Can we predict weaning failure from ventilator though evaluate cardiac function parameter?

引言人：陳紹恩 呼吸治療師

指導者：邊苗瑛 教授

報告日期：2023.08.18

評讀文章

BJA

IF : 11.719

British Journal of Anaesthesia, 126 (1): 319–330 (2021)

doi: 10.1016/j.bja.2020.07.059

Advance Access Publication Date: 25 September 2020

Review Article

RESPIRATION AND THE AIRWAY

Association of weaning failure from mechanical ventilation with transthoracic echocardiography parameters: a systematic review and meta-analysis

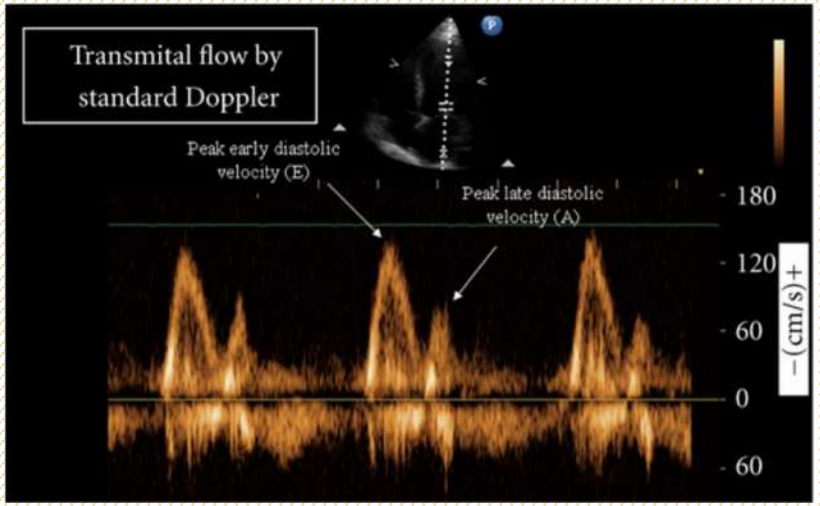
Filippo Sanfilippo[1,*], Davide Di Falco[2], Alberto Noto[3], Cristina Santonocito[1], Andrea Morelli[4], Elena Bignami[5], Sabino Scolletta[6], Antoine Vieillard-Baron[7,8] and Marinella Astuto[1,2,9]

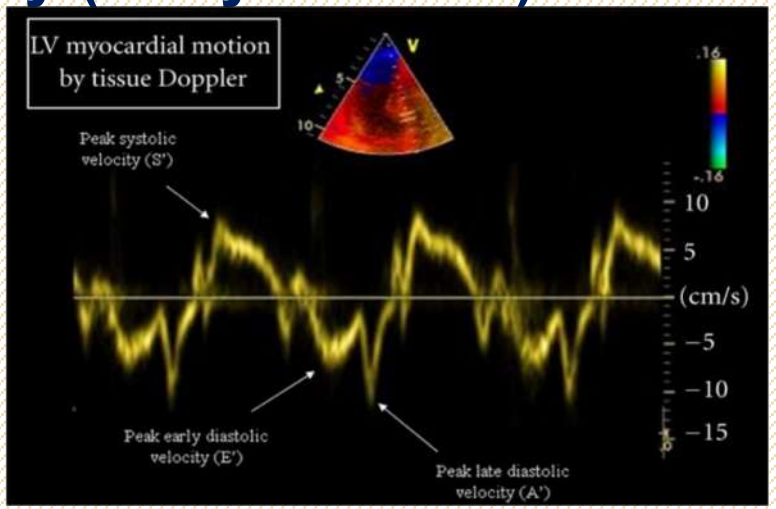
Ventilator weaning

- **Weaning failure and prolonged MV**
  - **ICU length of stay ↑**
  - **Healthcare costs ↑**
  - **Morbidity and mortality ↑**
  - **Reintubation → Life-threatening complications**
- **The main causes of weaning failure**
  - Respiratory origin
  - Diaphragmatic dysfunction
  - Cardiac dysfunction
    - 👉 Weaning- induced pulmonary edema (most common, 60%)
    - 👉 Hemodynamic changes
    - 👉 Myocardial ischemia seems uncommon

Transthoracic echocardiography parameters

- Provides real-time measurements
- Increasingly used in the ICU
- Parameters
  - ➢ E wave → Peak velocity in early diastole (Passive flow)
  - ➢ A wave → Peak velocity in late diastole (Atrial contraction)
  - ➢ e'→ mitral annulus velocity (Early diastole)





- Case Reports in Medicine 2012(8):476903

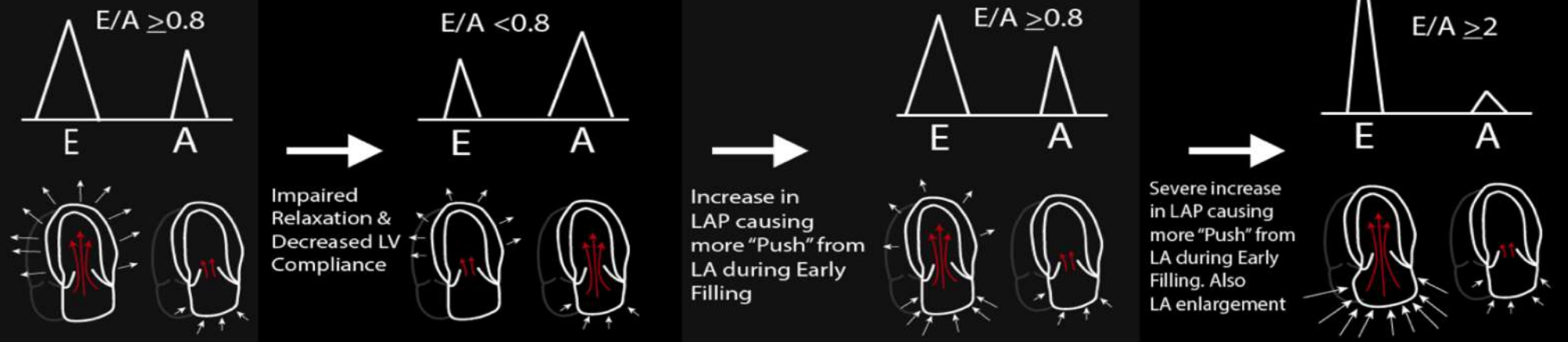
Left ventricular diastolic function

INTERPRETATION:	Grade 0 (Normal)	Grade 1 (Impaired Relaxation)	Grade 2 (Pseudonormal)	Grade 3 (Restrictive)
	E/A ≥0.8 e′ ≥ 8 cm/s E/e′ < 8	E/A <0.8 e′ < 8 cm/s E/e′ < 8	E/A ≥0.8 e′ < 8 cm/s E/e′ 8 - 15	E/A ≥2 e′ << 8 cm/s E/e′ > 15

MITRAL INFLOW

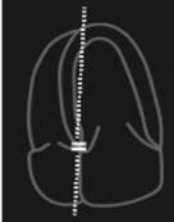
Measures **BLOOD FLOW** coming into the Left Ventricle

PULSE Wave gate at Mitral Valve Tips



TISSUE DOPPLER

Measures **MUSCLE MOVEMENT** of the Left Ventricle AWAY from probe during Diastole



Tissue Doppler gate at Septal Annulus

POCUS 101

Methods - Eligibility criteria

PICOS	
1. Participants	Patients undergoing weaning with SBT (T-tube trial or low level PSV)
2. Intervention	Transthoracic echocardiography performed before the weaning trial is started
3. Comparison	Measurements of echocardiographic parameters of LV and RV function
4. Outcomes	Weaning failure (failed SBT, reintubated, or both within 48 h) *vs* weaning success (studies with longer timeframe for reintubation used for sensitivity analysis)
5. Study design	Prospective clinical studies (retrospective studies only for sensitivity analysis)

- **Pediatric studies were excluded.**
- **Adult case series were included only if they provided acceptable data for at least 10 patients.**
- **Low-level PSV : PS ≦ 10 cm H_2O**
  PEEP ≦ 5 cm H_2O

Methods - Identification of studies

- Two electronic databases
  - MEDLINE (2011-2019)
  - EMBASE (2013-2019)
  - Final update: December 4, 2019.
- First group
  - ‘weaning’ OR ‘spontaneous breathing trial’ OR ‘mechanical ventilation’
- Second group
  - ‘echocardiography’ OR ‘ejection fraction’ OR ‘systol*’ OR ‘diastol*’
- Language restriction
  - only English
- Manual search by four authors (FS, DDF, AN, CS).

Methods - Analysis of outcomes (1)

- Primary : Left ventricular function
- Left ventricular systolic dysfunction (LVSD)
  - LV ejection fraction (LVEF)
- Left ventricular diastolic dysfunction (LVDD)
  - Left atrial volume
  - Tricuspid regurgitant jet velocity
  - E wave velocity
  - E/A ratio
  - e’
  - E/e’
- Secondary outcomes: Right ventricular function
  - ‘weaning’ OR ‘spontaneous breathing trial’ OR ‘mechanical ventilation’

Methods - Analysis of outcomes (2)

- Four types of sensitivity analyses
  - Including studies with criteria for reintubation extended to a longer timeframe (i.e. 1 week)
  - Including studies with non-prospective design
  - Excluding studies with a high risk of bias
  - Performed with ‘leave-one-out at a time’

Methods - Study selection and data extraction

1. Screened titles and abstracts produced by the automated search. (FS, DDF, CS)
2. Full text articles that were identified as relevant were then assessed against the eligibility criteria (FS, DDF, CS)
3. Discrepancies (AN, MA)
4. Extracted data from individual studies, contacted corresponding authors, and entered information into a pre-designed data collection form (FS, DDF)
5. Cross-checked (AN, CS, AM)

Methods - Quality assessment

- the Newcastle-Ottawa scale (NOS)
  - Selection
  - Comparability
  - Outcome
- Maximum of nine points
  - High-risk of bias : 1-3 points
  - Intermediate-risk of bias : 4 -5 points
  - Low- risk of bias :6 - 9points

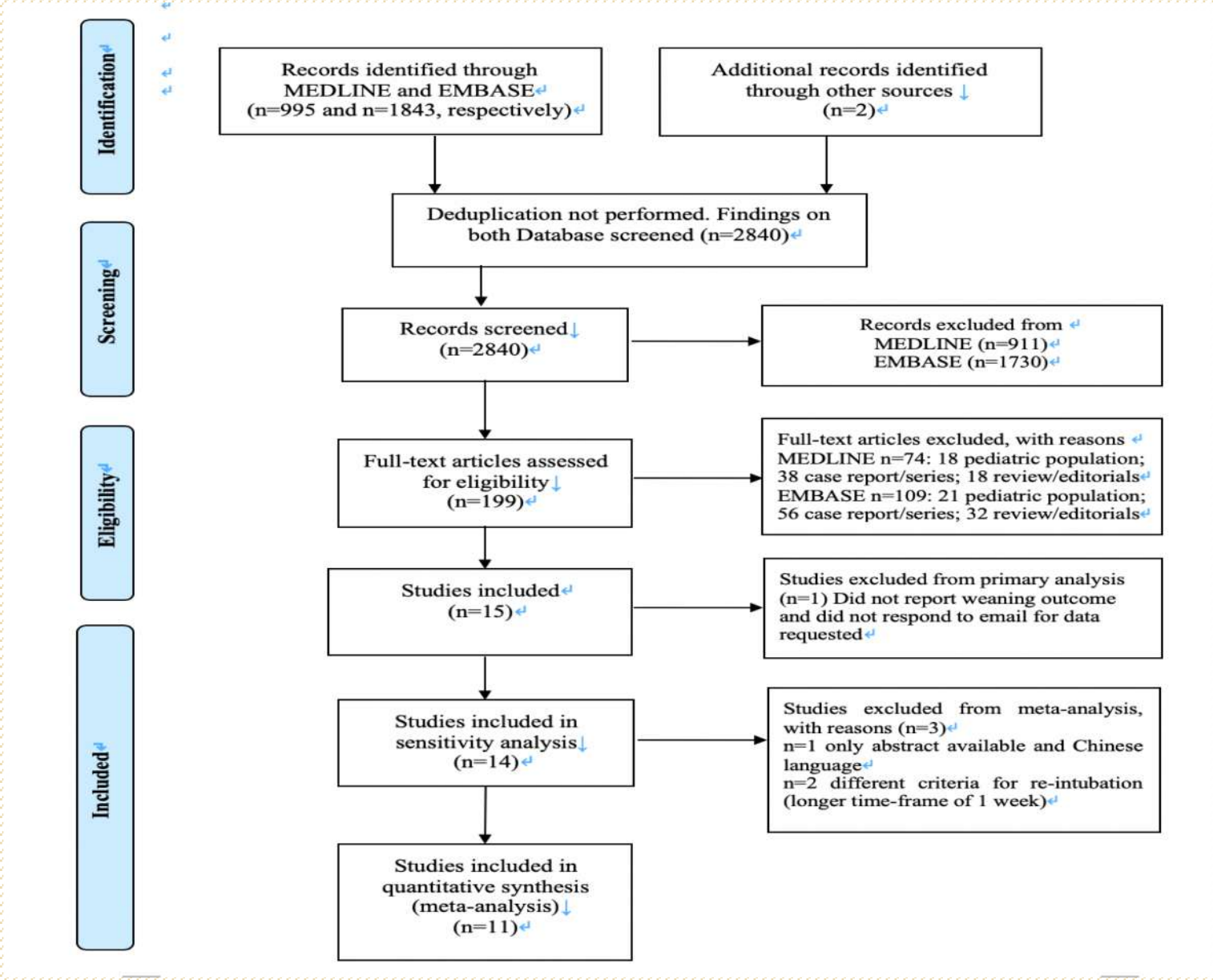
Methods - Statistical analysis (1)

- the variables
  - Mean values and standard deviation
  - If data were reported only as median and inter-quartile range or confidence interval (CI) → followed the Cochrane's recommendation to approximate the values of mean and standard deviation.
- Continuous outcome differences
  - Inverse variance model with a 95% CI.
  - Values : standard mean difference (SMD)
  - P-values : two-tailed and considered significant if <0.05

Methods - Statistical analysis (2)

- **Statistical heterogeneity**
  - the x^2 (Cochran Q) test.
  - If Q > degrees of freedom suggested and confirmed if P ≦ 0.10
- **Quantification of heterogeneity : I^2 statistic**
  - None heterogeneity : 0 - 24.9%
  - Low heterogeneity : 25 - 49.9%
  - Moderate heterogeneity : 50 - 74.9%
  - High heterogeneity : >75%
  - If heterogeneity was quantified as low or above→ more conservative random model was used.
  - Publication bias was investigated inspecting the funnel plot.

Results - Systematic search



Results – the Characteristics of the studies

- LVEF, n = 10
- E/e’ ratio, n = 10
- E/A ratio, n = 9
- E wave, n = 8
- TDI e’ wave, n = 7
- Left atrial size, n = 1
- Tricuspid regurgitant jet velocity, n = 0

Study (journal and year)	Type of patients/ Total patients (success *vs* fail) SBT method SBT duration	Criteria for SBT failure/ Criteria for reintubation	Echocardiography data reported	Severity scores, overall value (success and failure values)
Caille and colleagues[22] (*Crit Care*, 2010)	Two general ICUs, mixed population Total 117 (94 *vs* 23) T-tube (semi-recumbent, 45°) Last 30 min	• Failed SBT if agitation or depressed mental state, Sp_{O_2} <90%, VF>35 bpm, HR>150 min^{-1} or arrhythmias, SAP>180 mm Hg or <90 mm Hg • Reintubated within 48 h The study included patients at their first SBT	LVEF E/A, DT, E/e′ RV/LV-EDA	SAPS II overall 53, 47–58
TypeZapata and colleagues[30] (*Intensive Care Med*, 2011)	General ICU, mixed population Total 100 (42 *vs* 58) T-tube (semi-recumbent) Last 30 min–2 h	• Failed SBT if VF≥35 bpm with signs of increased work of breathing, Pa_{O_2} ≤60 mm Hg with O_2>4 L min^{-1}, arterial pH≤7.30; SAP≥180 mm Hg or <90 mm Hg; HR≥140 min^{-1} or ΔHR≥25%, acute arrhythmia; agitation, anxiety, or diaphoresis • Reintubated within 48 h	LVEF, LV-EDD, LV-ESD E/A, DT	SAPS II (44.2 [13.1] *vs* 45 [15]) APACHE II (18.6 [7.1] *vs* 19.2 [9.3])
Papanikolaou and colleagues[28] (*Intensive Care Med*, 2011)	General ICU, mixed population Total 50 (22 *vs* 28) T-tube Last 30 min	• Failed SBT if VF>35 bpm, Sa_{O_2} <90%, HR>140 min^{-1}, SAP>200 mm Hg or <80 mm Hg, acidosis, arrhythmias, diaphoresis, agitation, depressed mental status, distress • Reintubated within 48 h	LVEF, s′ E, A, E/A, DT, e′, E/e′, Vp, RVFAC, RV/LV-EDA	SOFA overall 5.5 [0.2] APACHE II overall 17.7 [0.5] (16.7 [0.7] *vs* 18.5 [0.7])
Gerbaud and colleagues[23] (*Minerva Anestesiol*, 2010)	Cardiology ICU Total 44 (34 *vs* 10) PS (7 cm H_2O), no PEEP Last 2 h	• Failed SBT if diaphoresis, respiratory distress, discomfort, VF>35 bpm, Sp_{O_2} <90%, HR>140 min^{-1}, SAP>180 mm Hg or <80 mm Hg • Do not report reintubation	LVEF, LV-EDV, LV-ESV E/A, E/e′	SAPS II overall 76 (26)
Moschietto and colleagues[27] (*Crit Care*, 2010)	Medical ICU, mixed population Total 68 (48 *vs* 20) PS (7 cm H_2O), no PEEP Last 1 h	• Failed SBT if VF>35 bpm, Sa_{O_2} <90%, HR>140 min^{-1}, SAP>200 mm Hg or <80 mm Hg, diaphoresis, distress • Reintubated within 48 h	LVEF DT, E/e′, e′	SAPS II (54, 48–72 *vs* 51, 45–55)

Study (journal and year)	Type of patients/ Total patients (success *vs* fail) SBT method SBT duration	Criteria for SBT failure/ Criteria for reintubation	Echocardiography data reported	Severity scores, overall value (success and failure values)
Thille and colleagues[29] (*Crit Care Med*, 2015)	General ICU, mixed population Total 225 (194 vs 31) PS 7–10 cm H_2O, no PEEP Last 1 h	• Failed SBT if VF>35 bpm, Sa_{O_2}<90%, HR>130 min^{-1}, SAP>180 or <90 mm Hg, increased accessory muscle activity, major dyspnea, agitation or depressed mental status • Reintubated within 7 days	LVEF	Not reported
Konomi and colleagues[24] (*Anaesth Intensive Care*, 2016)	General ICU, mixed population Total 42 (27 *vs* 15)* T-tube Last 2 h	• Failed SBT if VF>35 bpm, Sa_{O_2}<85–90%, HR>120–140 min^{-1} or ΔHR>20%, SAP>200 mm Hg or <90 mm Hg, arrhythmias, accessory muscles use, diaphoresis, discomfort • Reintubated within 48 h	LVEF E, A, E/A, DT, e′, E/e′	SOFA (8.1 [3.8] *vs* 13 [8.4]) APACHE II (15.6 [6] *vs* 17.7 [6])
Luo and colleagues[26] (*BMC Pulm Med*, 2017)	Four general ICU, mixed population Total 60 (31 *vs* 29) T-tube (supine 30°–45°) Last 30 min	• Failed extubation if onset within 48 h of at least two criteria: acidosis with Pa_{CO_2}>45 mm Hg or ΔPa_{CO_2}>20%; VF>30 bpm or ΔVF≥50%; Pa_{O_2}<60 mm Hg or Sp_{O_2}<90% at Fi_{O_2}≥0.5; decreased consciousness, agitation, or diaphoresis; clinical signs suggestive of respiratory muscle fatigue or increased work of breathing • Reintubated within 48 h (and also within 7 days) The study included only patients passing the SBT and extubated	LVEF E, E/e′	APACHE II (20 [6.4] *vs* 23.9 [4.7])
Haji and colleagues[34] (*Crit Ultrasound J*, 2018)	General ICU, mixed population Total 53 (42 *vs* 11) PS (up to 10 cm H_2O), PEEP (5 cm H_2O) Last 1 h	• Failed SBT if diaphoresis, RASS≥3 or ≤−3, increasing respiratory efforts, Pa_{O_2}<60 mm Hg or Sp_{O_2}<90% with Fi_{O_2}≥0.4, Pa_{CO_2}>50 mm Hg or ΔPa_{CO_2}>8 mm Hg, pH<7.32 or ΔpH≤0.07, Rapid Shallow Breathing Index>105, VF>35 bpm, HR>140 min^{-1} or ΔHR>20%, SAP>180 mm Hg or ΔSAP>20%, SAP<90 mm Hg, arrhythmias • Reintubation, NIV or death within 48 h after extubation	LVEF, E, E/A, DT, E/e′, e′ LA area	SAPS II (46, 36–57 *vs* 42, 33–46) APACHE II (20, 15–23 *vs* 20, 17–23)
Tongyoo and colleagues[35]	General ICU, mixed population		LVEF, LV-EDA E, A, E/A, e′, E/e′	

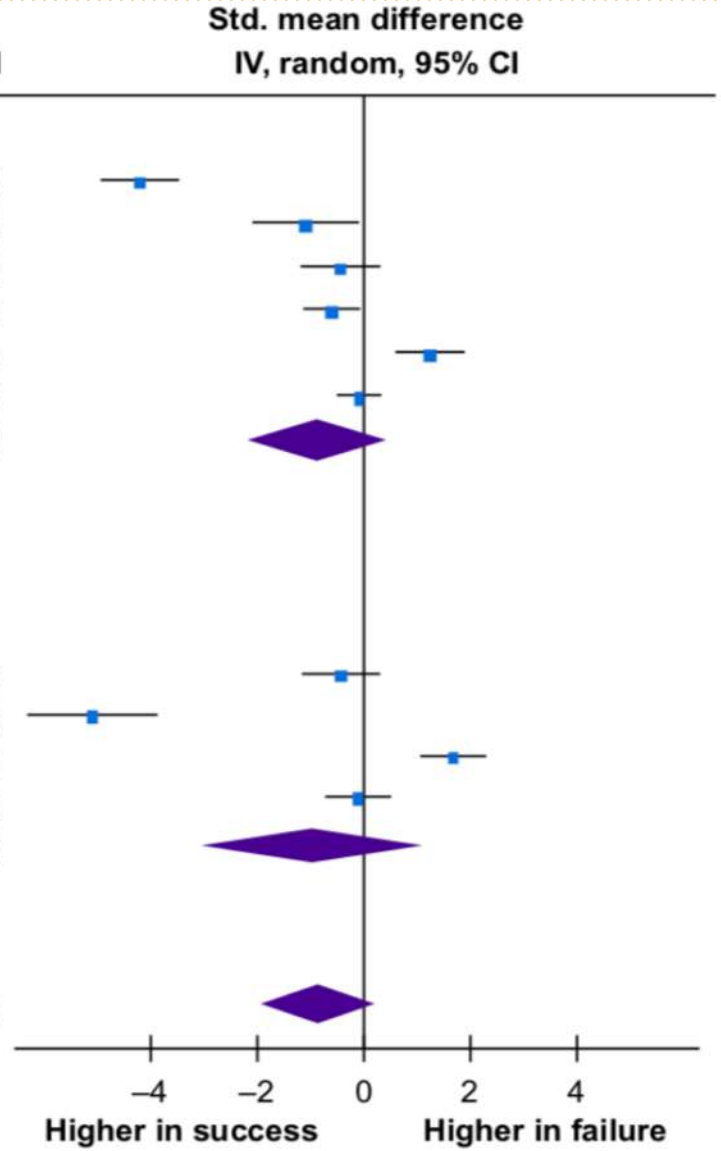
Study (journal and year)	Type of patients/ Total patients (success *vs* fail) SBT method SBT duration	Criteria for SBT failure/ Criteria for reintubation	Echocardiography data reported	Severity scores, overall value (success and failure values)
(*Echocardiography*, 2019)	Total 52 (38 *vs* 14) PS 8 cm H_2O, PEEP 5 cm H_2O Last 1–2 h	• Failed SBT if VF>35 bpm, HR>150 min^{-1}, Sa_{O_2} <95%, SAP>180 mm Hg or <90 mm Hg, or deterioration of level of consciousness, or all • Reintubated within 48 h for respiratory distress	RV-EDA, RV/LV-EDA	SOFA overall 4.1 (2.5) (3.9 [2.5] *vs* 4.7 [2.5])
Amarja and colleagues[32] (*Indian J Crit Care Med*, 2019)	General ICU Total 161 (140 *vs* 21) PS with PEEP (support unclear) Duration unclear	• Do not report SBT failure since the study included only patients with successful SBT (clinicians decided to extubate) • Reintubation within 48 h	Eyeball systolic function E, A, E/A, DT, e′, E/e′, a′ TAPSE	APACHE II (18 [6.6] *vs* 20.8 [5.6])
Kaltsi and colleagues[36] (*Crit Care Res Pract*, 2019)	General ICU and CCU, mixed population Total 19 (8 *vs* 11) T-tube Last 2 h	• Failed SBT if VF>35 bpm, $Sp_{O_2} \leq 90\%$, HR>120 min^{-1} or ΔHR>20%, SAP>180–200 mm Hg or <90 mm Hg, increased accessory muscles use, diaphoresis, discomfort, arrhythmias • Do not report reintubation	LVEF E, A, E/A, e′, E/e′, DT	Not reported
Bedet[33] (Crit Care, 2019)	General ICU, mixed population *Total 208 (76 vs 132)* *T-tube* *Last 2 h*	• Failed SBT if VF≥35 bpm or ΔVF≥50%, HR≥140 min^{-1}, $Sp_{O_2} \leq 90\%$, SAP>180 or <90 mm Hg, arrhythmia, diaphoresis, respiratory distress, diaphoresis, alteration of consciousness • Reintubation within 7 days or death Included patients failing a first SBT (undergoing a second SBT)	LVEF E, E/A, E/e′	SOFA overall 3, 3–5

Results - Methodological quality

Quality Assessment Criteria	Acceptable(*)	Caille 2010	Zapata 2011	Papanikolaou 2011	Gerbaud 2012	Moschietto 2012	Konomi 2016	Luo 2017	Haji 2018	Tongyoo 2018	Amarja 2019	Kaltsi 2019	Thille 2015	Bedet 2019
	Selection													
Representative of exposed cohort	Representative of average adult patients that undergoing a weaning process with SBT	*	*	*	*	*	*	*	*	*	*	*	*	*
Selection of the non-exposed cohort	Drawn from same community as exposed cohort	*	*	*	*	*	*	*	*	*	*	*	*	*
Ascertainment of exposure	Secured records	*	*	*	*	*	*	*	*	*	*	*	*	*
Demonstration that outcome of interest was not present at start of study	Patients with baseline echocardiographic data	*	*	*	*	*	*	*	-	*	*	*	*	*
	Comparability													
Complete echocardiographic report	yes	*	*	*	*	*	*	*	*	*	*	*	*	*
Study controls for at least one SAPS / APACHE II / SOFA	yes	-	*	*	-	*	*	*	*	*	*	-	*	*
	Outcome													
Assessment	Independent blind assessment/record linkage	*	-	*	*	*	*	*	-	-	-	*	-	-
Was follow up enough for outcome to occur	Follow up at 48h	*	*	*	*	*	*	*	*	*	*	*	-	*
Adequacy of follow up for cohort	Complete follow up, or subjects lost to follow up unlikely to introduce bias	*	*	*	*	*	*	*	*	*	*	*	*	*
Overall quality score		**8**	8	**9**	8	9	**9**	9	7	8	8	8	7	8

Results - LV systolic function, LVEF

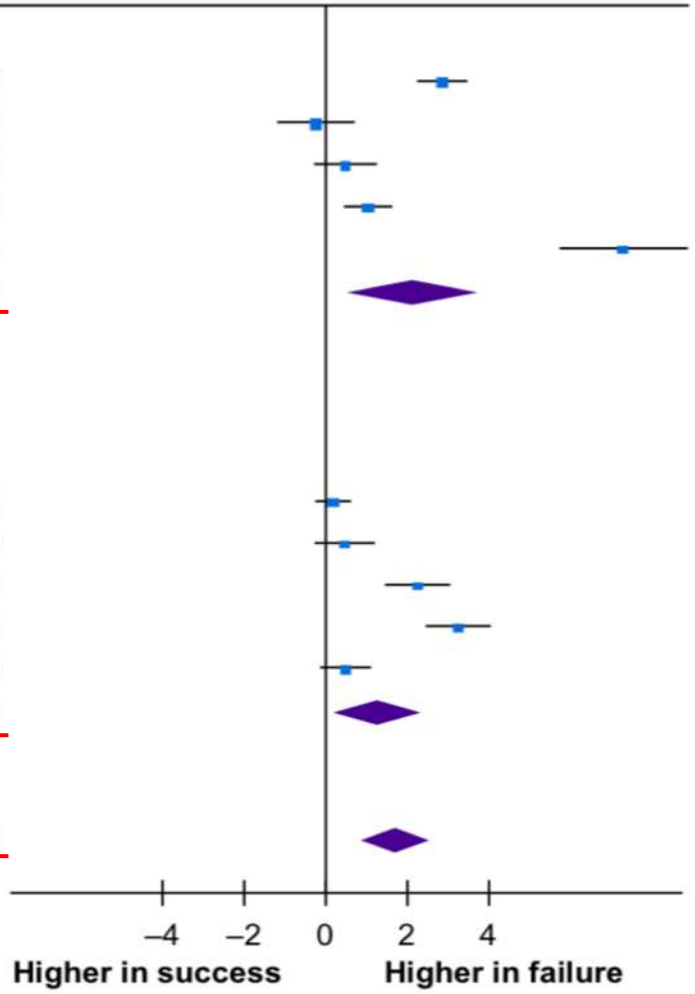
Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
1.1.1 T-tube trial								
Caille et al, 2010	36	7	23	51	2	94	10.0	–4.20 (–4.91 to –3.48)
Kaltsi et al, 2019	30	4	11	38	10	8	9.6	–1.07 (–2.06 to –0.09)
Konomi et al, 2016	52.6	15.6	12	58	9.7	22	10.0	–0.44 (–1.15 to 0.27)
Luo et al, 2017	57	14	29	64	9	31	10.2	–0.59 (–1.11 to –0.07)
Papanikolaou et al, 2011	60.4	1.2	28	58.8	1.3	22	10.1	1.27 (0.65 to 1.88)
Zapata et al, 2011	56.3	12.1	42	57	9	58	10.3	–0.07 (–0.46 to 0.33)
Subtotal (95% CI)			**145**			**235**	**60.4**	**0.84 (–2.15 to 0.48)**
Heterogeneity: Tau^2=2.58; χ^2=141.06, df=5 (*P*<0.00001); I^2=96%								
Test for overall effect: Z=1.25 (*P*=0.21)								
1.1.2 Pressure support trial								
Gerbaud et al, 2012	39	1.375	10	40.5	4	34	10.0	–0.41 (–1.12 to 0.30)
Haji et al, 2018	50	2.5	11	65	3	42	9.2	–5.08 (–6.29 to –3.88)
Moschietto et al, 2012	60	3.75	20	55	2.5	48	10.2	1.70 (1.10 to 2.29)
Tongyoo et al, 2019	56.2	15	14	57.7	14.9	38	10.1	–0.10 (–0.71 to 0.51)
Subtotal (95% CI)			**55**			**162**	**39.6**	**–0.91 (–3.01 to 1.19)**
Heterogeneity: Tau^2=4.42; χ^2=100.51, df=3 (*P*<0.00001); I^2=97%								
Test for overall effect: Z=0.85 (*P*=0.39)								
Total (95% CI)			**200**			**397**	**100.0**	**–0.86 (–1.92, 0.20)**
Heterogeneity: Tau^2=2.79; χ^2=248.23, df=9 (*P*<0.00001); I^2=96%								
Test for overall effect: Z=1.58 (*P*=0.11)								
Test for subgroup differences: χ^2=0.00, df=1 (*P*=0.95), I^2=0%								



Results - LV diastolic function, E/e' ratio

a

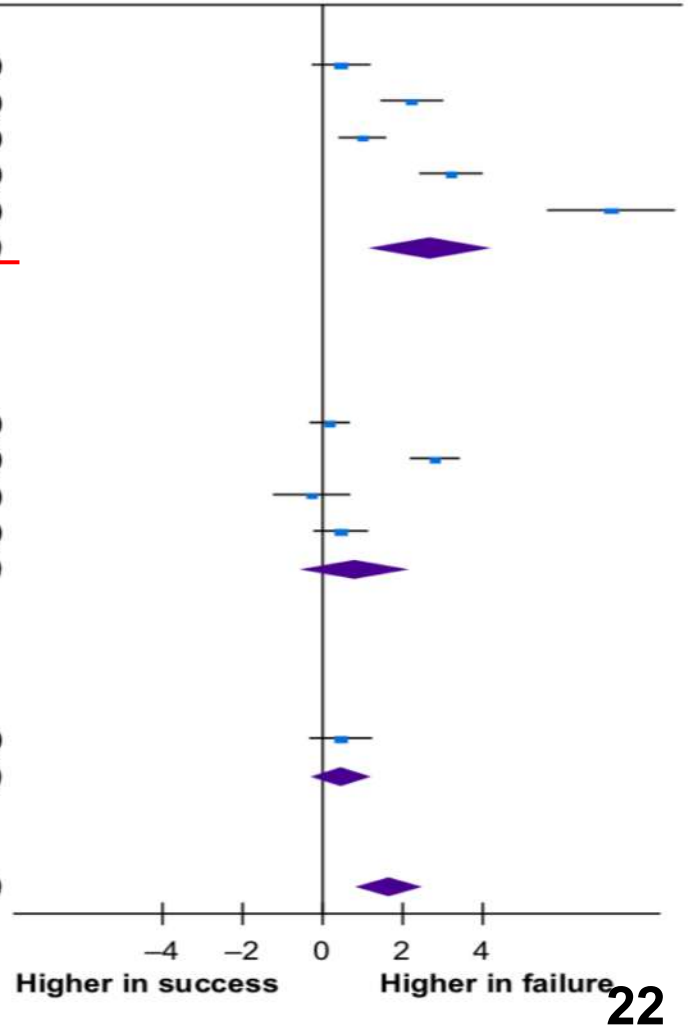
Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.7.1 T-tube trial								
Caille et al, 2010	7	1.05	23	5.6	0.18	94	10.4	2.86 (2.27-3.44)
Kaltsi et al, 2019	10.51	3.18	11	11.2	2.32	8	9.8	–0.23 (–1.15-0.68)
Konomi et al, 2016	11.04	4.71	12	9.29	2.6	22	10.2	0.49 (–0.22-1.21)
Luo et al, 2017	14.7	5.6	29	10.1	2.8	31	10.4	1.04 (0.49-1.58)
Papanikolaou et al, 2011	10.98	0.83	28	6.18	0.28	22	8.2	7.27 (5.69-8.86)
Subtotal (95% CI)			**103**			**177**	**48.9**	**2.16 (0.52-3.80)**
Heterogeneity: Tau^2=3.27; χ^2=95.35, df=4 (P<0.00001); I^2=96%								
Test for overall effect: Z=2.58 (P=0.010)								
2.7.2 Pressure support trial								
Amarja et al, 2019	8.21	2.95	21	7.68	2.79	140	10.5	0.19 (–0.27-0.65)
Gerbaud et al, 2012	10.7	3.45	10	9.5	2.175	34	10.2	0.47 (–0.24-1.18)
Haji et al, 2018	10.9	2.325	11	7.7	1.05	42	10.0	2.26 (1.46-3.06)
Moschietto et al, 2012	13.4	1.975	20	8.9	1.025	48	10.1	3.25 (2.48-4.02)
Tongyoo et al, 2019	19	8.3	14	15.5	6.5	38	10.3	0.49 (–0.13-1.11)
Subtotal (95% CI)			**76**			**302**	**51.1**	**1.31 (0.19-2.43)**
Heterogeneity: Tau^2=1.51; χ^2=59.26, df=4 (P<0.00001); I^2=93%								
Test for overall effect: Z=2.29 (P=0.02)								
Total (95% CI)			**179**			**479**	**100.0**	**1.70 (0.78-2.62)**
Heterogeneity: Tau^2=2.04; χ^2=162.06, df=9 (P<0.00001); I^2=94%								
Test for overall effect: Z=3.62 (P=0.0003)								
Test for subgroup differences: Chi^2=0.70, df=1 (P=0.40), I^2=0%								



Results - LV diastolic function, different e' of E/e' ratio

b

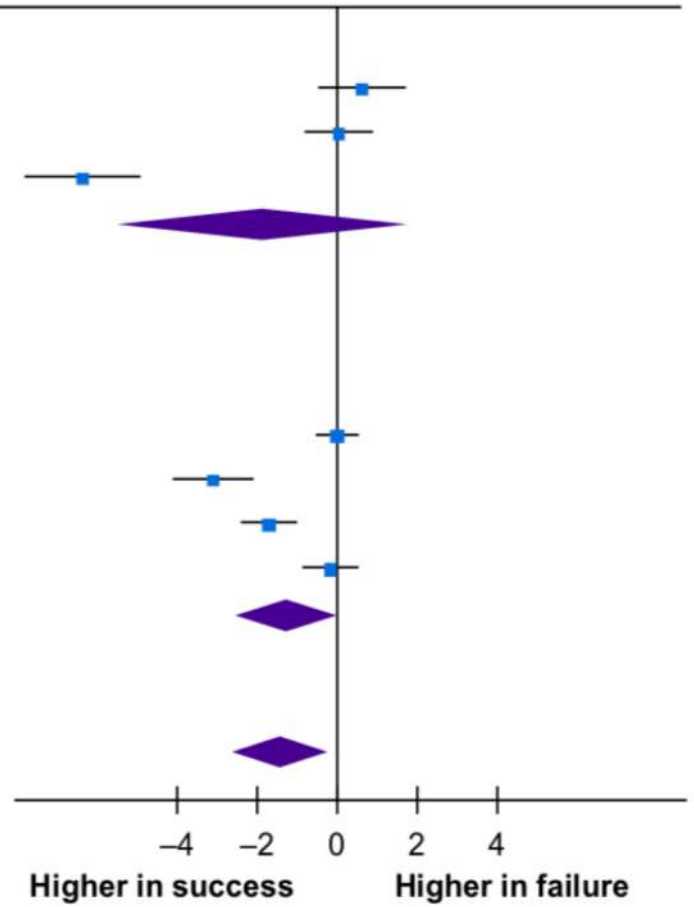
Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.1.1 Average								
Gerbaud et al, 2012	10.7	3.45	10	9.5	2.175	34	10.2	0.47 (–0.24-1.18)
Haji et al, 2018	10.9	2.325	11	7.7	1.05	42	10.0	2.26 (1.46-3.06)
Luo et al, 2017	14.7	5.6	29	10.1	2.8	31	10.4	1.04 (0.49-1.58)
Moschietto et al, 2012	13.4	1.975	20	8.9	1.025	48	10.1	3.25 (2.48-4.02)
Papanikolaou et al, 2011	10.98	0.83	28	6.18	0.28	22	8.2	7.27 (5.69-8.86)
Subtotal (95% CI)			**98**			**177**	**48.8**	**2.72 (1.15-4.30)**
Heterogeneity: Tau^2=3.01; χ^2=81.73, df=4 (P<0.00001); I^2=95%								
Test for overall effect: Z=3.38 (P=0.0007)								
2.1.2 Lateral								
Amarja et al, 2019	8.21	2.95	21	7.68	2.79	140	10.5	0.19 (–0.27-0.65)
Caille et al, 2010	7	1.05	23	5.6	0.18	94	10.4	2.86 (2.27-3.44)
Kaltsi et al, 2019	10.51	3.18	11	11.2	2.32	8	9.8	–0.23 (–1.15-0.68)
Tongyoo et al, 2019	19	8.3	14	15.5	6.5	38	10.3	0.49 (–0.13-1.11)
Subtotal (95% CI)			**69**			**280**	**41.0**	**0.84 (–0.53-2.21)**
Heterogeneity: Tau^2=1.83; χ^2=59.21, df=3 (P<0.00001); I^2=95%								
Test for overall effect: Z=1.21 (P=0.23)								
2.1.3 Septal								
Konomi et al, 2016	11.04	4.71	12	9.29	2.6	22	10.2	0.49 (–0.22-1.21)
Subtotal (95% CI)			**12**			**22**	**10.2**	**0.49 (–0.22-1.21)**
Heterogeneity: Not applicable								
Test for overall effect: Z=1.35 (P=0.18)								
Total (95% CI)			**179**			**479**	**100.0**	**1.70 (0.78-2.62)**
Heterogeneity: Tau^2=2.04; χ^2=162.06, df=9 (P<0.00001); I^2=94%								
Test for overall effect: Z=3.62 (P=0.0003)								
Test for subgroup differences: χ^2=6.38, df=2 (P=0.04), I^2=68.6%								



Results - LV diastolic function, TDI e' wave

a

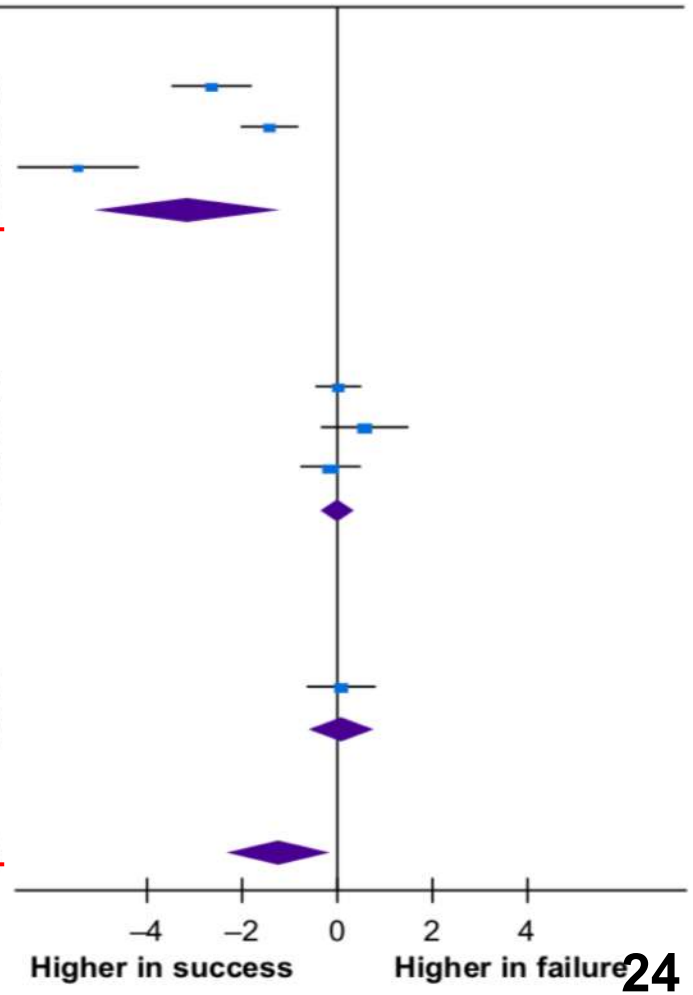
Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.8.1 T-tube trial								
Kaltsi et al, 2019	8	2	11	7	1	8	13.9	0.57 (–0.36 to 1.51)
Konomi et al, 2016	13.8	18.9	12	12.3	15.4	22	14.5	0.09 (–0.62 to 0.79)
Papanikolaou et al, 2011	9.8	0.8	28	14.5	0.9	22	12.9	–5.47 (–6.72 to –4.22)
Subtotal (95% CI)			**51**			**52**	**41.3**	**–1.57 (–4.72 to 1.59)**
Heterogeneity: Tau^2=7.53; χ^2=68.04, df=2 (*P*<0.00001); I^2=97%								
Test for overall effect: Z=0.97 (*P*=0.33)								
2.8.2 Pressure support trial								
Amarja et al, 2019	11.43	3.17	21	11.38	3.24	140	15.0	0.02 (–0.44 to 0.47)
Haji et al, 2018	7	1.5	11	10	1	42	14.1	–2.65 (–3.49 to –1.80)
Moschietto et al, 2012	7	0.5	20	8	0.75	48	14.8	–1.44 (–2.02 to –0.86)
Tongyoo et al, 2019	6.4	3.9	14	6.8	2.8	38	14.7	–0.13 (–0.74 to 0.49)
Subtotal (95% CI)			**66**			**268**	**58.7**	**–1.01 (–2.10 to 0.08)**
Heterogeneity: Tau^2=1.13; χ^2=39.37, df=3 (*P*<0.00001); I^2=92%								
Test for overall effect: Z=1.82 (*P*=0.07)								
Total (95% CI)			**117**			**320**	**100.0**	**–1.22 (–2.33 to –0.11)**
Heterogeneity: Tau^2=2.09; χ^2=107.41, df=6 (*P*<0.00001); I^2=94%								
Test for overall effect: Z=2.15 (*P*=0.03)								
Test for subgroup differences: χ^2=0.11, df=1 (*P*=0.75), I^2=0%								



Results - LV diastolic function, different regional of TDI e' wave

b

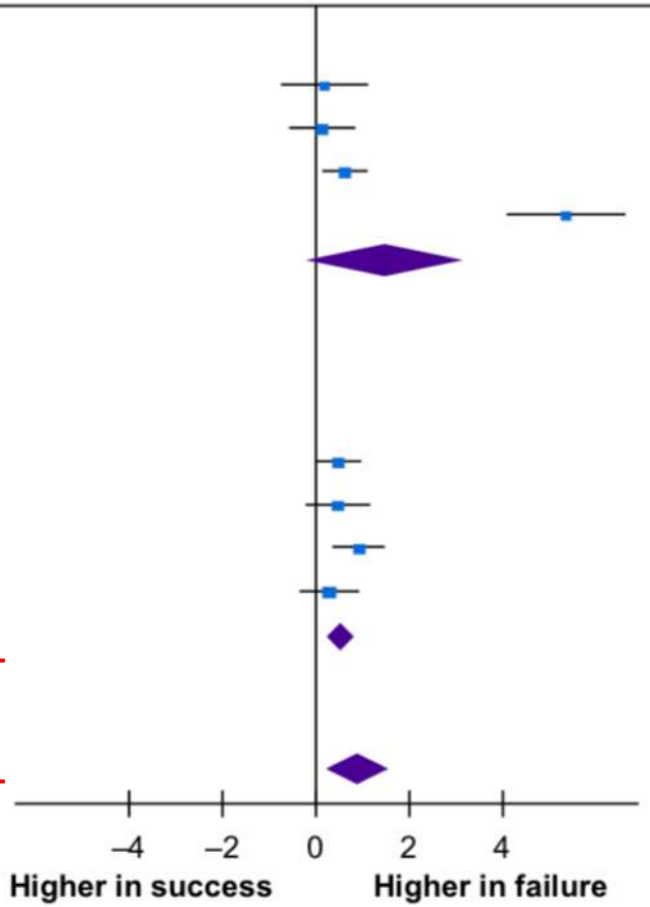
Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.2.1 Average								
Haji et al, 2018	7	1.5	11	10	1	42	14.1	–2.65 (–3.49 to –1.80)
Moschietto et al, 2012	7	0.5	20	8	0.75	48	14.8	–1.44 (–2.02 to –0.86)
Papanikolaou et al, 2011	9.8	0.8	28	14.5	0.9	22	12.9	–5.47 (–6.72 to –4.22)
Subtotal (95% CI)			**59**			**112**	**41.8**	**–3.12 (–5.15 to –1.09)**
Heterogeneity: Tau^2=2.99; χ^2=33.97, df=2 (*P*<0.00001); I^2=94%								
Test for overall effect: Z=3.01 (*P*=0.003)								
2.2.2 Lateral								
Amarja et al, 2019	11.43	3.17	21	11.38	3.24	140	15.0	0.02 (–0.44 to 0.47)
Kaltsi et al, 2019	8	2	11	7	1	8	13.9	0.57 (–0.36 to 1.51)
Tongyoo et al, 2019	6.4	3.9	14	6.8	2.8	38	14.7	–0.13 (–0.74 to 0.49)
Subtotal (95% CI)			**46**			**186**	**43.6**	**0.05 (–0.30 to 0.39)**
Heterogeneity: Tau^2=0.00; χ^2=1.55, df=2 (*P*=0.46); I^2=0%								
Test for overall effect: Z=0.27 (*P*=0.79)								
2.2.3 Septal								
Konomi et al, 2016	13.8	18.9	12	12.3	15.4	22	14.5	0.09 (–0.62 to 0.79)
Subtotal (95% CI)			**12**			**22**	**14.5**	**0.09 (–0.62 to 0.79)**
Heterogeneity: Not applicable								
Test for overall effect: Z=0.24 (*P*=0.81)								
Total (95% CI)			**117**			**320**	**100.0**	**–1.22 (–2.33 to –0.11)**
Heterogeneity: Tau^2=2.09; χ^2=107.41, df=6 (*P*<0.00001); I^2=94%								
Test for overall effect: Z=2.15 (*P*=0.03)								
Test for subgroup differences: χ^2=9.19, df=2 (*P*=0.01), I^2=78.2%								



Results - LV diastolic function, E wave

a

Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.3.1 T-tube trial								
Kaltsi et al, 2019	86	34	11	80	15	8	11.5	0.21 (–0.71-1.12)
Konomi et al, 2016	81	26	12	77	22	22	12.6	0.17 (–0.54-0.87)
Luo et al, 2017	92.9	25.6	29	78.2	18.4	31	13.4	0.65 (0.13-1.18)
Papanikolaou et al, 2011	90.6	3.6	28	74	2	22	9.8	5.43 (4.19-6.68)
Subtotal (95% CI)			**80**			**83**	**47.3**	**1.54 (–0.19-3.27)**
Heterogeneity: Tau^2=2.90; χ^2=58.37, df=3 (P<0.00001); I^2=95%								
Test for overall effect: Z=1.75 (P=0.08)								
2.3.2 Pressure support trial								
Amarja et al, 2019	92.5	24.9	21	81.9	19.3	140	13.6	0.53 (0.06-0.99)
Haji et al, 2018	87	9	11	83	7.75	42	12.7	0.49 (–0.18-1.16)
Moschietto et al, 2012	80	10.25	20	72	7.25	48	13.3	0.96 (0.41-1.51)
Tongyoo et al, 2019	96.5	30.8	14	87.3	27.5	38	13.0	0.32 (–0.30-0.94)
Subtotal (95% CI)			**66**			**268**	**52.7**	**0.59 (0.31-0.87)**
Heterogeneity: Tau^2=0.00; χ^2=2.67, df=3 (P=0.45); I^2=0%								
Test for overall effect: Z=4.15 (P<0.0001)								
Total (95% CI)			**146**			**351**	**100.0**	**0.97 (0.29-1.65)**
Heterogeneity: Tau^2=0.84; χ^2=62.40, df=7 (P<0.00001); I^2=89%								
Test for overall effect: Z=2.78 (P=0.005)								
Test for subgroup differences: χ^2=1.13, df=1 (P=0.29), I^2=11.8%								

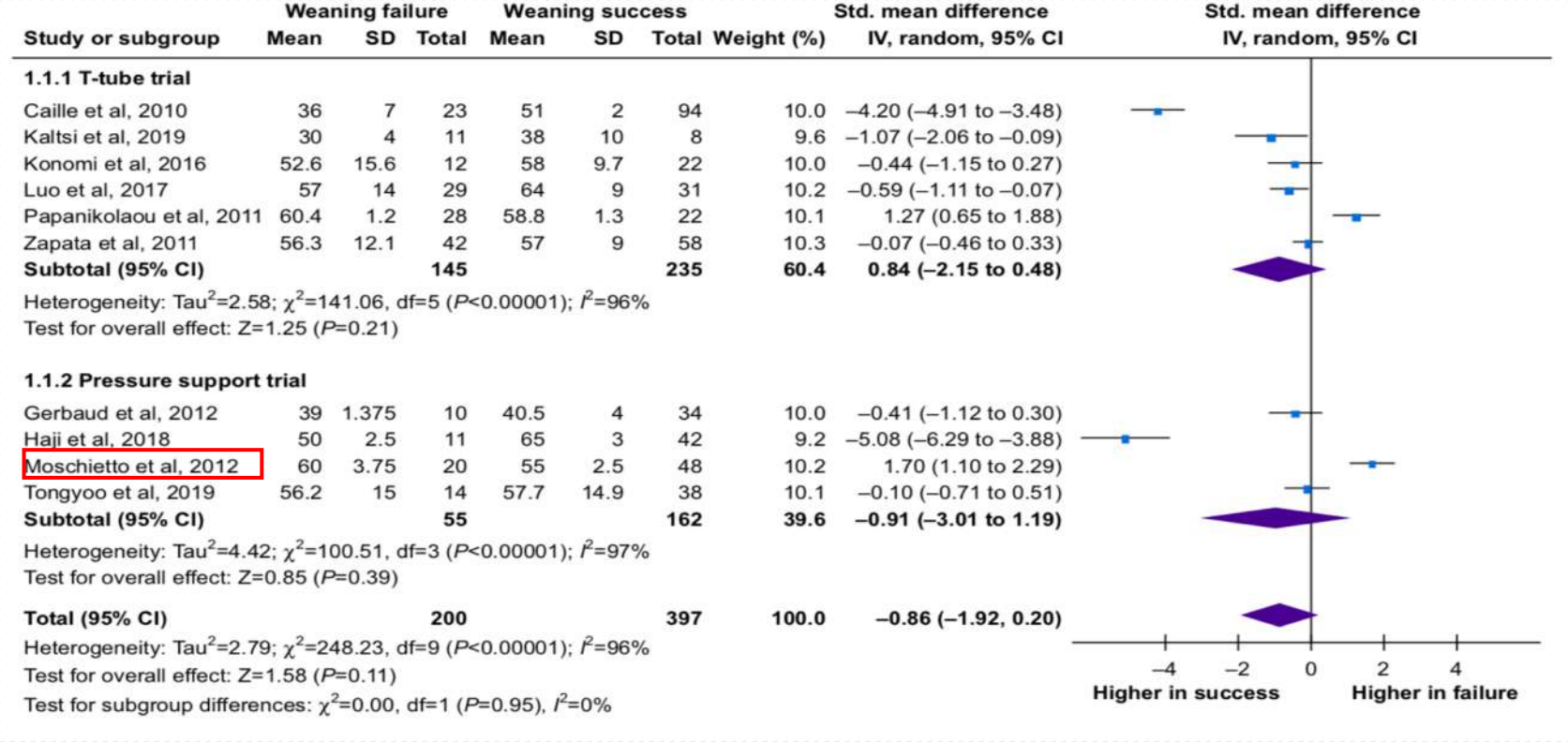


Results - Sensitivity analyses (1)

- Including studies with criteria for reintubation extended to a longer timeframe (1 week rather than 48 hours) , n = 2
  - ➢ no statistical change
- Inclusion of the study by Wang and colleagues (Chinese language, only abstract available in English)
  - ➢ no statistical change
- All the included studies scored with a low risk of bias
  - ➢ Including studies with non-prospective design
  - ➢ Excluding studies with a high risk of bias
  - ➢ Performed with ‘leave-one-out at a time’

Results - Sensitivity analyses (2)

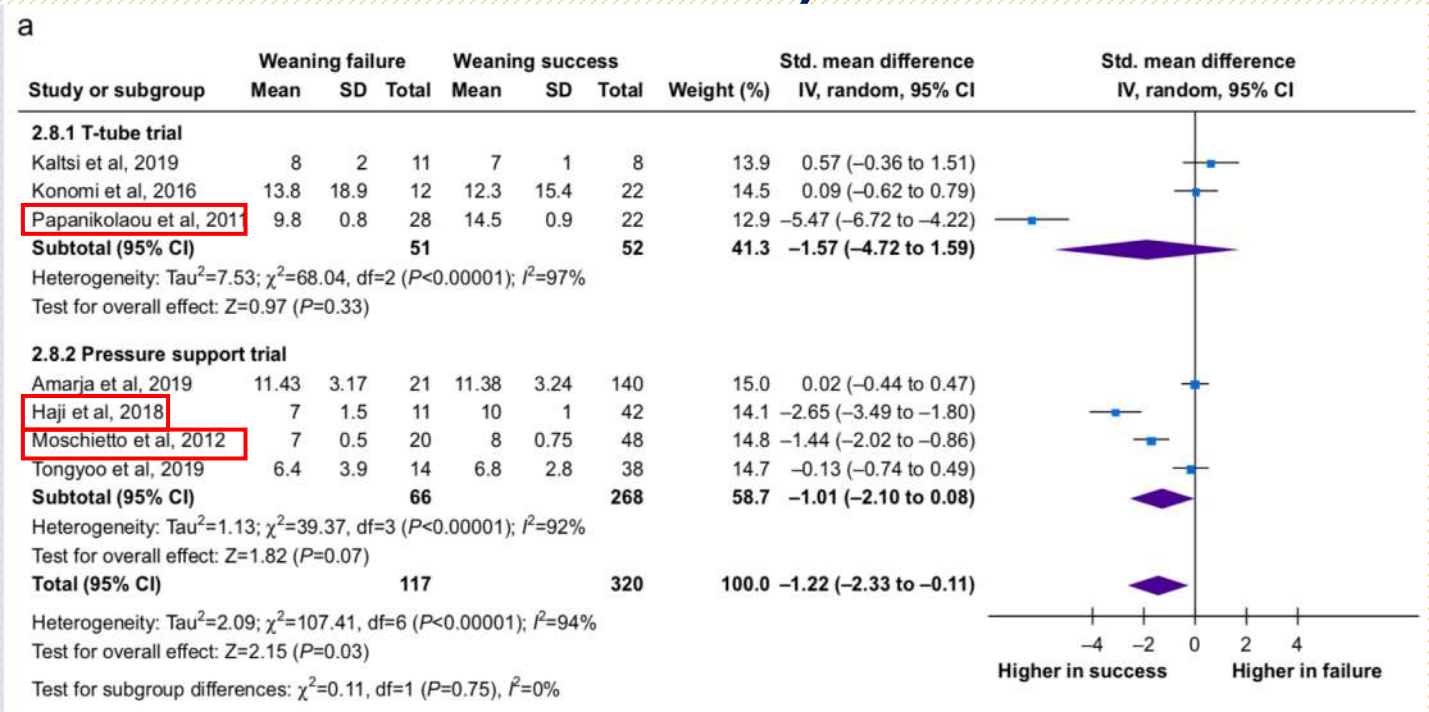
- **Performed with 'leave-one-out at a time'**
  - **LVEF, where the exclusion of the study by Moschietto and colleagues changed the result to significant association between lower LVEF and weaning failure (P=0.04)**



Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
1.1.1 T-tube trial								
Caille et al, 2010	36	7	23	51	2	94	10.0	−4.20 (−4.91 to −3.48)
Kaltsi et al, 2019	30	4	11	38	10	8	9.6	−1.07 (−2.06 to −0.09)
Konomi et al, 2016	52.6	15.6	12	58	9.7	22	10.0	−0.44 (−1.15 to 0.27)
Luo et al, 2017	57	14	29	64	9	31	10.2	−0.59 (−1.11 to −0.07)
Papanikolaou et al, 2011	60.4	1.2	28	58.8	1.3	22	10.1	1.27 (0.65 to 1.88)
Zapata et al, 2011	56.3	12.1	42	57	9	58	10.3	−0.07 (−0.46 to 0.33)
Subtotal (95% CI)			**145**			**235**	**60.4**	**0.84 (−2.15 to 0.48)**
Heterogeneity: Tau²=2.58; χ²=141.06, df=5 (P<0.00001); I²=96%								
Test for overall effect: Z=1.25 (P=0.21)								
1.1.2 Pressure support trial								
Gerbaud et al, 2012	39	1.375	10	40.5	4	34	10.0	−0.41 (−1.12 to 0.30)
Haji et al, 2018	50	2.5	11	65	3	42	9.2	−5.08 (−6.29 to −3.88)
Moschietto et al, 2012	60	3.75	20	55	2.5	48	10.2	1.70 (1.10 to 2.29)
Tongyoo et al, 2019	56.2	15	14	57.7	14.9	38	10.1	−0.10 (−0.71 to 0.51)
Subtotal (95% CI)			**55**			**162**	**39.6**	**−0.91 (−3.01 to 1.19)**
Heterogeneity: Tau²=4.42; χ²=100.51, df=3 (P<0.00001); I²=97%								
Test for overall effect: Z=0.85 (P=0.39)								
Total (95% CI)			**200**			**397**	**100.0**	**−0.86 (−1.92, 0.20)**
Heterogeneity: Tau²=2.79; χ²=248.23, df=9 (P<0.00001); I²=96%								
Test for overall effect: Z=1.58 (P=0.11)								
Test for subgroup differences: χ²=0.00, df=1 (P=0.95), I²=0%								

Results - Sensitivity analyses (3)

- **Performed with 'leave-one-out at a time'**
  - **TDI e' wave, where the exclusion of any one of these three studies changed the result to no significant association between e' wave values and weaning failure (P values ranging between 0.08 and 0.17)**



Discussions – The physiological change between ex- and post extubation

- From positive to negative pressure ventilation → ↑venous return
  - Higher filling pressures if LV compliance is reduced.
  - Increase in LV afterload significant when inspiratory.
  - RV dilatation
    - 👉 Increase cardiac workload

Discussions – The association between weaning failure and higher values of E/e' ratio

- E/e' ratio is indicated by the newest guidelines for the diagnosis of LV diastolic dysfunction.
- E/e' is the marker of increased LV end-diastolic pressure (filling pressure)
- The increased pool of blood returning to the LV may not be accommodated by if the compliance of LV is poor.

Discussions – E/A was not associated with weaning failure

- E/A ratio are useful in the grading of dysfunction.
- E/A ratio should not be interpreted as a continuous variable.
  - Semi-quantitative approach
- The ‘pseudo-normalisation’ issue
  - Increased left atrial pressures in patients with LVDD of second degree produces an E/A ratio with similar values to patients with normal LV diastolic function

Limitations

- Not able to adjust for confounders by regression/multivariate analyses
- Included critically ill patients with different pathologies and patients with significant clinical heterogeneity
  - another confounding effect is probably generated by the ‘noncardiac’ causes of weaning failure

Conclusion

Weaning failure from MV is significantly associated with parameters indicating worse LV diastolic function and increased LV filling pressure.

評讀文章-步驟1：系統性文獻回顧探討的問題為何？

PICOS	
1. Participants	Patients undergoing weaning with SBT (T-tube trial or low level PSV)
2. Intervention	Transthoracic echocardiography performed before the weaning trial is started
3. Comparison	Measurements of echocardiographic parameters of LV and RV function
4. Outcomes	Weaning failure (failed SBT, reintubated, or both within 48 h) *vs* weaning success (studies with longer timeframe for reintubation used for sensitivity analysis)
5. Study design	Prospective clinical studies (retrospective studies only for sensitivity analysis)

評讀文章-步驟2：系統性文獻回顧的品質如何？(FAITH)

- F - 研究是否找到 (Find) 所有的相關證據？
  - 至少包括二個主要的資料庫，並加上文獻引用檢索且應不只限於英文。
    - 👉 評讀結果: □是 ■否 □不清楚
  - 應同時使用 MeSH 字串及一般檢索詞彙(text words)。在文章的方法(Methods)章節，可以找到詳細搜尋策略的說明。
    - 👉 評讀結果: ■是 □否 □不清楚
  - 是否評估的摘要及全文文獻數目、文獻納入與排除 的數量及原因。
    - 👉 評讀結果: ■是 □否 □不清楚
  - 有圖表或PRISMA的流程圖呈現。
    - 👉 評讀結果: ■是 □否 □不清楚

評讀文章-步驟2：系統性文獻回顧的品質如何？(FAITH)

- H-試驗的結果是否相近-異質性(Heterogeneity)？
  - 各個試驗的結果應相近或具同質性，若具有異質性，作者應評估差異是否顯著(卡方檢定)。根據每篇個別研究中不同的PICO及研究方法，探討造成異質性的原因

    👉 評讀結果: □是 ■否 ■不清楚

能依系統性文獻回顧之結論回答問題嗎?

Can we predict weaning failure from ventilator though evaluate cardiac function parameter?

Thank you

Results

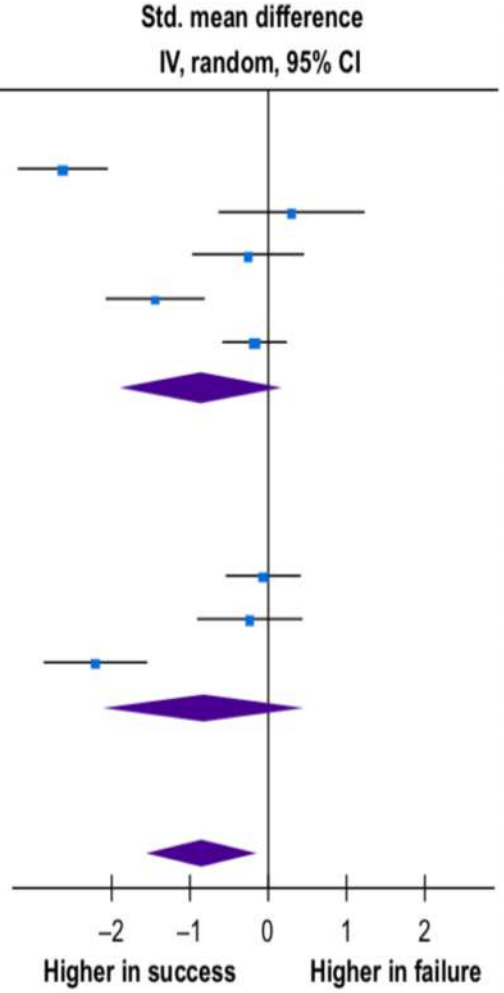
The two independent literature searches produced 995 titles on Medline and 1843 on EMBASE. The PRISMA flowchart of the systematic search and qualitative synthesis and the PRISMA checklist are reported as Supplementary material. After screening of titles and abstracts from Medline, 911 articles were excluded because they were not relevant, and a further 74 were subsequently excluded for various reasons (18 paediatric studies, 18 reviews, and 38 case reports/series or letter to editor/editorials), leaving only 10 findings for inclusion,[22–30] but one was excluded because the baseline echocardiography data were collected with very high PSV (15–20 cm H_2O).[31] The search on EMBASE produced a further four studies not identified on MEDLINE.[32–35] Two extra findings were retrieved by the independent manual search.[36,37]

Therefore, we identified 15 studies as potentially eligible in our study, but four were not included in the primary analysis. One study did not explicitly report echocardiographic findings according to weaning failure or success. We contacted the corresponding authors but we were not successful in retrieving data of interest, and therefore the study was fully excluded.[25] Three other studies were included only in sensitivity analysis, the first one because it was published in Chinese language (only abstract available)[37] while the other two since reported reintubation at 1 week (longer timeframe).[29,33] The remaining 11 studies were included for the primary analysis. All the studies included were performed with transthoracic echocardiography and none with transoesophageal echocardiography.

Results - LV diastolic function, DT

b

Study or subgroup	Weaning failure Mean	SD	Total	Weaning success Mean	SD	Total	Weight (%)	Std. mean difference IV, random, 95% CI
2.5.1 T-tube trial								
Caille et al, 2010	138	24.2	23	170	6.5	94	12.7	−2.63 (−3.20 to −2.06)
Kaltsi et al, 2019	234	66	11	214	60	8	11.4	0.30 (−0.62 to 1.22)
Konomi et al, 2016	173.8	76.5	12	192.5	63.4	22	12.2	−0.27 (−0.97 to 0.44)
Papanikolaou et al, 2011	194	9	28	205	5	22	12.5	−1.44 (−2.07 to −0.81)
Zapata et al, 2011	193	49	42	202	52	58	13.2	−0.18 (−0.57 to 0.22)
Subtotal (95% CI)			**116**			**204**	**62.1**	**−0.86 (−1.91 to 0.19)**
Heterogeneity: Tau^2=1.33; χ^2=60.41, df=4 (P<0.00001); I^2=93%								
Test for overall effect: Z=1.60 (P=0.11)								
2.5.2 Pressure support trial								
Amarja et al, 2019	116.5	36	21	119.2	38.2	140	13.1	−0.07 (−0.53 to 0.39)
Haji et al, 2018	175	33.5	11	180	15.5	42	12.4	−0.24 (−0.91 to 0.42)
Moschietto et al, 2012	170	15.7	20	215	21.7	48	12.5	−2.21 (−2.85 to −1.56)
Subtotal (95% CI)			**52**			**230**	**37.9**	**−0.83 (−2.14 to 0.48)**
Heterogeneity: Tau^2=1.24; χ^2=29.84, df=2 (P<0.00001); I^2=93%								
Test for overall effect: Z=1.25 (P=0.21)								
Total (95% CI)			**168**			**434**	**100.0**	**−0.85 (−1.60 to −0.10)**
Heterogeneity: Tau^2=1.06; χ^2=91.19, df=7 (P<0.00001); I^2=92%								
Test for overall effect: Z=2.23 (P=0.03)								
Test for subgroup differences: χ^2=0.00, df=1 (P=0.97), I^2=0%								



Secondary outcomes

As secondary outcome, we evaluated two other parameters. DT data were available from 602 patients from eight studies,[22,24,27,28,30,32,34,36] with an overall weaning failure of 27.9% (n=168). Weaning failure was significantly associated with lower DT: SMD −0.85, 95% CI −1.60 to −0.10; P=0.03, Figure 4b, with high heterogeneity (I^2=92%, P<0.0001). There were no subgroup differences according to the type of SBT, with no heterogeneity.

The second parameter evaluated as secondary outcome was the RV/LV end-diastolic area ratio. This parameter was reported by three studies with data on 219 patients,[22,28,35] with an overall weaning failure of 29.7% (n=65), and was not significantly different between weaning failure and success (SMD 0.23, 95% CI −0.27–0.74; P=0.37), with moderate heterogeneity (I^2=62%, P<0.007). As there were only three studies, analysis in subgroups was not performed.