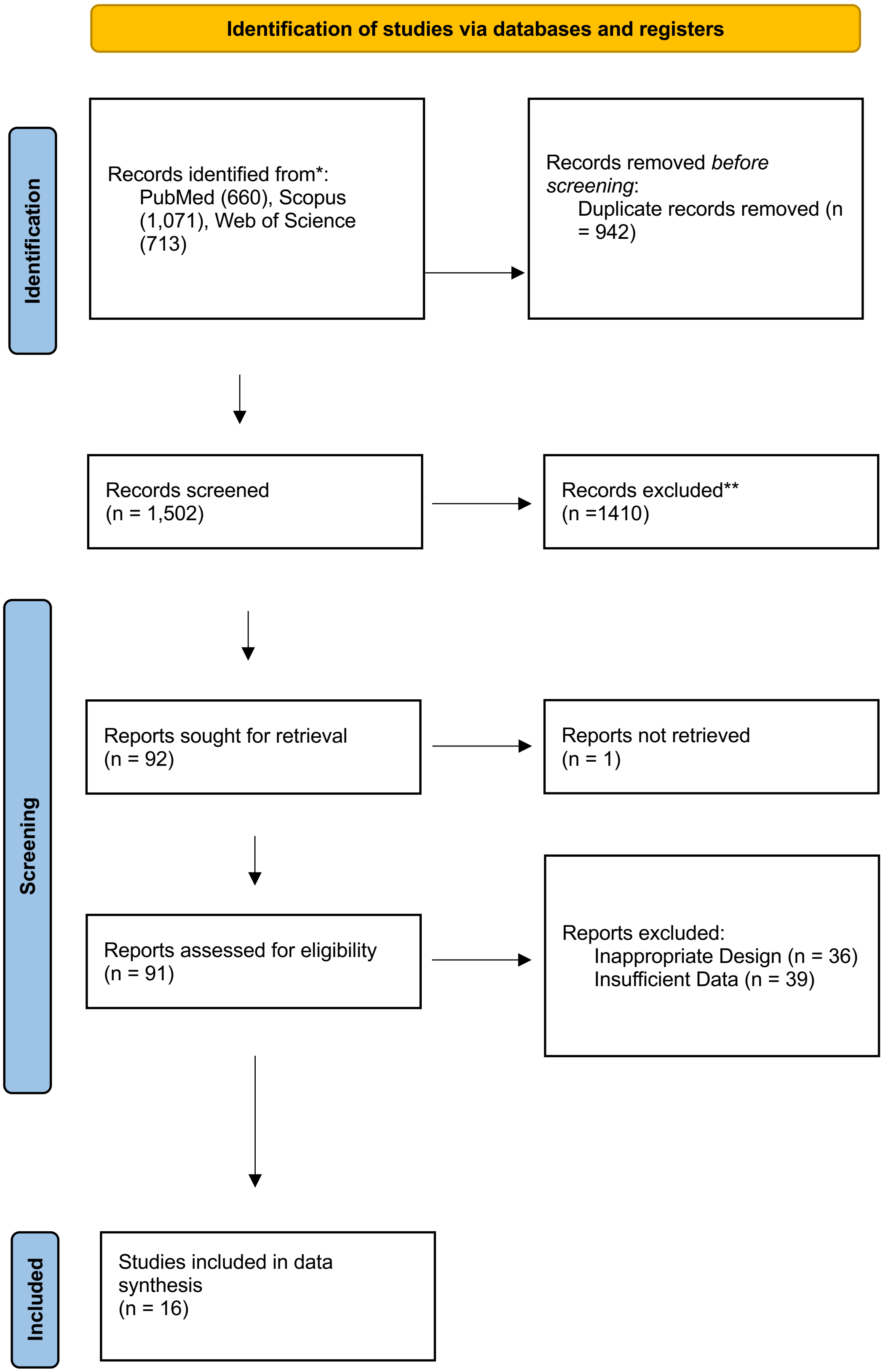

Figure 2. Forest plot of pooled mean difference of DE among the two groups

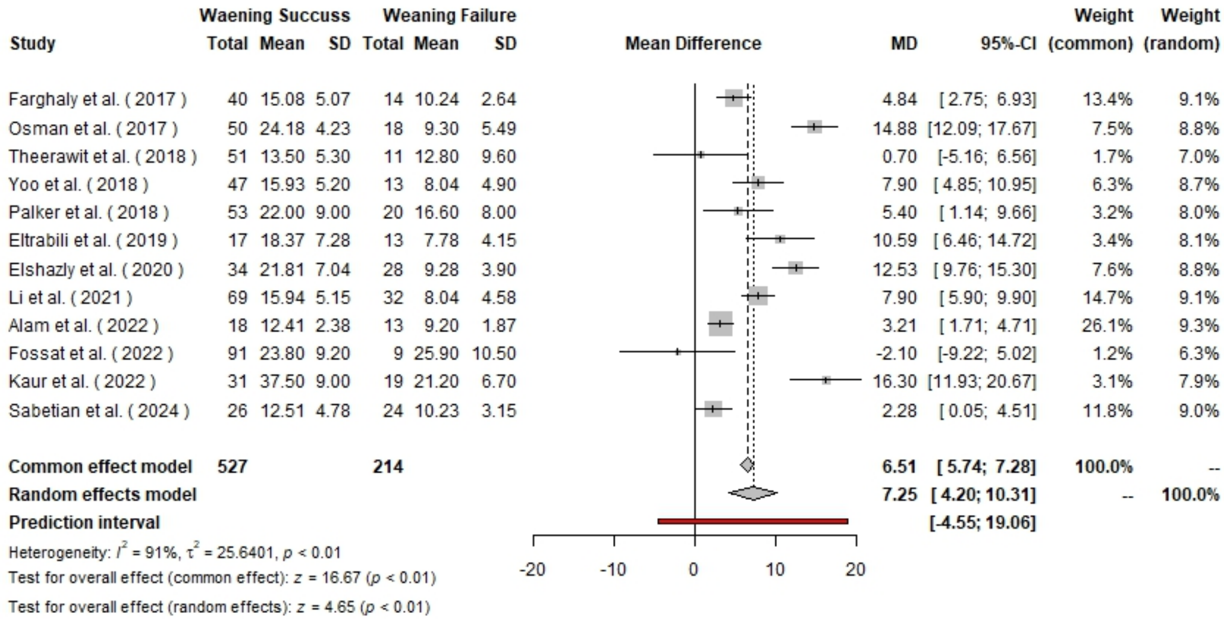

Figure 3. Funnel plot of mean difference of DE among the included studies

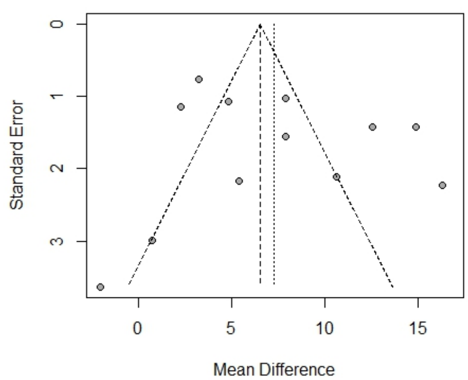

Figure 4. Forest plot of pooled mean difference of DTF among the two groups

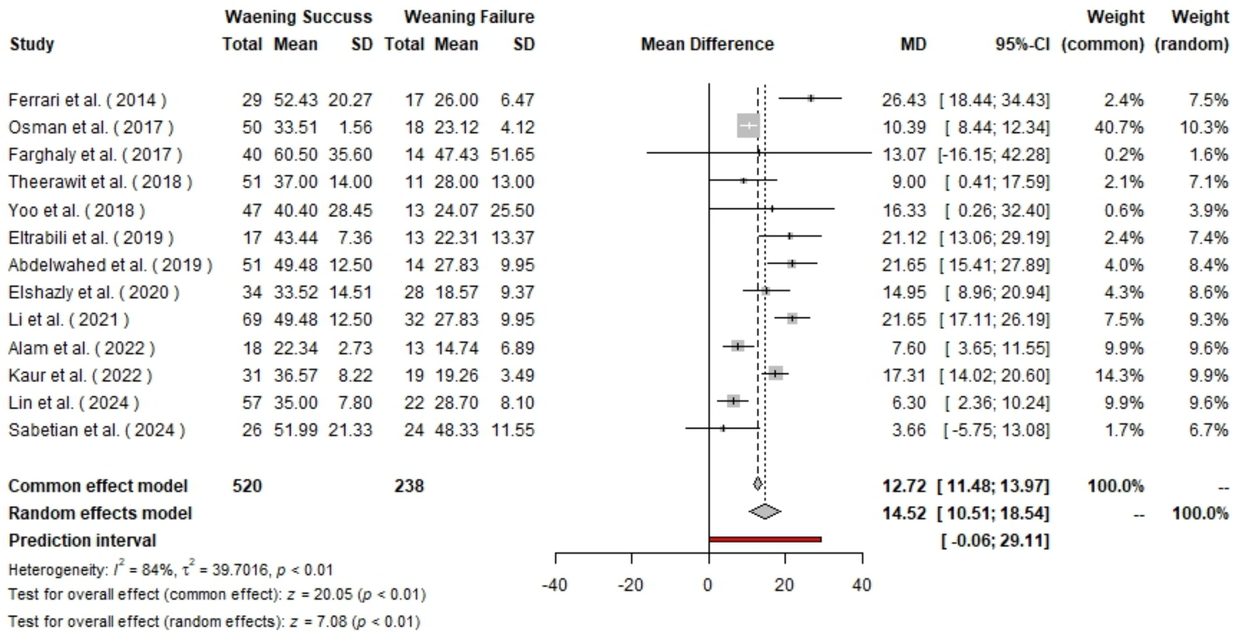

Figure 5. Funnel plot of mean difference of DTE among the included studies