Difficult Weaning – Pathophysiology and Management

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SR Pulmonary Medicine

- Difficult weaning: Definition and epidemiology
- Pathophysiology and management
    - Respiratory causes
    - Cardiac causes
    - Neuromuscular causes
    - Psychological causes
    - Nutrition in ICU
    - Post extubation causes

Problem statement

- Time spent in weaning process represents 40-50% of total duration of MV
- Mortality increases with increasing duration of MV
- Subjects receiving prolonged MV – 6% of all ventilated patients but consume 37% of ICU resources

B ´eduneau, Pham, Schortgen, et al.ATS 2017
Esteban A et al
Kollef MH et al

Definitions

- **Weaning** – Starting from 1st attempt at separating the patient from the ventilator to the successful separation of the patient
- **Spontaneous Breathing Trial (SBT)** – Test of spontaneous ventilation without or with minimal level of support
- **Separation attempt** –

  For intubated patients – SBT with or without extubation or an extubation without identified SBT

  For tracheostomized patients - ≥24 hrs with spontaneous ventilation through tracheostomy without any MV

J.M Boles et al ERS 2007

Definitions

- **Successful weaning** –

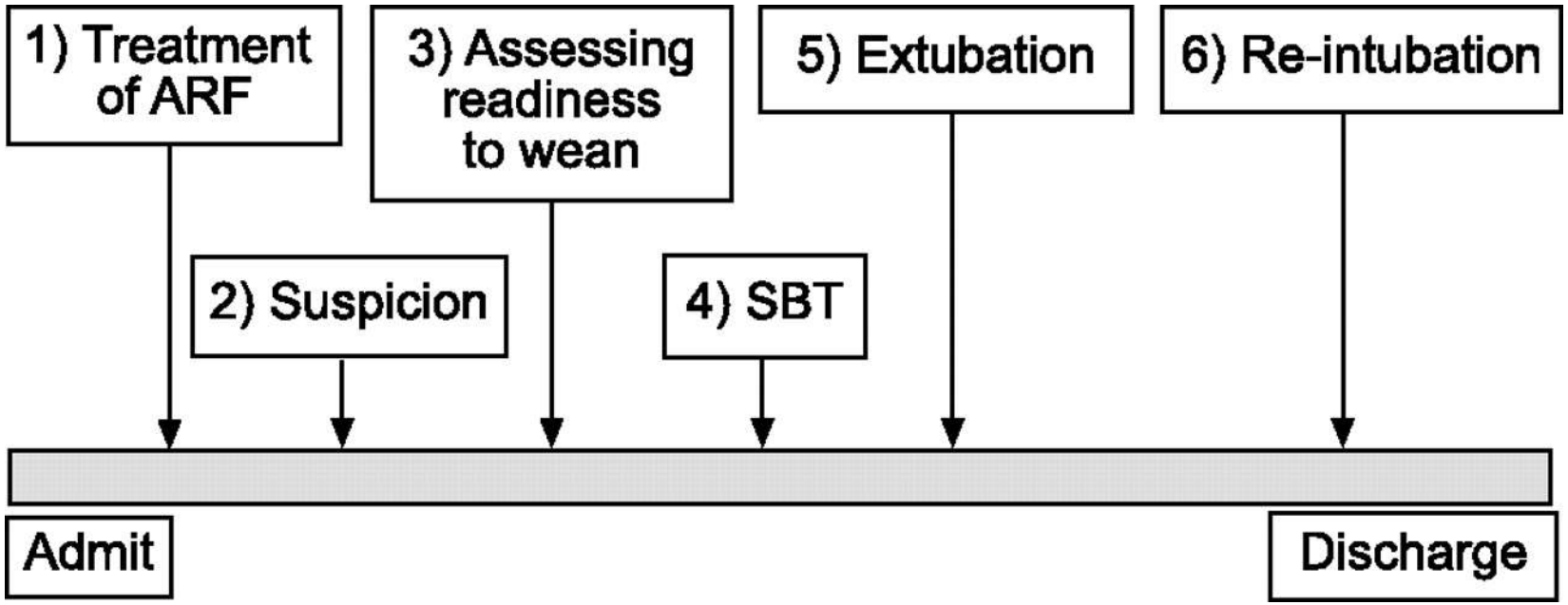
  Intubated patients – Extubation without death or reintubation within 7 days after extubation

  Tracheostomized patients – Spontaneous ventilation through tracheostomy without any MV during 7 days

- **Weaning failure** – Either failure of SBT or the need for reintubation within 48 h following extubation

J.M Boles et al ERS 2007

Schematic representation of the different stages occurring in a mechanically ventilated patient



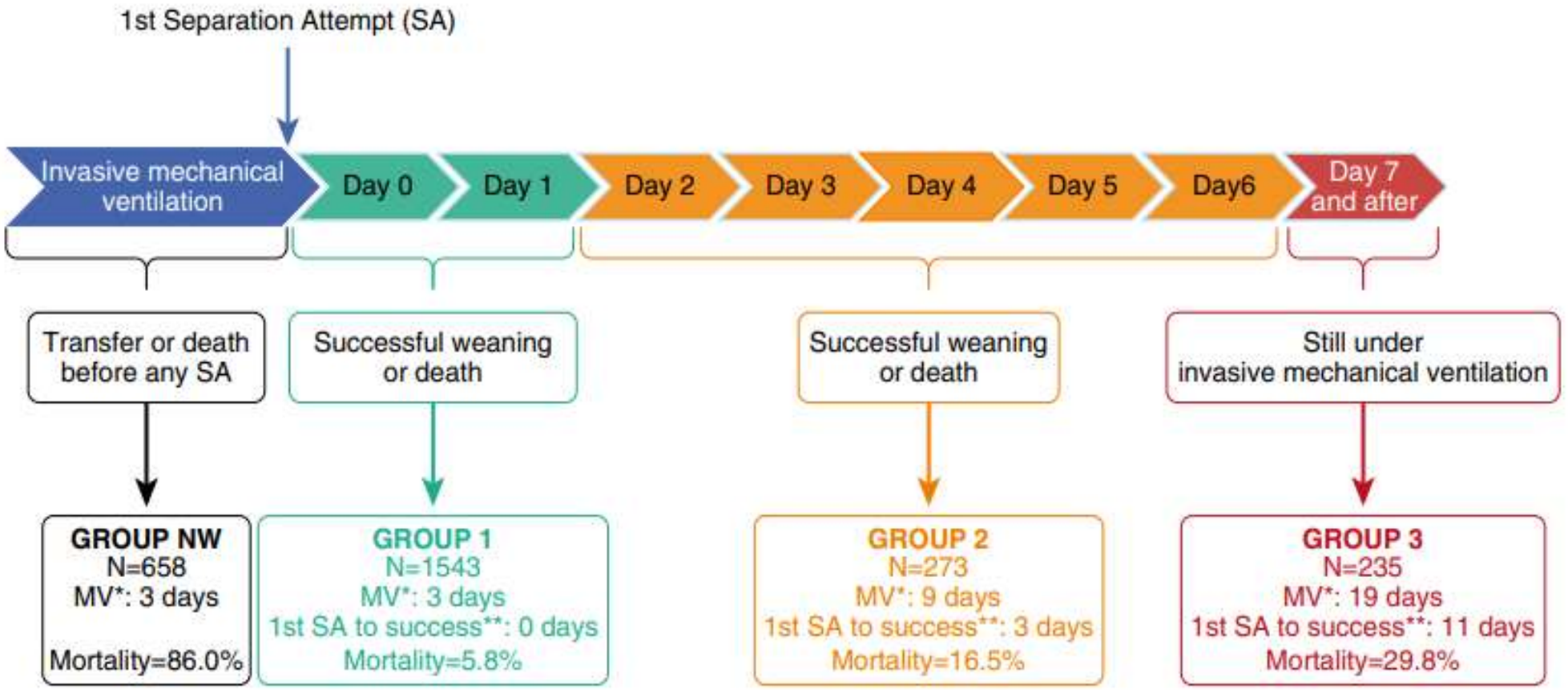
J.M Boles et al ERS 2007

Classification of patients according to the weaning process

- Simple weaning – Patients who proceed from initiation of weaning to successful extubation on the first attempt without difficulty
- Difficult weaning – patients who fail initial weaning and require upto 3 SBT or as long as 7 days from the first SBT to achieve successful weaning
- Prolonged weaning – Patients who fail at least 3 weaning attempts or require >7 days of weaning after the first SBT

J.M Boles et al ERS 2007

Epidemiology



B ´eduneau, Pham, Schortgen, et al.: Epidemiology of Weaning ATS 2017

Epidemiology

- Incidence of unplanned extubation – 0.3-16% -83% initiated by pt, 17% accidental
- 30-40% of the patients with self-extubation during weaning do not require reintubation
- Mortality increases if there is delay in extubation – 12% when there was no delay vs 27%

Ebstein et al AJRCCM
Copplin et al AJRCCM

Process of weaning

Consideration for assessing readiness to wean

Clinical assessment	Adequate cough
	Absence of excessive tracheobronchial secretion
	Resolution of disease acute phase for which the patient was intubated
Objective measurements	Clinical stability
	Stable cardiovascular status (*i.e.* f_C ⩽140 beats·min^{-1}, systolic BP 90–160 mmHg, no or minimal vasopressors)
	Stable metabolic status
	Adequate oxygenation
	S_{a,O_2} >90% on ⩽F_{I,O_2} 0.4 (or $P_{a,O_2}/F_{I,O_2}$ ⩾150 mmHg)
	PEEP ⩽8 cmH_2O
	Adequate pulmonary function
	f_R ⩽35 breaths·min^{-1}
	MIP ⩽-20– -25 cmH_2O
	V_T >5 mL·kg^{-1}
	VC >10 mL·kg^{-1}
	f_R/V_T <105 breaths·min^{-1}·L^{-1}
	No significant respiratory acidosis
	Adequate mentation
	No sedation or adequate mentation on sedation (or stable neurologic patient)

J.M. Boles weaning from mechanical ventilation ERJ 2007

	Effect of PSV vs T piece during SBT on successful extubation Carles Subira et al JAMA 2019	Spontaneous breathing trial with PSV or a T piece Thille et al NEJM 2022
Study	Multicentre RCT ,18 Spanish ICU	Multicentre RCT, 31 ICUs in France
Population	N = 1153,	N = 969
Intervention & comparison	2 hr T piece SBT (N=575) vs 30 min SBT (N= 578) with PS 8 cm H2o, PEEP – 0	PSV (484) – PS – 8, PEEP - 0 T piece (485) -1 hr
Inclusion Criteria	Pts on MV for at least 24 hrs who fulfilled the weaning criteria	Pts with **high risk for extubation failure** >24 hr MV, who fulfilled weaning criteria
Primary outcome	**Successful extubation** – 473 (82.3%) in PSV vs 428 (74%) in T piece grp (Diff-8.2%, 95% CI 3.4 – 13%, **P = 0.001**) [Post extubation NIV/HFNC – Non protocolised]	**Total time alive and without IMV (VFD)** – 27 (24-27) in PSV vs 27 (23-27) in T piece grp (Diff-0days, 95%CI -0.5 to 1, p=0.31) [80% patients received post extubation NIV]
Secondary outcomes	Extubation after 1st SBT – 532(92.5%) vs 486(84.1%) {8.4, P<0.001} Hospital mortality- 60(10.4) vs 86(14.9) [-4.4, p=0.02] 90 day mortality 76(13.2) vs100(17.3) p=004] Reintubation, ICU & hosp length of stay, tracheostomy - Nonsignificant	Extubation <24 hrs – 376(77.7%) in PSV vs 350(72.2%) in T piece grp (Diff-5.5%, CI -0.8-5.9) 24 hr to 7days -97(20) vs 108(22.2) >7 days- 11(2.3) vs 27(5.6) Reintubation ≤ 7days – 72(14.9) vs 65 (13.6) Median length of stay and mortality – similar

Failure criteria for SBT

Clinical assessment and subjective indices	Agitation and anxiety
	Depressed mental status
	Diaphoresis
	Cyanosis
	Evidence of increasing effort
	Increased accessory muscle activity
	Facial signs of distress
	Dyspnoea
Objective measurements	P_{a,O_2} ⩽50–60 mmHg on F_{I,O_2} ⩾0.5 or S_{a,O_2} <90%
	P_{a,CO_2} >50 mmHg or an increase in P_{a,CO_2} >8 mmHg
	pH <7.32 or a decrease in pH ⩾0.07 pH units
	f_R/V_T >105 breaths·min^{-1}·L^{-1}
	f_R >35 breaths·min^{-1} or increased by ⩾50%
	f_C >140 beats·min^{-1} or increased by ⩾20%
	Systolic BP >180 mmHg or increased by ⩾20%
	Systolic BP <90 mmHg
	Cardiac arrhythmias

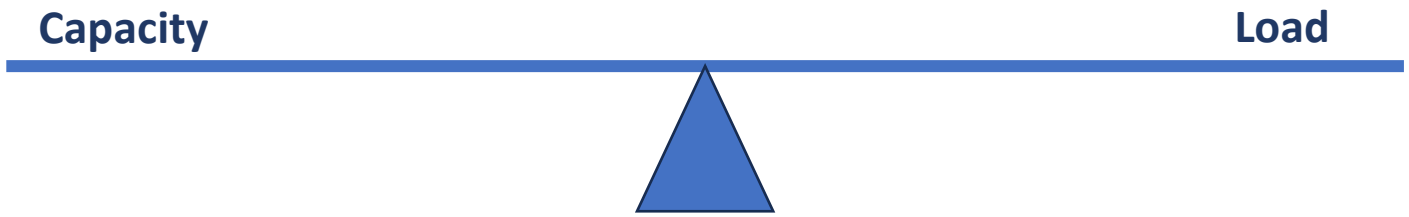
J.M. Boles weaning from mechanical ventilation ERJ 2007

Pathophysiology of difficult weaning

Pathophysiology

Respiratory Drive
Respiratory muscle function
O2 transport
Systolic function
Diastolic function
Cognitive function
Metabolic/Endocrine function

Respiratory resistance
Respiratory elasticity
Intrinsic PEEP
Gas exchange
O2 consumption



Increase respiratory workload

- Elastic workload

  Lung parenchyma – ARDS, pneumonia, fibrosis

  Chest wall – Kyphoscoliosis, flail chest, pleural effusion, pneumothorax, ascites etc

- Resistive load –

  Airways – Bronchospasm, mucosal edema, excess secretions, DHI

  ETT resistance – Kinking, small ETT

  Ventilator – Inappropriate settings, malfunctioning valves

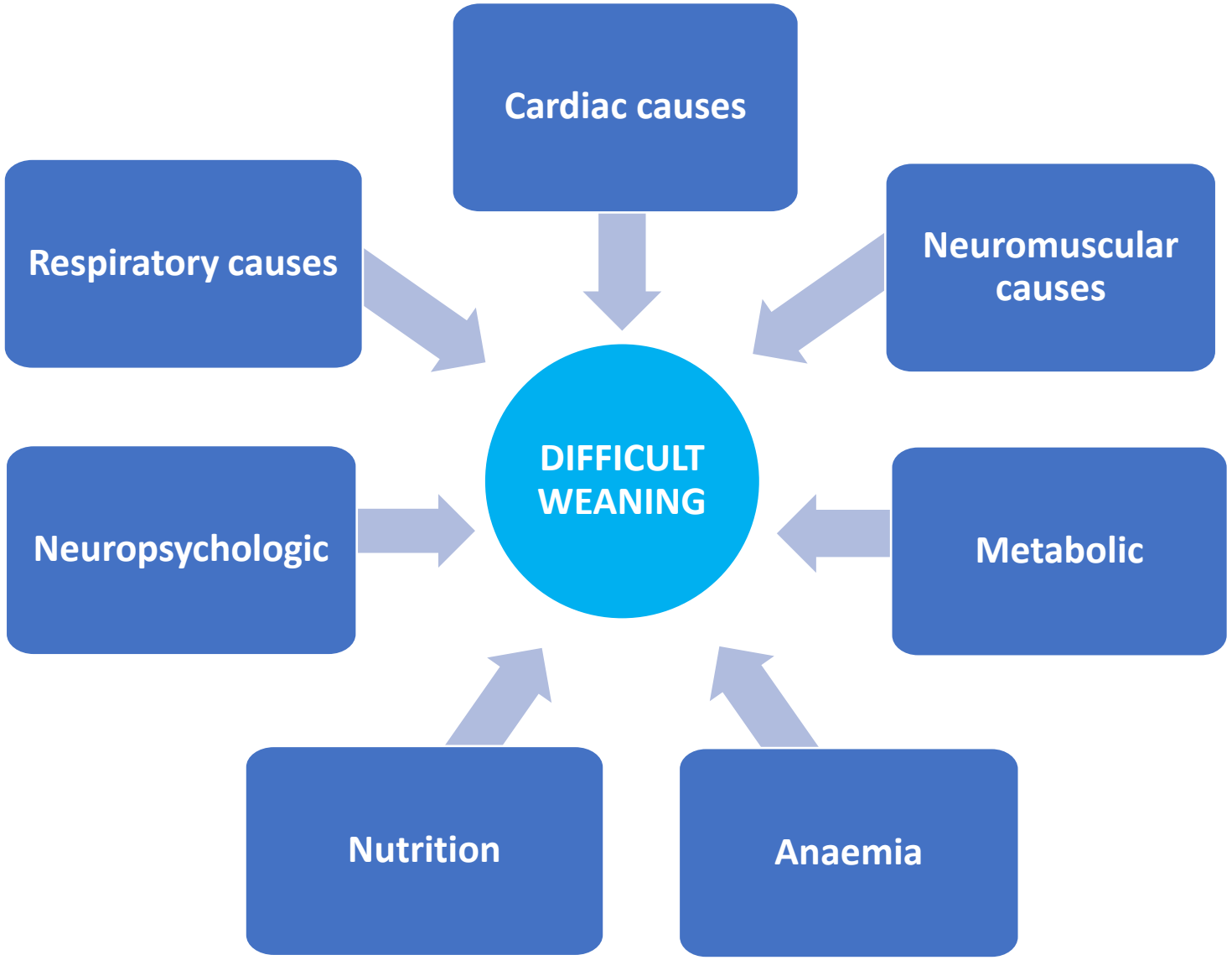
- Ventilatory needs

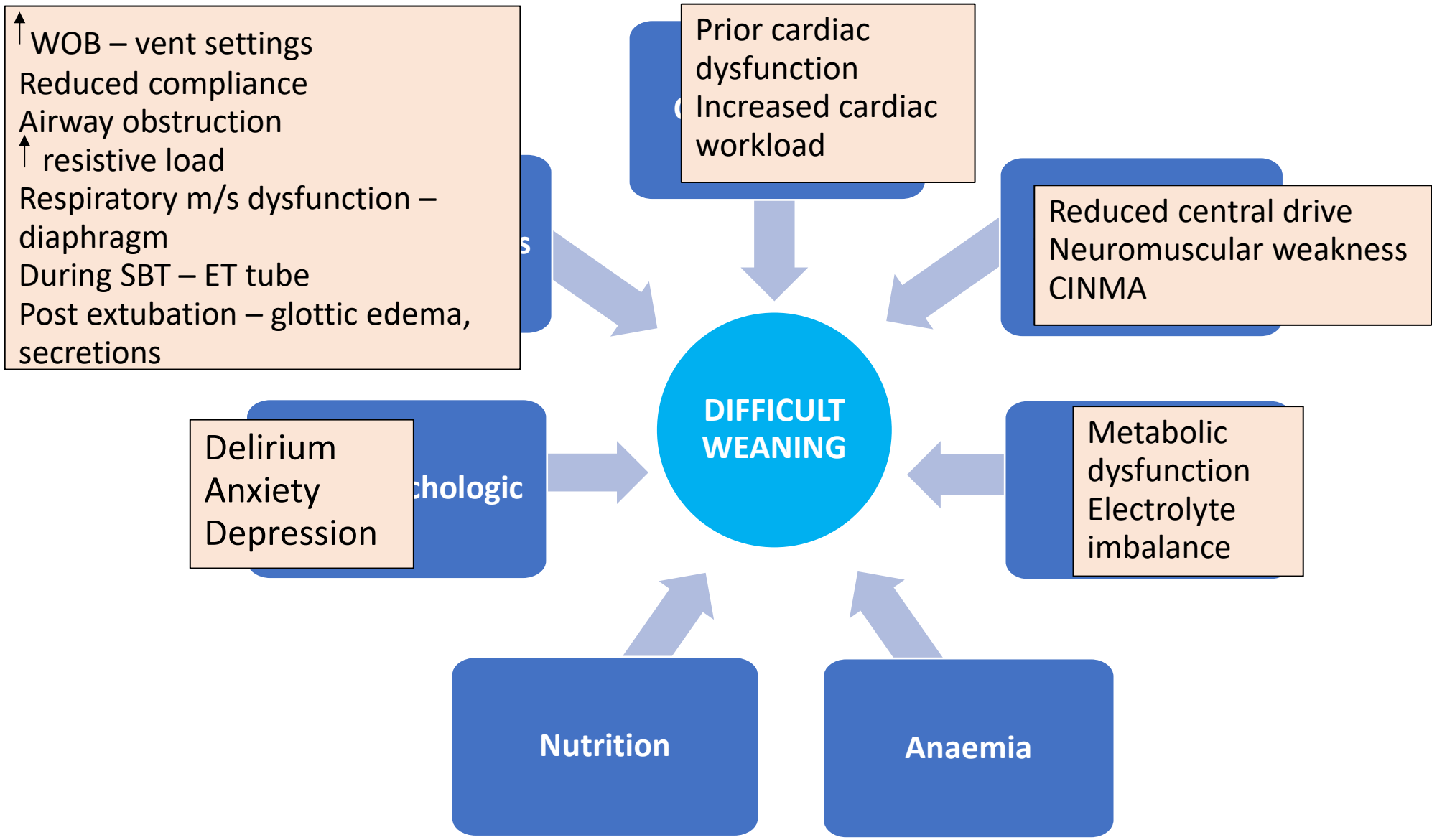
  High MV – hyperventilation, fever, V/Q mismatch

  Vent dyssynchrony

Decrease respiratory capacity

- Decreased central drive – Sedatives, narcotics, metabolic – urea, met alkalosis, Infection – encephalitis, meningitis
- Decreased signal conduction – spine lesions, GBS, MG, AIP, phrenic n/v involvement – traumatic/iatrogenic, critical illness polyneuropathy
- Reduced strength and endurance – critical illness myopathy, disuse atropy, metabolic – decreased PO4, Mg, K, Ca, Endocrine – thyroid disturbances and adrenal insufficiency


Cardiac causes
Respiratory causes
Neuromuscular causes
DIFFICULT WEANING
Neuropsychologic
Metabolic
Nutrition
Anaemia


↑ WOB – vent settings
Reduced compliance
Airway obstruction
↑ resistive load
Respiratory m/s dysfunction – diaphragm
During SBT – ET tube
Post extubation – glottic edema, secretions
Prior cardiac dysfunction
Increased cardiac workload
Reduced central drive
Neuromuscular weakness
CINMA
Delirium
Anxiety
Depression
DIFFICULT WEANING
Metabolic dysfunction
Electrolyte imbalance
Nutrition
Anaemia

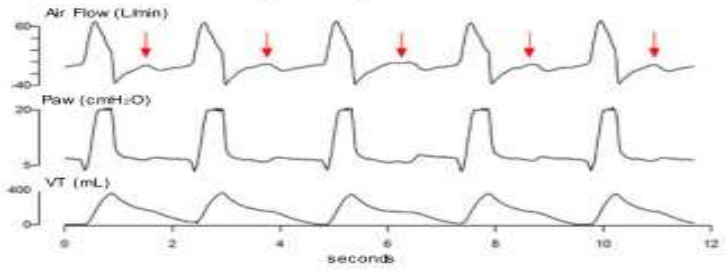
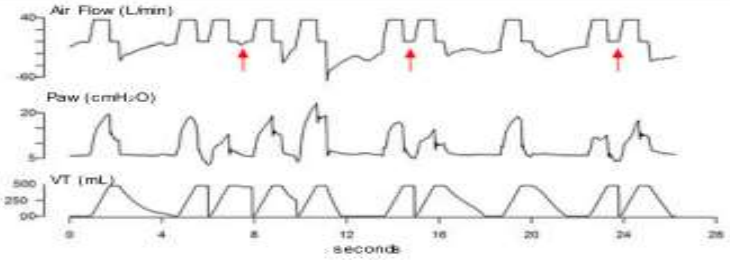
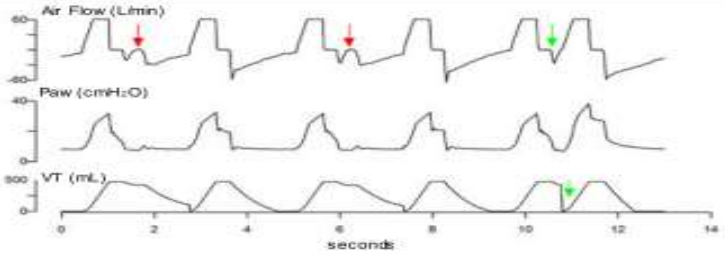
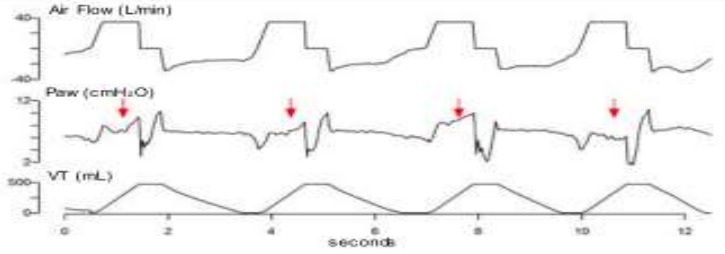
1)Respiratory causes -

Increased airway resistance	Reduced compliance
Tube (small diameter, sputum retention)	Chest wall
Central airways	Edema
Tracheostomy malposition	Elevated abdominal pressure
Sputum plug	Pleural fluid and ascites
Corpus alienum (after trauma)	Obesity
Tracheomalacia or tracheal stenosis	Lung
Small airways	Intrinsic positive end-expiratory pressure
Asthma and chronic obstructive pulmonary disease	Alveolar filling (edema, pus, and collapse)
Acute respiratory distress syndrome	Pneumonia
	Interstitial lung disease and fibrosis

Management of respiratory causes

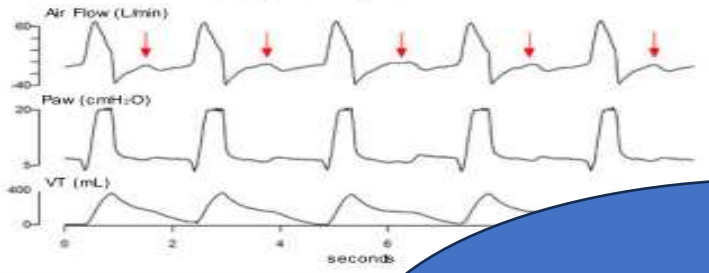
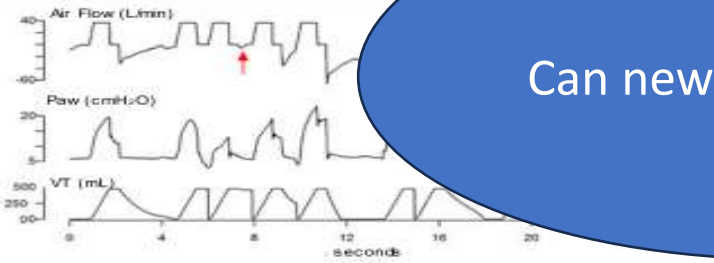
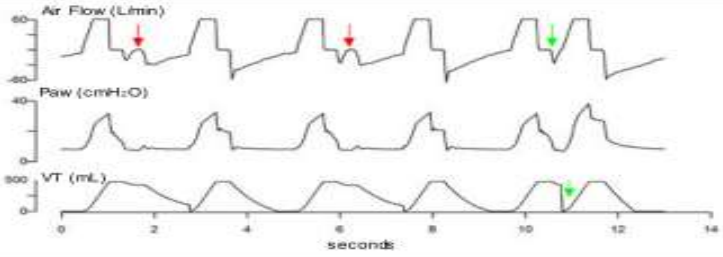
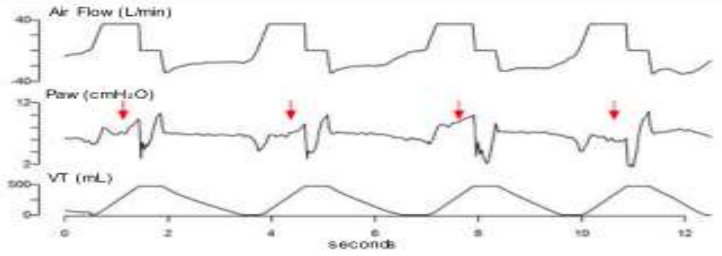
- Management of factors that increase elastic workload such as ascites, abdominal distention, pleural effusion, pneumothorax
- Management of factors that increase resistive load such as bronchospasm, excessive secretions, intrinsic peep, ventilatory circuit, malfunctioning vent valves
- Identification of patient-ventilator dyssynchrony and manage accordingly
- Newer modes – NAVA, Automated – SmartCare, ASV
- Post extubation – NIV vs HFNC

Patient-ventilator dyssynchrony

Asynchrony	Graphic representation	Description	Causes
Ineffective Efforts		Inspiratory muscle efforts not followed by a ventilator breath (red arrows)	Inadequate trigger sensitivity Excessive assistance Overdistension/Air trapping Low respiratory drive Low level of pCO2 Oversedation
Double Cycling		Inspiratory effort that continues beyond the ventilator inspiratory time producing a second or a third ventilator breath (red arrows) without expiration. Consequently, the volume of the first breath is added to the second or third breath.	Inadequate setting of ventilator inspiratory time Inadequate trigger sensitivity (too sensible) Inadequate circuit pressurization Patient effort too strong Reverse triggering
Reverse Triggering		Ventilator insufflations that trigger diaphragmatic muscle contractions (red arrows) in response to passive insufflation of the lungs. When the diaphragmatic muscle contraction occurs at the end of inspiration a double cycled breath can occur (green arrow) .	Oversedation Overdistension/Air trapping
Inspiratory Airflow Dyssynchrony		Strong patient inspiratory effort (concavity in pressure tracing) due to insufficient inspiratory airflow in a patient ventilated in assist-volume controlled mode.	Inadequate gas flow Dyspnea Delirium/Pain

Candelaria de Haro et al ICM 2019

Patient-ventilator dyssynchrony

Asynchrony	Graphic representation	Description	Causes
Ineffective Efforts		Inspiratory muscle efforts not followed by a ventilator breath (red arrows)	Inadequate trigger sensitivity Excessive assistance Overdistension/Air trapping Low respiratory drive Low level of pCO2 Oversedation
Double Cycling		...es beyond ...oducing a ...eath (red ...nsequently, ...n is added to	Inadequate setting of ventilator inspiratory time Inadequate trigger sensitivity (too sensible) Inadequate circuit pressurization Patient effort too strong Reverse triggering
Reverse Triggering		Ventilator insufflations that trigger diaphragmatic muscle contractions (red arrows) in response to passive insufflation of the lungs. When the diaphragmatic muscle contraction occurs at the end of inspiration a double cycled breath can occur (green arrow) .	Oversedation Overdistension/Air trapping
Inspiratory Airflow Dyssynchrony		Strong patient inspiratory effort (concavity in pressure tracing) due to insufficient inspiratory airflow in a patient ventilated in assist-volume controlled mode.	Inadequate gas flow Dyspnea Delirium/Pain

Can newer modes help?

Candelaria de Haro et al ICM 2019

Neurally Adjusted Ventilatory Assist vs. Conventional Mechanical Ventilation in Adults and Children With Acute Respiratory Failure: A Systematic Review and Meta-Analysis

Mengfan Wu, Xueyan Yuan, Ling Liu and Yi Yang**

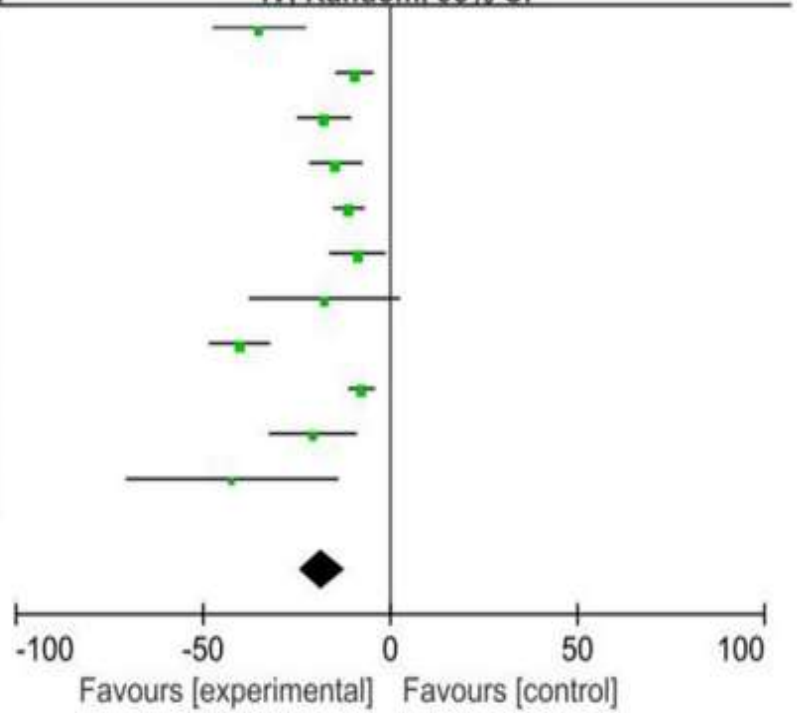
- Eighteen eligible studies (n = 926 patients of ARF)
- Primary outcome was asynchrony index (AI)
- Secondary outcomes- duration of MV, ICU mortality, incidence rate of VAP, pH, and PaCO2 in ABG
- NAVA vs PSV

Primary outcome - AI

Study or Subgroup	NAVA Mean	NAVA SD	NAVA Total	CMV Mean	CMV SD	CMV Total	Weight	Mean Difference IV, Random, 95% CI
Baudin 2014	3	3	11	38	21	11	8.0%	-35.00 [-47.54, -22.46]
Bertrand PM 2013	3.8	3.8	13	13.4	8.6	13	11.2%	-9.60 [-14.71, -4.49]
Doorduin 2014	5.3	2.5	12	23	12.6	12	10.3%	-17.70 [-24.97, -10.43]
Giovanna Chidini 2016	1.08	2.41	18	15.64	15.28	18	10.4%	-14.56 [-21.71, -7.41]
Juliana C. Ferreira 2017	11.68	4.86	20	22.77	8.56	20	11.5%	-11.09 [-15.40, -6.78]
Lise Piquilloud 2011	5.76	5.78	22	14.58	17.11	22	10.2%	-8.82 [-16.37, -1.27]
Lise Piquilloud 2012	6	6.6	13	23.6	36.6	13	5.2%	-17.60 [-37.82, 2.62]
Prasad KT 2021	7.37	11.68	50	47.67	27.25	50	9.9%	-40.30 [-48.52, -32.08]
Tajamul S 2020	4.42	2.03	20	12.06	7.98	20	11.7%	-7.64 [-11.25, -4.03]
Vignaux 2013	6.52	8.57	19	27.21	24.83	19	8.3%	-20.69 [-32.50, -8.88]
Vignaux L 2013	2.72	4.1	6	44.97	35.28	6	3.3%	-42.25 [-70.67, -13.83]
Total (95% CI)			**204**			**204**	**100.0%**	**-18.31 [-24.38, -12.25]**

Heterogeneity: Tau² = 78.69; Chi² = 73.98, df = 10 (P < 0.00001); I² = 86%

Test for overall effect: Z = 5.92 (P < 0.00001)

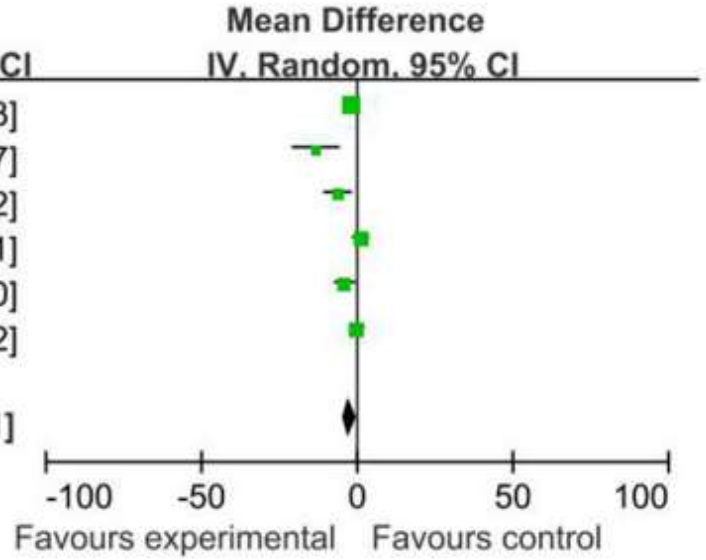


Duration of MV

Study or Subgroup	NAVA Mean	NAVA SD	NAVA Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
A. Demoule 2016	6.27	2.04	62	8.15	1.7	66	26.1%	-1.88 [-2.53, -1.23]
Hadfeld DJ 2020	5.79	3	39	19.16	24.04	38	6.4%	-13.37 [-21.07, -5.67]
Ling Liu 2020	8.27	5.74	47	14.6	15.86	52	12.5%	-6.33 [-10.94, -1.72]
Prasad KT 2021	4.61	8.73	50	3.58	4.96	50	18.9%	1.03 [-1.75, 3.81]
Robert M 2020	7.8	8.1	103	11.9	16.2	103	16.1%	-4.10 [-7.60, -0.60]
Tajamul S 2020	3.64	2.39	20	3.82	5.19	20	20.0%	-0.18 [-2.68, 2.32]
Total (95% CI)			**321**			**329**	**100.0%**	**-2.64 [-4.88, -0.41]**

Heterogeneity: Tau² = 4.87; Chi² = 19.64, df = 5 (P = 0.001); I² = 75%

Test for overall effect: Z = 2.32 (P = 0.02)

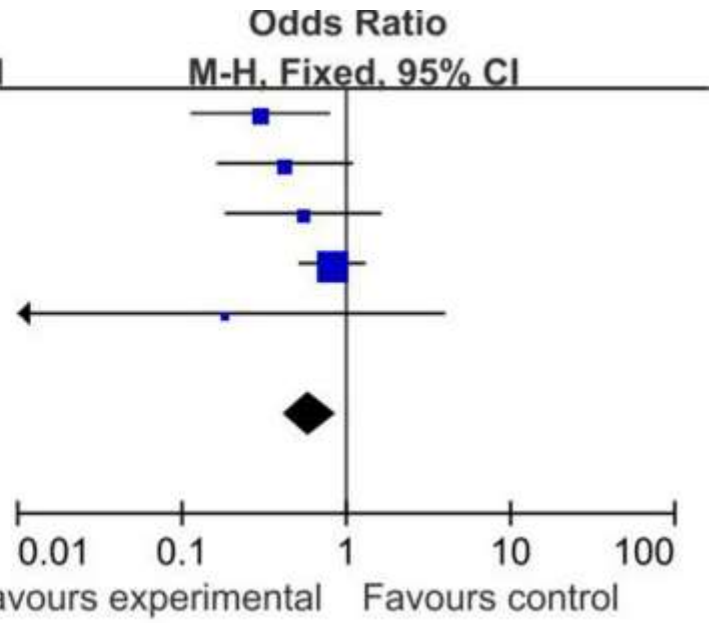


ICU mortality

Study or Subgroup	NAVA Events	NAVA Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Hadfeld DJ 2020	9	39	19	38	19.0%	0.30 [0.11, 0.80]
Ling Liu 2020	8	47	17	52	17.2%	0.42 [0.16, 1.10]
Prasad KT 2021	6	50	10	50	11.3%	0.55 [0.18, 1.64]
Robert M 2020	41	194	50	203	49.4%	0.82 [0.51, 1.31]
Tajamul S 2020	0	20	2	20	3.1%	0.18 [0.01, 4.01]
Total (95% CI)		**350**		**363**	**100.0%**	**0.60 [0.42, 0.86]**
Total events	64		98			

Heterogeneity: Chi² = 4.74, df = 4 (P = 0.31); I² = 16%

Test for overall effect: Z = 2.78 (P = 0.006)



Clinical outcomes in patients undergoing invasive mechanical ventilation using NAVA and other ventilation modes - A systematic review and meta-analysis

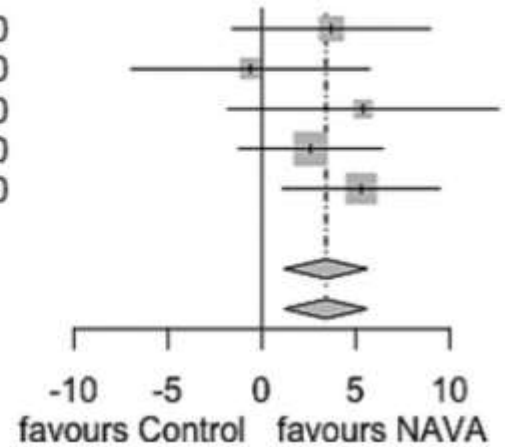
Clarissa Both Pinto [a], Debora Leite [b], Mariana Brandão [b], Wagner Nedel [a,c,d,*]

- RCTs comparing NAVA vs the standard ventilation mode in critically ill adult patients admitted to the ICU with invasive MV
- The main outcome was 28-day ventilatory-free days (VFD)
- Secondary outcomes were weaning failure, mortality, ICU and hospital length of stay, and need for tracheostomy

Study	Population	Intervention	Outcome
Liu et al 2020 unicentric	Patient on IMV who failed 1st SBT or reintubated after successful SBT	N = 99 NAVA -47, PSV - 52	Weaning duration: 3.0 (1.2 to 8) vs 7.4 (2 to 28) days; 95% CI -9.2 to 1.4, p = 0.039 Successful weaning – 70%(33/47) vs 48%(25/52) p=0.02
Kuo et al 2016 unicentric	COPD patients who endured weaning failure for >21 days	N = 33 NAVA -14, PSV - 19	Asynchrony index: 0% vs 11.9%(p= 0.001) Ineffective trigger 0% vs 52% (p= 0.001) Delayed trigger 0% vs 36% (p = 0.001), Flow asynchrony 0% vs 26%,
Demoule et al 2016 multicentric - 11	MV >24 hrs for ARF of resp cause, able to sustain psv and estimated remaining MV >48 hr	N = 128 NAVA = 61, PSV = 66	Proportion of patients remaining in NAVA or PSV throughout the first 48 h without any return to assist control ventilation: 67.2 vs 63.3% (p = 0.66)
Hadfield et al 2020 Multicentric - 4	Patients at risk of prolonged MV – COPD, HF, ARDS	N = 78 NAVA = 39, PSV = 39	Median (95% CI) mode adherence was 83% (64–97%) and 100% (100–100%), and protocol compliance was 66% (50–80%) and 100% (89% - 100%)
Kacmarek et al 2020 Multicentric - 15	Pts with ARF expected to be MV for >72 Hr	N = 306 NAVA = 153, PSV = 153	Median VFDs: 22 vs 18 days, between-group difference 4 days (95% CI 0 to 8 days), p = 0.016 No mortality difference

Study	NAVA Total	Mean	SD	Control Total	Mean	SD	Mean Difference	MD	95%-CI
Demoule 2016	62	17.30	13.6000	66	13.60	16.7000		3.70	[-1.56; 8.96]
Kuo 2016	14	11.60	9.0000	19	12.20	9.4000		-0.60	[-6.93; 5.73]
Hadfield 2020	39	12.70	17.0000	38	7.30	15.2000		5.40	[-1.80; 12.60]
Kacmarek 2020	153	16.40	16.3000	153	13.80	17.8000		2.60	[-1.22; 6.42]
Liu 2020	47	20.30	9.6000	52	15.00	11.6000		5.30	[1.12; 9.48]
Common effect model	**315**			**328**				**3.42**	**[1.21; 5.62]**
Random effects model								**3.42**	**[1.21; 5.62]**

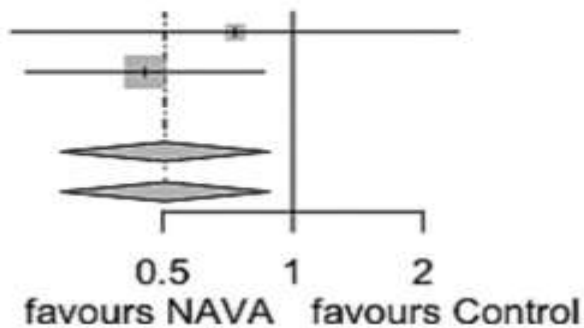
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.59$



VFD

Study	NAVA Events	Total	Control Events	Total	Odds Ratio	OR	95%-CI
Hadfield 2020	7	25	9	26		0.73	[0.22; 2.41]
Kacmarek 2020	17	153	33	153		0.45	[0.24; 0.86]
Common effect model		**178**		**179**		**0.50**	**[0.29; 0.88]**
Random effects model						**0.51**	**[0.29; 0.88]**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.49$



Weaning Failure

No difference in mortality, hospital length of stay and need for tracheostomy

PHYSIOLOGICAL CHANGES IN OBSTRUCTIVE AIRWAY DISEASES RELEVANT TO MECHANICAL VENTILATION

- Expiratory flow limitation – It leads to the development of inspiratory muscle fatigue
- Dynamic hyperinflation and auto-PEEP – The airflow obstruction, low elastic recoil, high ventilatory demand, and short expiratory time result in air trapping and consequent DH
- DH is the main factor explaining the increased ITP, increased WOB, ventilator dependency, and weaning failure

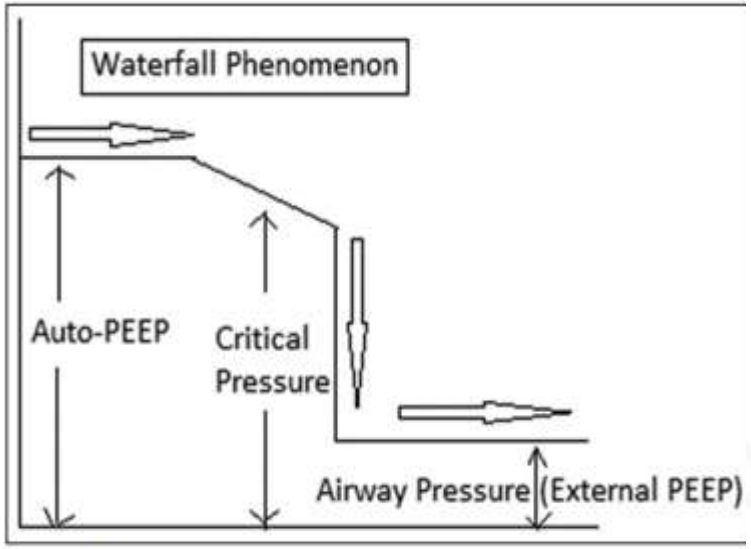
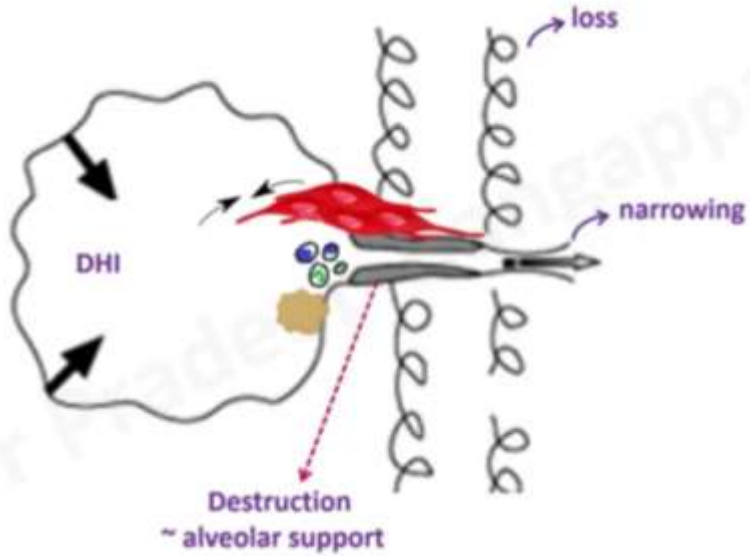
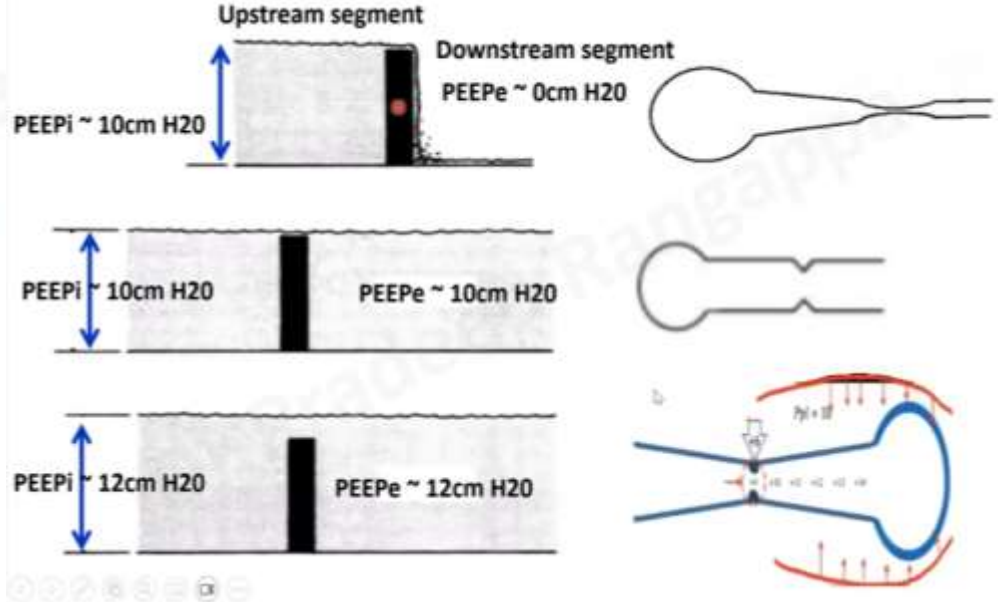
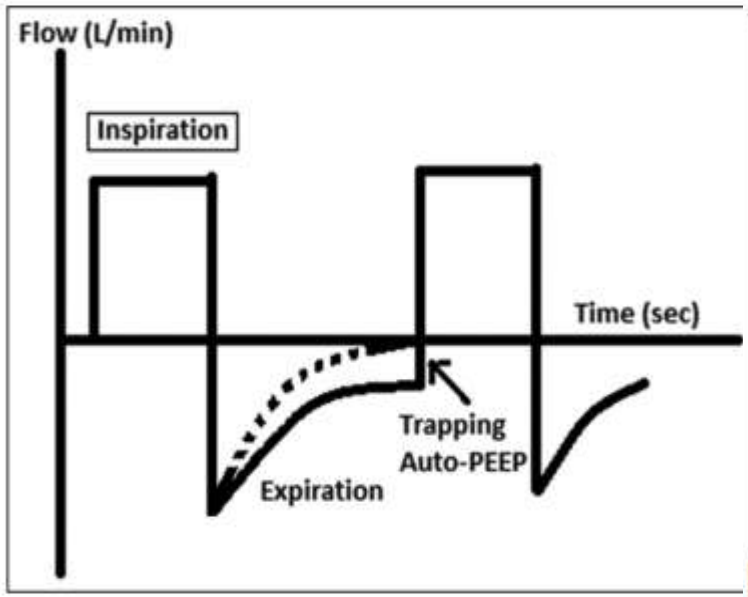


Figure 1: Waterfall phenomenon and its relation with critical pressure







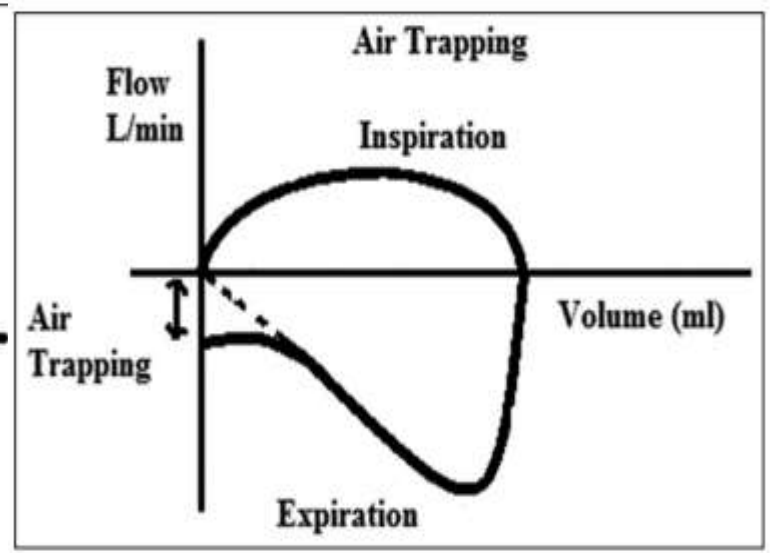
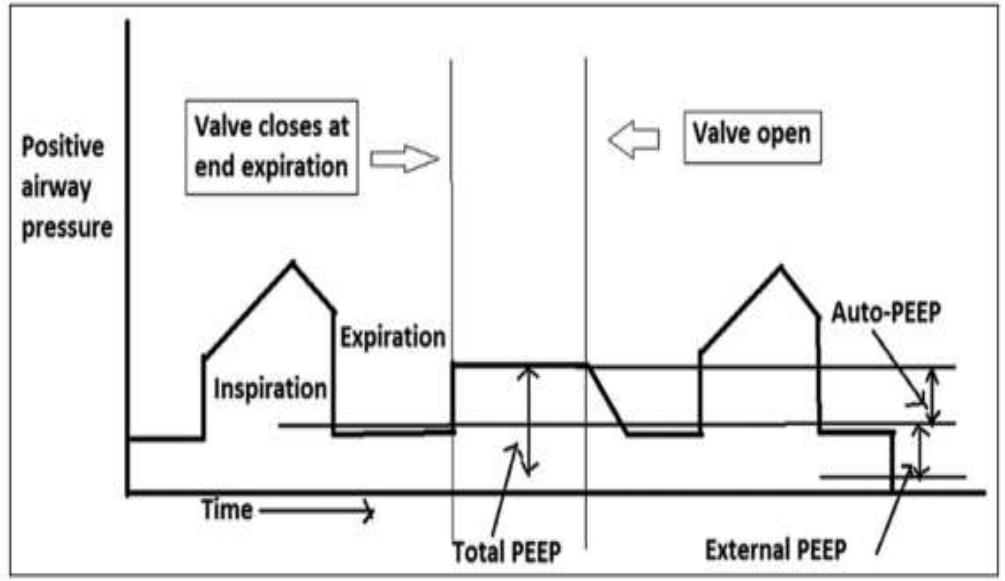
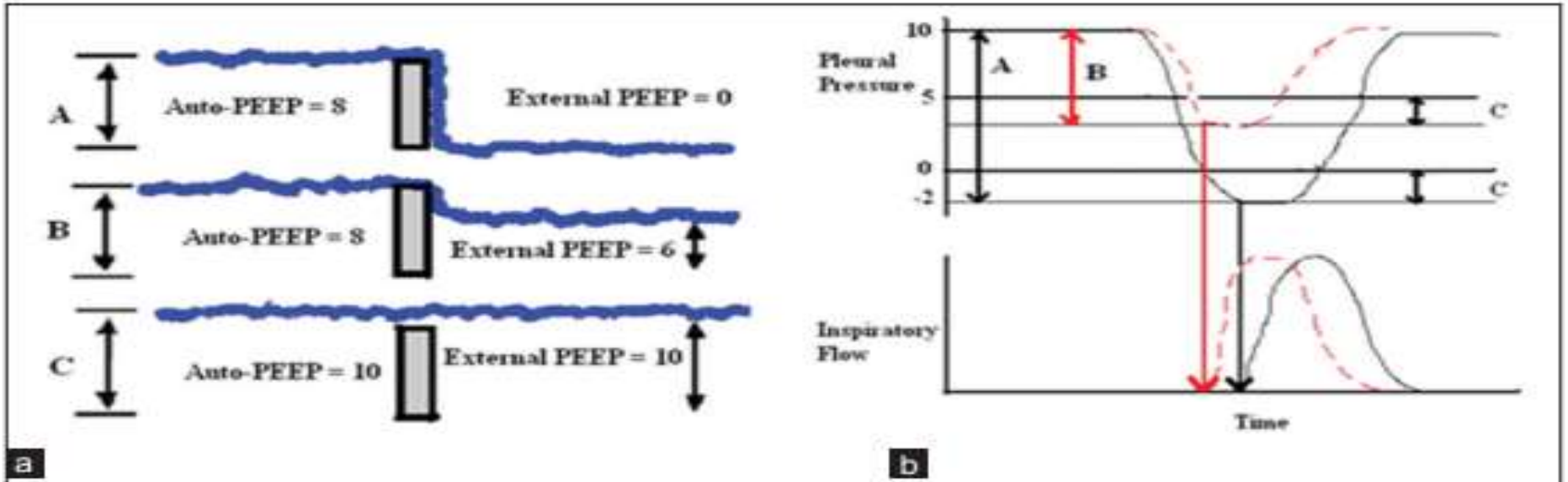


Figure 4: Air trapping in flow-volume loop





Panel	Auto-PEEP cm H2O	Ventilator Trigger Sensitivity	External PEEP cm H2O	Negative Pressure required to initiate ventilator breath
A	8	2	0	8 + 2 - 0 = 10
B	8	2	6	8 + 2 – 6 = 4
C	8	2	10	8 +2 – 10 = 0

Adaptive support ventilation for faster weaning in COPD: a randomised controlled trial

ERJ 2011

C. Kirakli*, I. Ozdemir#, Z.Z. Ucar*, P. Cimen*, S. Kepil# and S.A. Ozkan#

- Single centre RCT
- Enrolled intubated COPD patients who met the inclusion criteria and were ready for weaning
- N = 97, ASV =49, PSV =48
- Patients with previous use of NIV were not included in the study

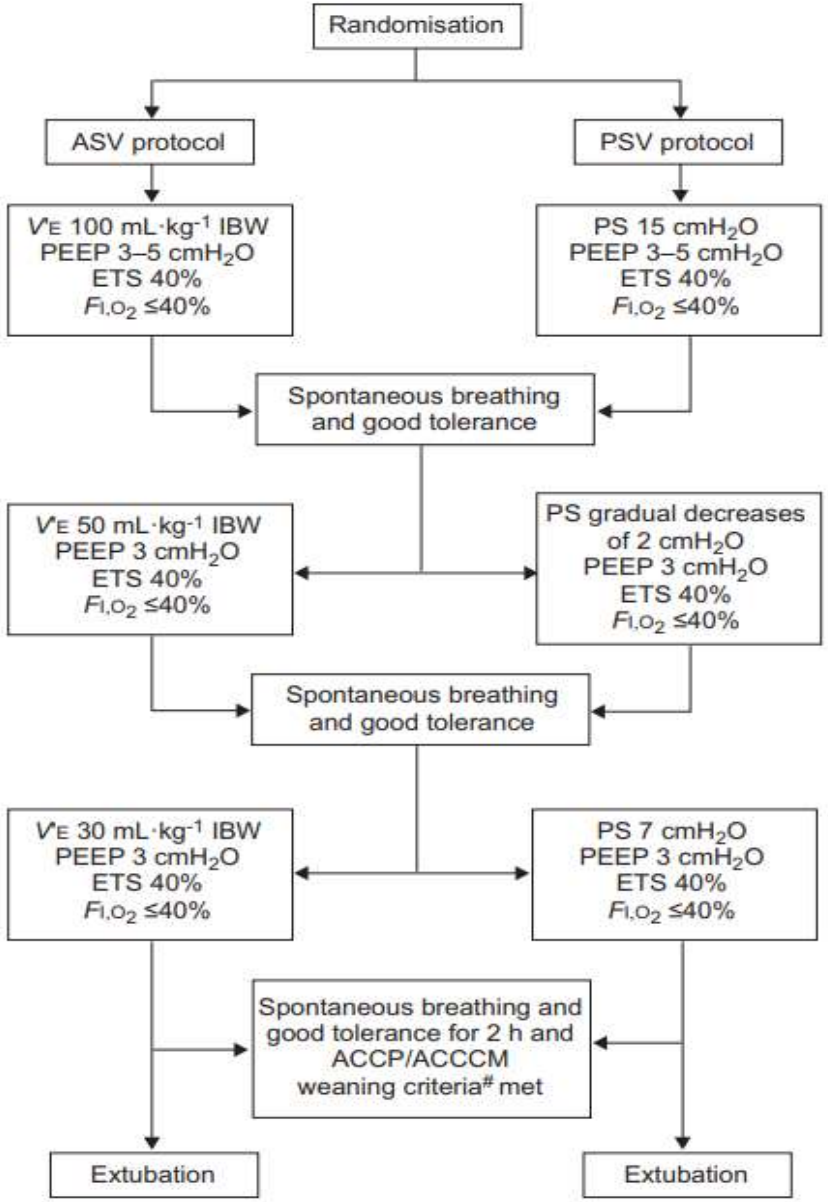


TABLE 3 Comparison of adaptive support ventilation (ASV) and the pressure support ventilation (PSV) groups

Outcomes	ASV	PSV	p-value
Subjects n	49	48	
Weaning duration h	24 (20–62)	72 (24–169)	**0.041**
Weaning failure	15 (31)	16 (33)	0.47
Duration of MV h	120 (72–264)	156 (72–288)	0.56
LOS in ICU days	11 (6–15)	13 (8–14)	0.5
Mortality at day 28	9 (18)	9 (18)	0.58

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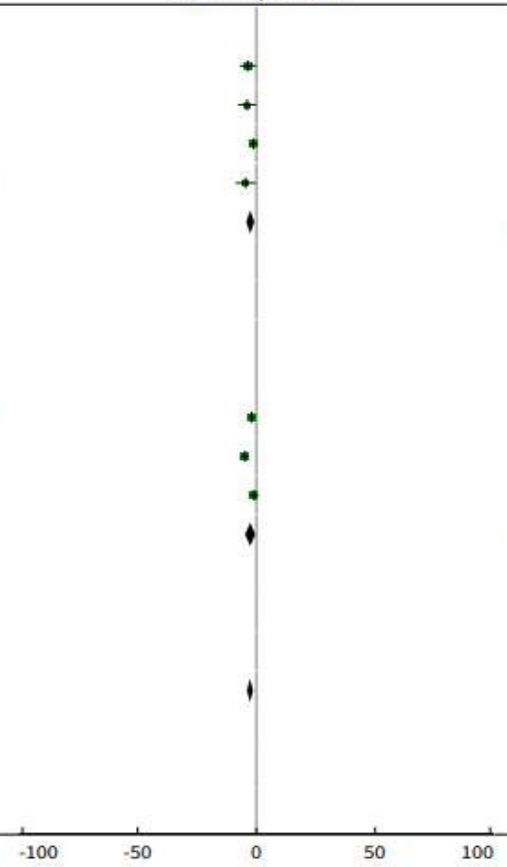
[Intervention Review]

Automated weaning and SBT systems versus non-automated weaning strategies for weaning time in invasively ventilated critically ill adults

- Included 10 RCTs comparing automated weaning and SBT systems versus non-automated weaning strategies
- Trials investigating predominantly critically ill adults requiring invasive mechanical ventilation
- The primary outcome was weaning time (time from randomization to extubation) as defined by the study authors

Analysis 1.1. Comparison 1 SmartCare™ versus non-automated weaning, Outcome 1 Weaning time (randomization to extubation) based on type of control arm.

Study or subgroup	SmartCare N	SmartCare Mean(SD)	Non-automated N	Non-automated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Predominantly protocolized control strategy							
Burns 2013a	43	4.7 (5.2)	37	8.3 (9.4)		9.2%	-3.56[-6.97,-0.15]
Lellouche 2006	74	4.4 (4.7)	70	8.3 (15.4)		8.1%	-3.9[-7.66,-0.14]
Liu 2013	19	1.7 (1.4)	20	3 (2.7)		19.49%	-1.29[-2.63,0.05]
Ma 2010	30	6.7 (7.9)	32	11.2 (8.8)		7.03%	-4.55[-8.72,-0.38]
Subtotal ***	**166**		**159**			**43.82%**	**-2.57[-4.26,-0.88]**
Heterogeneity: Tau^2=0.97; Chi^2=4.3, df=3(P=0.23); I^2=30.3%							
Test for overall effect: Z=2.98(P=0)							
1.1.2 Predominantly non-protocolized control strategy							
Bifulco 2008	15	3.5 (1.4)	15	5.5 (1.8)		20.54%	-2[-3.15,-0.85]
Jiang 2006	13	8.5 (2.1)	25	13.3 (2.2)		18.96%	-4.78[-6.2,-3.36]
Rose 2008	51	2.5 (3.7)	51	3.3 (5.5)		16.68%	-0.88[-2.69,0.93]
Subtotal ***	**79**		**91**			**56.18%**	**-2.59[-4.75,-0.43]**
Heterogeneity: Tau^2=3.09; Chi^2=13.5, df=2(P=0); I^2=85.18%							
Test for overall effect: Z=2.35(P=0.02)							
Total ***	**245**		**250**			**100%**	**-2.68[-3.99,-1.37]**
Heterogeneity: Tau^2=1.83; Chi^2=18.62, df=6(P=0); I^2=67.77%							
Test for overall effect: Z=4.01(P<0.0001)							
Test for subgroup differences: Chi^2=0, df=1 (P=0.99), I^2=0%							



Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weaning time (randomization to extubation) based on clinician type	7	495	Mean Difference (IV, Random, 95% CI)	-2.68 [-3.99, -1.37]

Patient or population: patients with weaning time in invasively ventilated critically ill adults
Settings:
Intervention: SmartCare™ versus non-automated weaning

Outcomes	Illustrative comparative risks* (95% CI)	
	Average duration	**Estimated duration**
	Control	**SmartCare™ versus non-automated weaning**
Weaning time (from randomization to extubation) based on ICU type: purely medical	Mean weaning time (from randomization to extubation) based on ICU type—purely medical—in the control groups was **13 days**	Mean weaning time (from randomization to extubation) based on ICU type—purely medical—in the intervention groups was **4.78 lower** (6.2 to 3.36 lower)
Weaning time (from randomization to extubation) based on ICU type: medical-surgical or surgical only	Mean weaning time (from randomization to extubation) based on ICU type—medical-surgical or surgical only—in the control groups was **3 to 11 days**	Mean weaning time (from randomization to extubation) based on ICU type—medical-surgical or surgical only—in the intervention groups was **1.85 lower** (2.67 to 1.04 lower)
Time to successful extubation	Mean time to successful extubation in the control groups was **1 to 10 days**	Mean time to successful extubation in the intervention groups was **0.99 lower** (1.89 to 0.09 lower)
Time to first successful spontaneous breathing trial	Mean time to first successful spontaneous breathing trial in the control groups was **0 to 6 days**	Mean time to first successful spontaneous breathing trial in the intervention groups was **1.72 lower** (6.23 lower to 2.78 higher)
Total duration of mechanical ventilation	Mean total duration of mechanical ventilation in the control groups was **3 to 17 days**	Mean total duration of mechanical ventilation in the intervention groups was **1.68 lower** (3.33 to 0.03 lower)
Intensive care unit length of stay (based on type of control arm): predominantly protocolized control strategy	Mean intensive care unit length of stay based on type of control arm—predominantly protocolized control strategy—in the control groups was **23 to 37 days**	Mean length of intensive care unit stay based on type of control arm—predominantly protocolized control strategy—in the intervention groups was **9.84 lower** (17.02 to 2.66 lower)
Intensive care unit length of stay (based on type of control arm): predominantly non-protocolized control strategy	Mean intensive care unit length of stay based on type of control arm—predominantly non-protocolized control strategy—in the control groups was **10 to 20 days**	Mean intensive care unit length of stay based on type of control arm—predominantly non-protocolized control strategy—in the intervention groups was **1.26 lower** (4.1 lower to 1.59 higher)

(MD -0.99 days, P value 0.03, seven trials, 516 participants, low-quality evidence)

SmartCare™ had no effect on time to first successful SBT, mortality or adverse events, specifically reintubation

Patient or population: patients with weaning time in invasively ventilated critically ill adults
Settings:
Intervention: SmartCare™ versus non-automated weaning

Outcomes	Illustrative comparative risks* (95% CI)	
	Average duration	**Estimated duration**
	Control	**SmartCare™ versus non-automated weaning**
Weaning time (from randomization to extubation) based on ICU type: purely medical	Mean weaning time (from randomization to extubation) based on ICU type—purely medical—in the control groups was **13 days**	Mean weaning time (from randomization to extubation) based on ICU type—purely medical—in the intervention groups was **4.78 lower** (6.2 to 3.36 lower)
Weaning time (from randomization to extubation) based on ICU type: medical-surgical or surgical only	Mean weaning time (from randomization to extubation) based on ICU type—medical-surgical or surgical only—in the control groups was **3 to 11 days**	Mean weaning time (from randomization to extubation) based on ICU type—medical-surgical or surgical only—in the intervention groups was **1.85 lower** (2.67 to 1.04 lower)
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P value 0.05, 7 trials, 521 participants

P value 0.02, 6 trials, 499 participants

(MD -0.99 days, P value 0.03, seven trials, 516 participants, low-quality evidence)

SmartCare™ had no effect on time to first successful SBT, mortality or adverse events, specifically reintubation

Comparison of advanced closed-loop ventilation modes with pressure support ventilation for weaning from mechanical ventilation in adults: A systematic review and meta-analysis

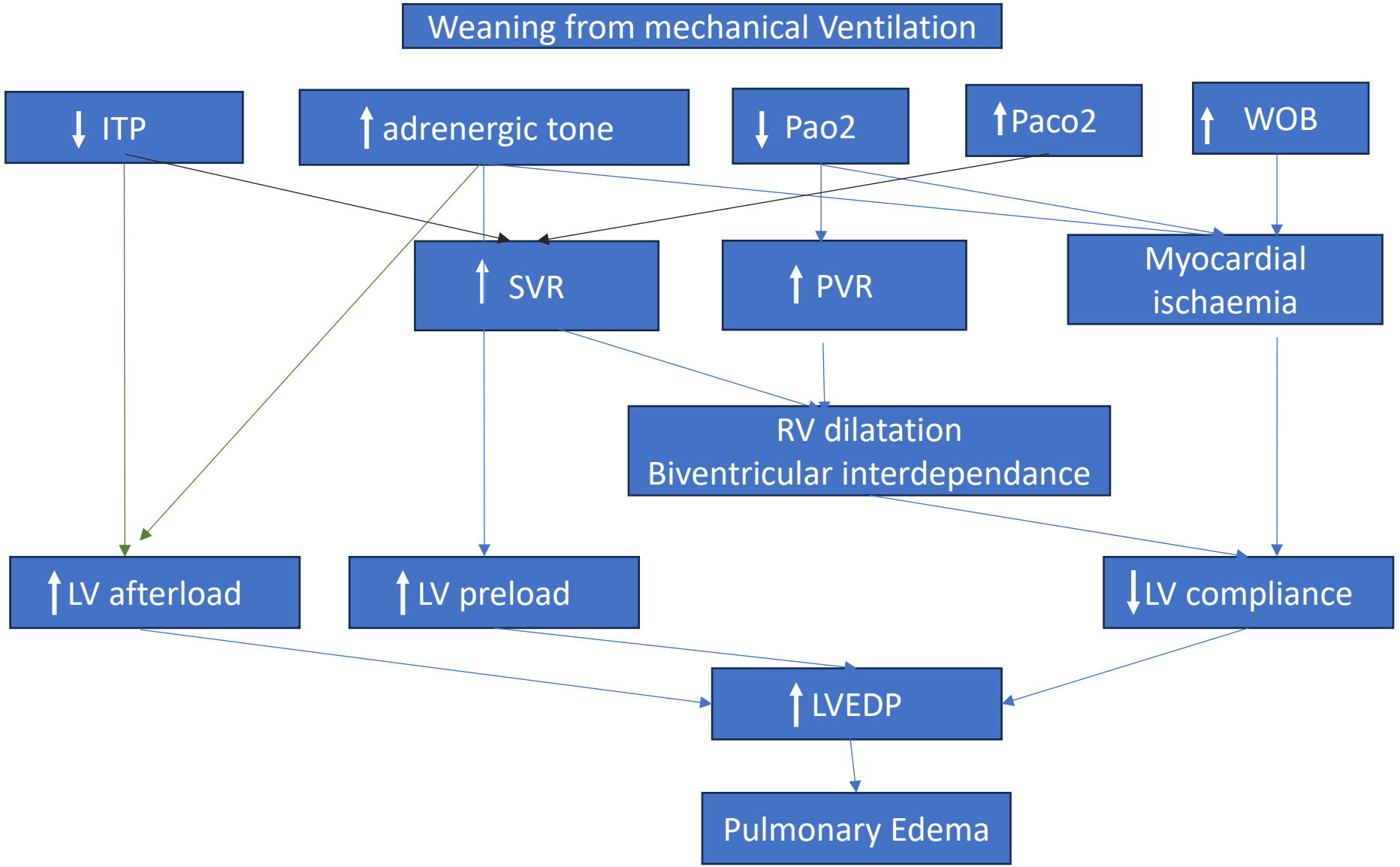
Christos F. Kampolis, MD, PhD [a,*], Maria Mermiri, MD [b], Georgios Mavrovounis, MD [b], Antonia Koutsoukou, MD, PhD [c], Angeliki A. Loukeri, MD, MSc [d], Ioannis Pantazopoulos, MD, PhD [b]

- Compare NAVA, PAV, ASV, and Smartcare/PS with standard PSV regarding their effectiveness for weaning in critically ill adults from IMV
- Primary outcome - weaning success
- Included 20 RCTs
- Secondary outcomes - weaning time, total MV duration, reintubation or use of non-invasive MV (NIMV) within 48 h after extubation, in-hospital and ICU mortality, in-hospital and ICU LOS

Summary estimates of effect and publication bias.

Outcome	ASV vs. PSV	NAVA vs. PSV	PAV vs. PSV	SmartCare vs. PSV
Successful weaning	RR: 1.00 (0.97, 1.03); $p = 0.98$ I^2: 0%; $p = 0.79$	RR: 1.15 (0.96, 1.38); $p = 0.14$ I^2: 31%; $p = 0.24$	*RR: 1.17 (1.04, 1.31); $p = 0.008$* *I^2: 0%; $p = 0.56$*	RR: 1.01 (0.92, 1.11); $p = 0.80$ I^2: 0%; $p = 0.66$
Weaning time (hours)	MD: −24.75 (−54.18, 4.69); $p = 0.10$ I^2: 98%; $p < 0.00001$	NA	MD: 0.03 (−1.44, 1.50); $p = 0.97$ I^2: 39%; $p = 0.20$	MD: −2.55 (−7.98, 2.88); $p = 0.36$ I^2: 66%; $p = 0.02$
Total duration of mechanical ventilation (days)	NA	MD: −4.89 (−10.80, 1.02); p = 0.10 I^2: 64%; $p = 0.04$	*MD: −2.31 (−2.85, −1.78); $p < 0.00001$* *I^2: 27%; $p = 0.25$*	MD: −0.37 (−0.94, 0.19); p = 0.20 I^2: 0%; $p = 0.51$
Need for re-intubation in the first 48 h after extubation	NA	NA	NA	RR: 1.09 (0.56, 2.13); $p = 0.81$ I^2: 0%; $p = 0.82$
Need for non-invasive mechanical ventilation in the first 48 h after extubation	NA	*RR: 0.67 (0.50, 0.89); $p = 0.005$* *I^2: 0%; $p = 0.40$*	NA	NA
In-hospital mortality	NA	*RR: 0.63 (0.46, 0.88); $p = 0.007$* *I^2: 0%; $p = 0.67$*	RR: 0.77 (0.54, 1.10); $p = 0.15$ I^2: 0%; $p = 0.47$	NA
ICU mortality	NA	*RR: 0.55 (0.36, 0.82); $p = 0.004$* *I^2: 0%; $p = 0.85$*	RR: 0.72 (0.44, 1.17); $p = 0.18$ I^2: 0%; $p = 0.42$	NA
Hospital stay (days)	NA	MD: −0.46 (−8.39, 7.46); $p = 0.91$ I^2: 56%; $p = 0.08$	MD: 1.40 (−2.17, 4.96); $p = 0.44$ I^2: 84%; $p < 0.0001$	MD: −1.01 (−4.31, 2.29); $p = 0.55$ I^2: 8%; $p = 0.34$
ICU stay (days)	MD: −1.82 (−4.40, 0.76); $p = 0.17$ I^2: 88%; $p = 0.0003$	MD: −1.17 (−4.42, 2.08); $p = 0.48$ I^2: 47%; $p = 0.13$	*MD: −1.67 (−2.29, −1.05); $p < 0.00001$* *I^2: 0%; $p = 0.53$*	MD: −0.99 (−2.19, 0.22); $p = 0.11$ I^2: 0%; $p = 0.70$

Cardiac Dysfunction



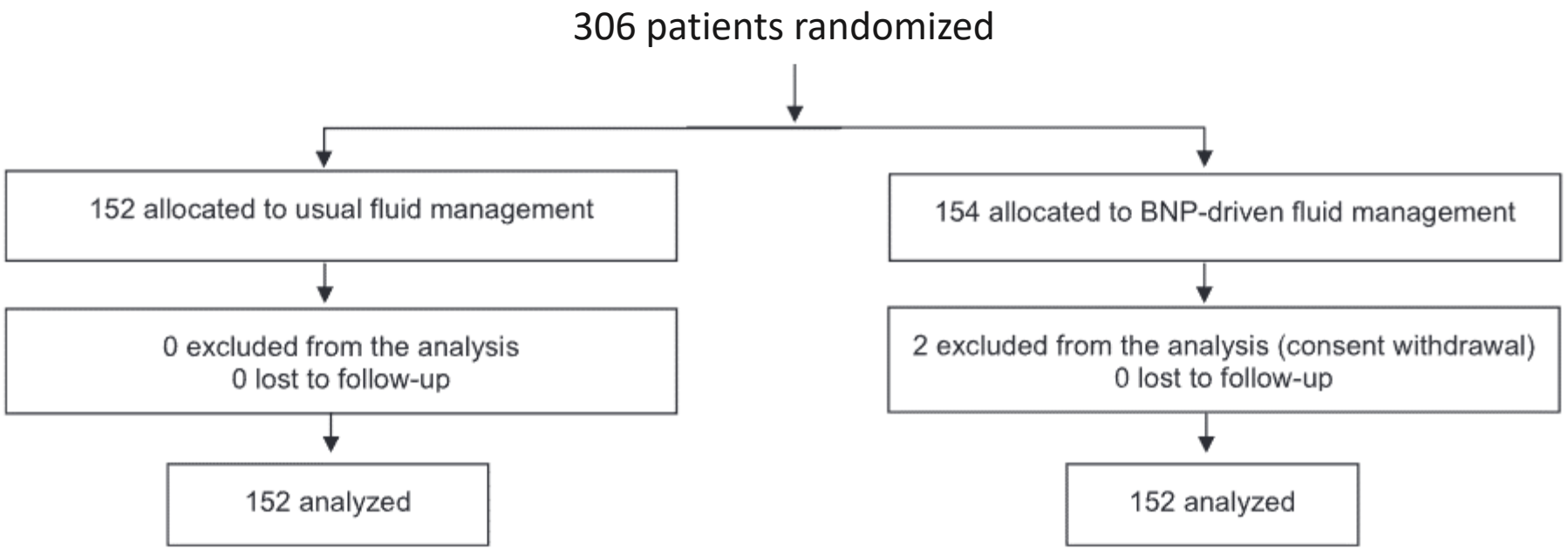
Routsi et al. Ann. Intensive Care (2019)

Natriuretic Peptide–driven Fluid Management during Ventilator Weaning

A Randomized Controlled Trial

ATS 2012

Armand Mekontso Dessap[1,2,3], Ferran Roche-Campo[1,4], Achille Kouatchet[5], Vinko Tomicic[6],

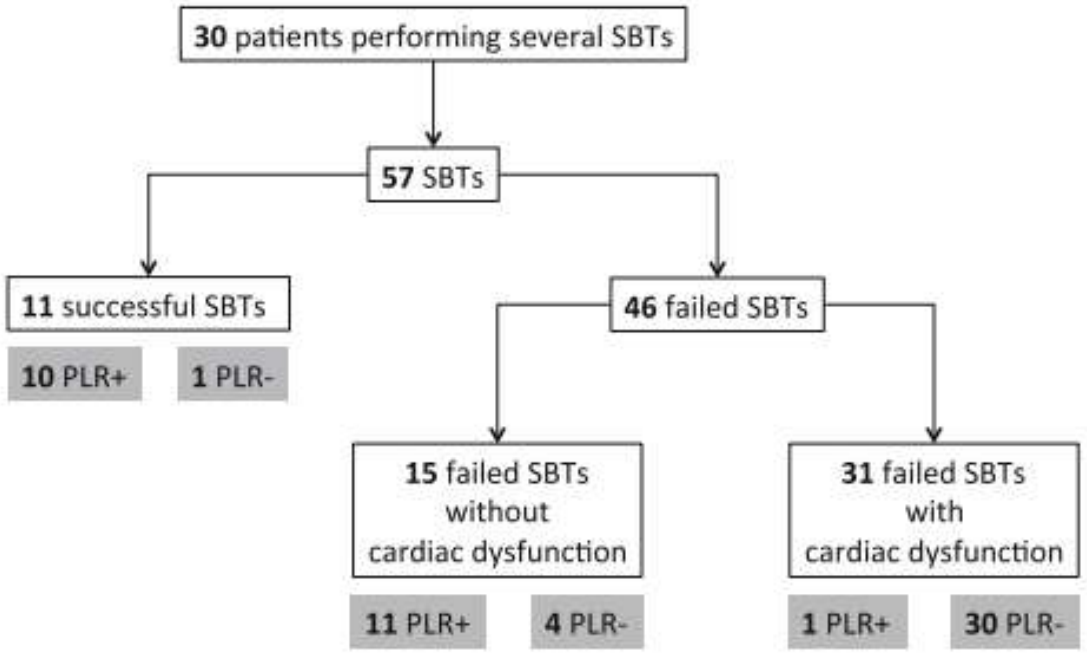


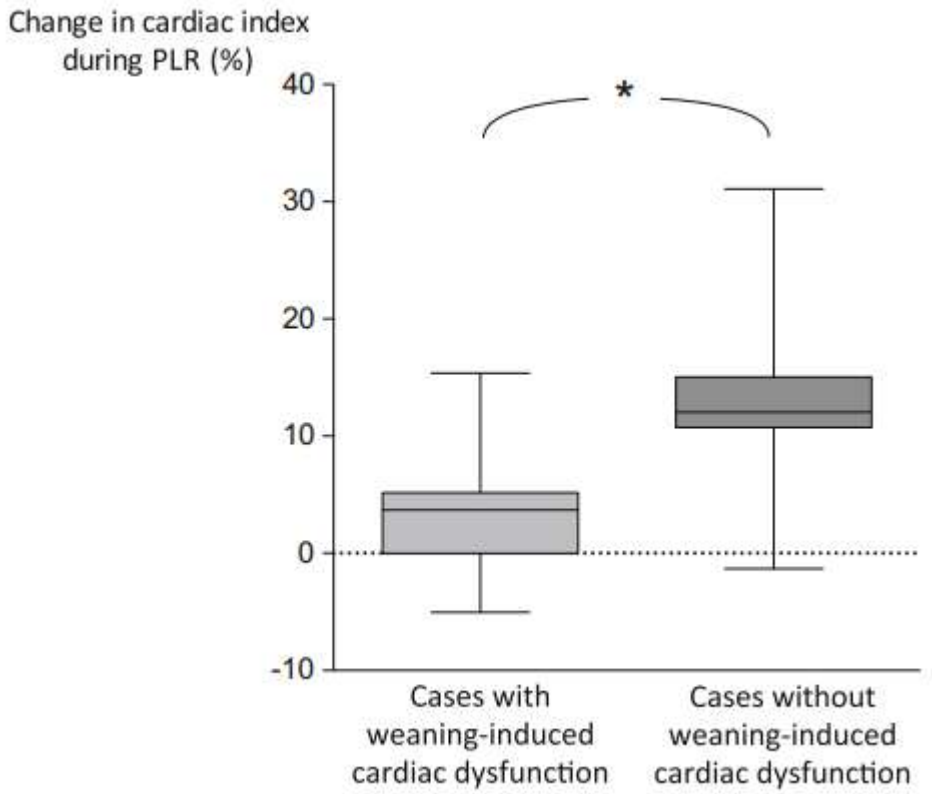
	Usual Care Group ($n = 152$)	BNP-guided Group ($n = 152$)	*P* Value
Time to first extubation, h			
Median (IQR)	47.7 (22.9–124.8)	39.8 (20.0–72.4)	0.019
Mean (SD)	92.8 (110.2)	70.6 (106.8)	
Time to successful extubation, h			
Median (IQR)	58.6 (23.3–139.8)	42.4 (20.8–107.5)	0.034
Mean (SD)	112.2 (147.1)	86.2 (127.9)	
Time to successful weaning from invasive and noninvasive ventilation, h			
Median (IQR)	74.4 (31.7–160.5)	49.3 (21.9–140.6)	0.051
Mean (SD)	134.3 (187.6)	107.1 (141.0)	
Ventilator-free days from randomization to Day 14, d			
Median (IQR)	9.7 (2.3–12.9)	12.0 (6.5–13.1)	0.026
Mean (SD)	8.2 (5.2)	9.3 (4.9)	
Ventilator-free days from randomization to Day 28, d			
Median (IQR)	23.3 (14.7–26.7)	25.9 (19.3–27.1)	0.038
Mean (SD)	18.9 (10.4)	20.3 (10.4)	
Ventilator-free days from randomization to Day 60, d			
Median (IQR)	54.9 (38.7–58.3)	57.9 (50.4–59.1)	0.015
Mean (SD)	42.8 (23.7)	45.7 (22.7)	
ICU stay length, d			
Median (IQR)	8.0 (4.0–13.0)	8.0 (4.0–14.0)	0.995
Mean (SD)	11.6 (12.3)	11.4 (11.2)	
Hospital stay length, d			
Median (IQR)	20.0 (12.0–33.0)	20.0 (13.0–33.0)	0.796
Mean (SD)	27.3 (37.3)	24.0 (14.2)	
ICU mortality	19 (12.5%)	18 (11.8%)	0.861
Hospital mortality	25 (16.4%)	20 (13.2%)	0.433
Day-60 mortality	28 (18.4%)	21 (13.8%)	0.275

Armand Mekontso Dessap ATS Journal 2012

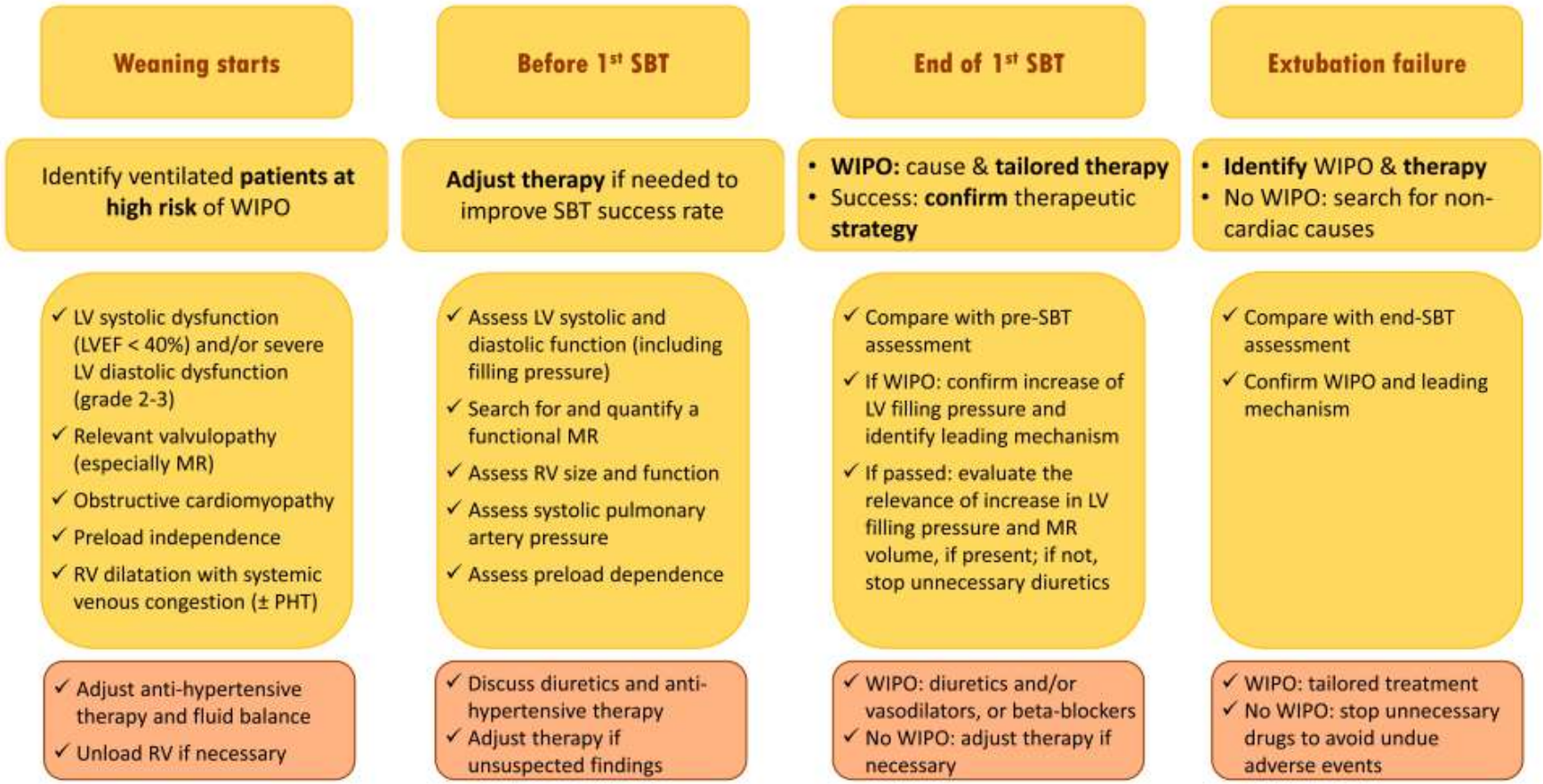
Passive leg raising performed before a spontaneous breathing trial predicts weaning-induced cardiac dysfunction

- Included 30 patients after a first failed 1-h T-tube SBT who had a transpulmonary thermodilution (PiCCO 2) already in place
- Preload independence - PLR was assessed before the second SBT





- If PLR did not increase the CI by > 10 % before the SBT, the occurrence of SBT failure related to cardiac dysfunction was predicted with a sensitivity of 97 % [95 % CI 83–100], specificity of 81 % (95 % CI 61–93) and AUC of 0.88 (95 % CI 0.78–0.98)



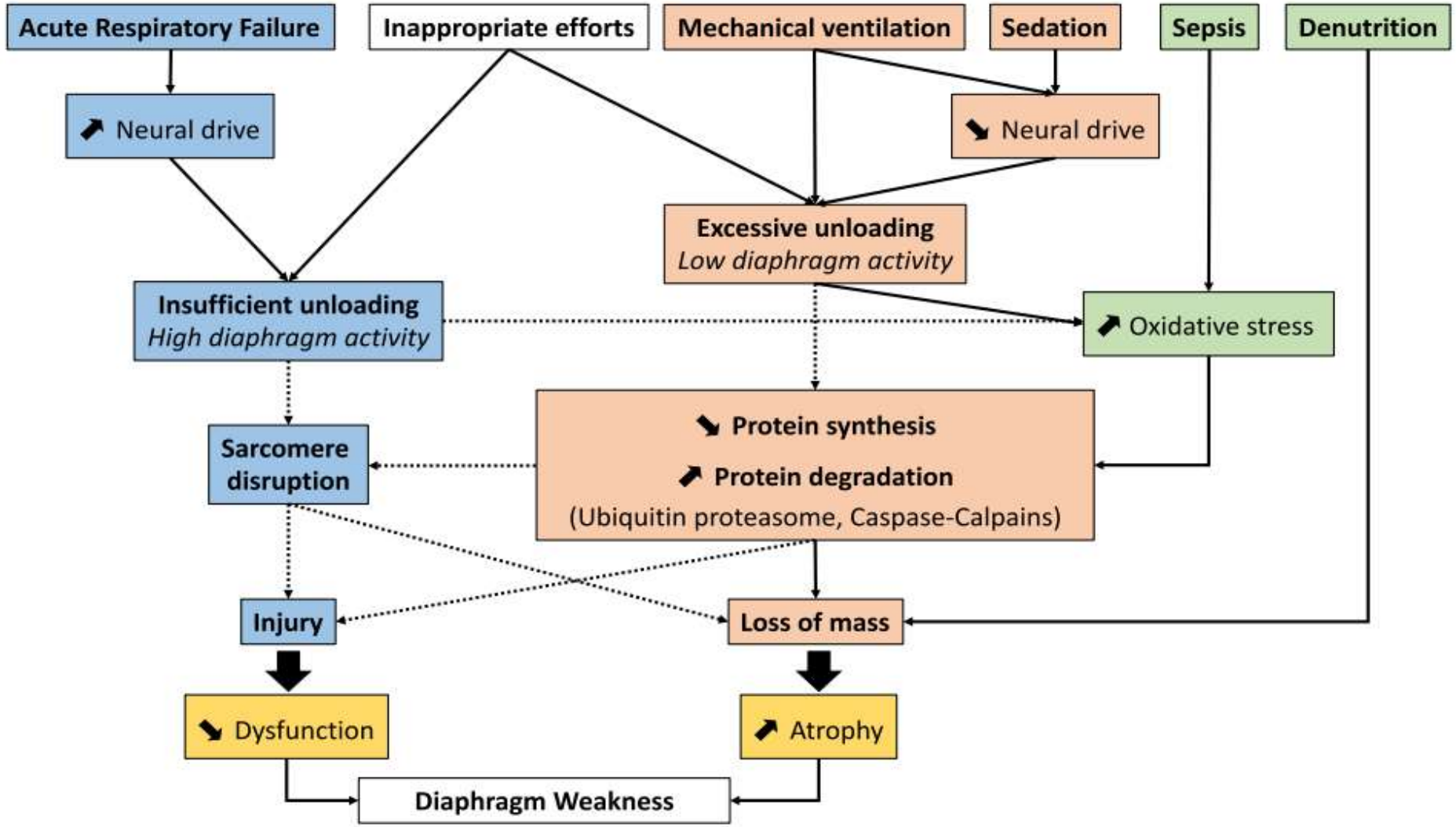
Routsi et al. Ann. Intensive Care (2019)

Neuromuscular causes

- Reduced central drive, Neuromuscular weakness, CINMA
- MV is associated with ICU-acquired complications, such as diaphragm weakness – VIDD
- At least 25% of patients who are intubated for more than 7 days develop ICU-acquired weakness
- Up to 80 - 100% of those who have severe sepsis and SIRS develop CINMA
- Development of ICUAW can lead to difficulty in weaning and prolonged MV

De Jonghe et al JAMA 2002
Bednarik et al J Neurol 2005
Narjeet et al IJCCM 2021

Pathways involved in the occurrence of diaphragm weakness in critically ill patients



Martin Dres et al ICM 2017

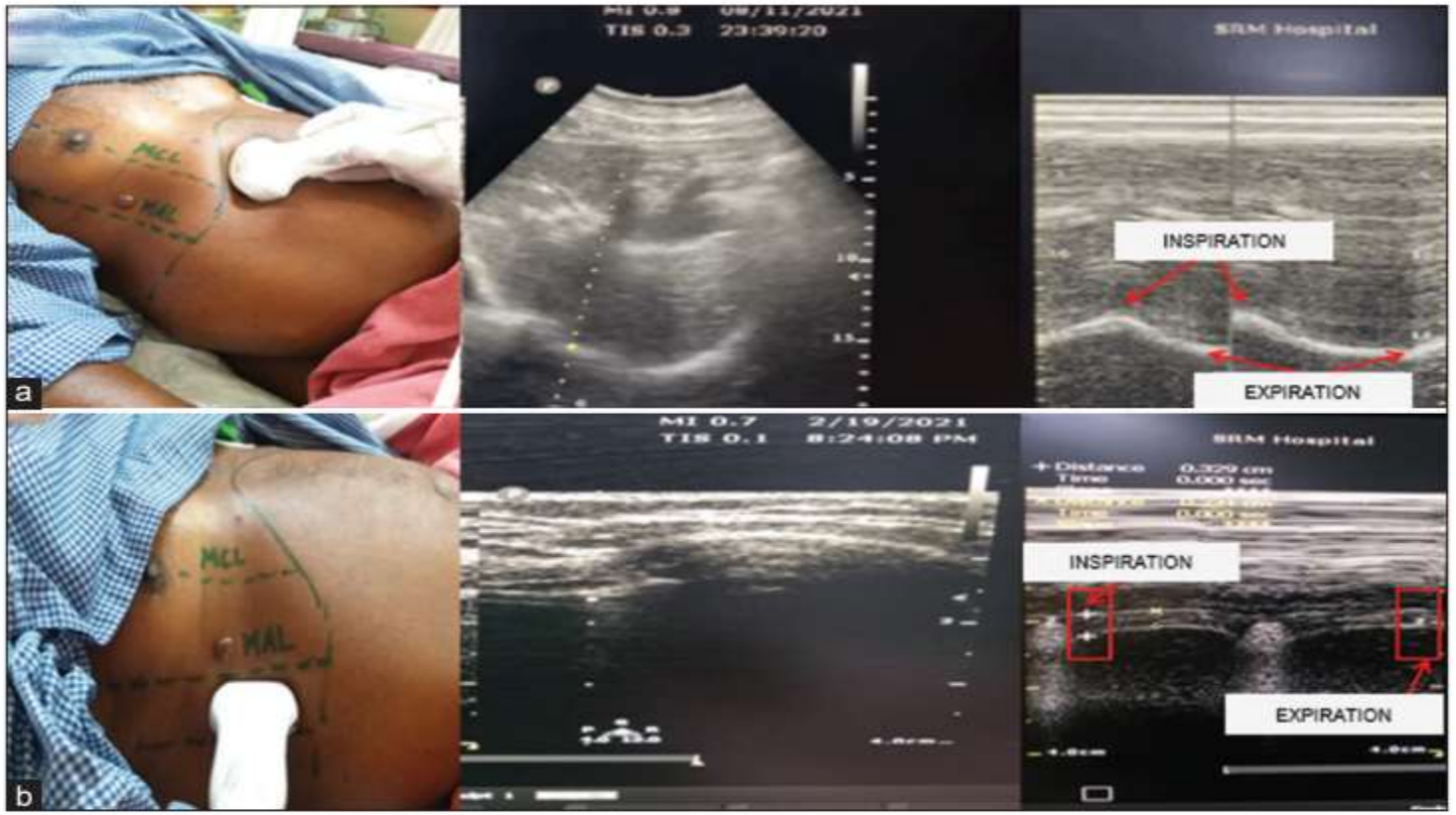
Role of diaphragm ultrasound in weaning mechanically ventilated patients: A prospective observational study

Ravi Saravanan, Krishnamurthy Nivedita, Krishnamoorthy Karthik, Rajagopalan Venkatraman

Department of Anaesthesiology, SRM Medical College Hospital and Research Institute, Potheri, Chennai, Tamil Nadu, India

- Prospective observational Cohort study
- 200 adult patients on MV were enrolled
- Patients assessed for readiness to wean

USG Diaphragm was done – Diaphragmatic excursion and DTF were calculated
[DTF = (TDmax − TDmin)/TDmin × 100]

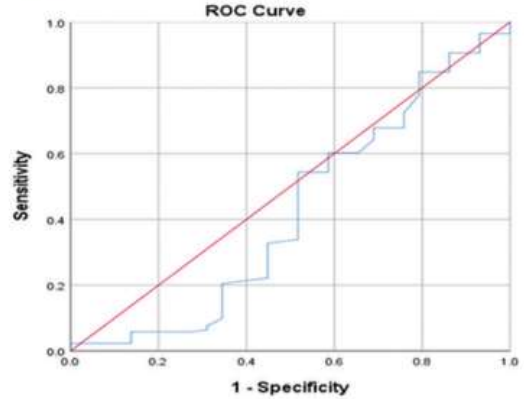


Parameters	Weaning Success (*n*=171)		Weaning Failure (*n*=29)		*P* value
RSBI	52.853±19.995	52.00 (40.00-65.00)	59.630±25.061	60.00 (41.15-85.00)	0.405 (NS)
DTF (%)	54.288±19.202	55.00 (39.00-64.00)	43.578±20.718	37.00 (27.25-62.00)	0.019
DE (cm)	1.933±0.682	1.73 (1.56-2.20)	1.215±0.662	1.12 (0.78-1.52)	<0.001

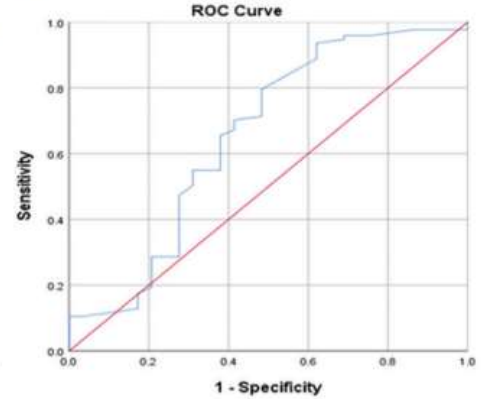
Table 2: Sensitivity, specificity, positive predictive value and negative predictive value for each parameter in predicting weaning success

Parameter	Cut off range	Sensitivity %	Specificity %	PPV %	NPV %	Youden's index	AUROC
RSBI	<82	94.0	31.0	89.0	45.0	0.25	0.422
DTF (%)	>37%	79.5	51.7	90.7	30.0	0.31	0.654
DE (cm)	>1.21	93.6	71.4	95.2	64.5	0.65	0.809
RSBI-DTF	>0.854	66.7	69.0	92.7	26.0	0.36	0.656
RSBI-DE	>0.738	93.0	71.4	95.2	62.5	0.64	0.807

RSBI:



DTF:



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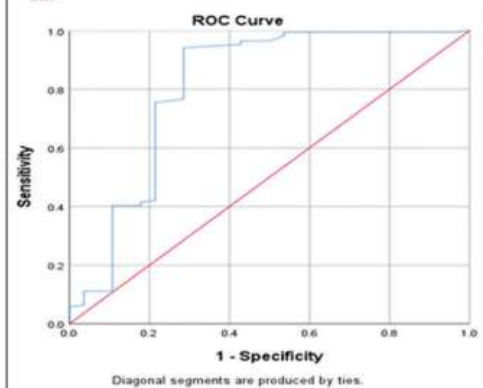

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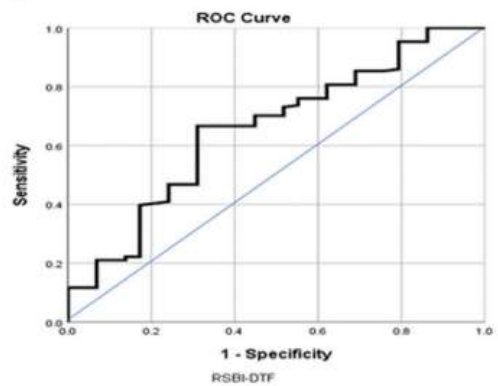


RSBI-DE:

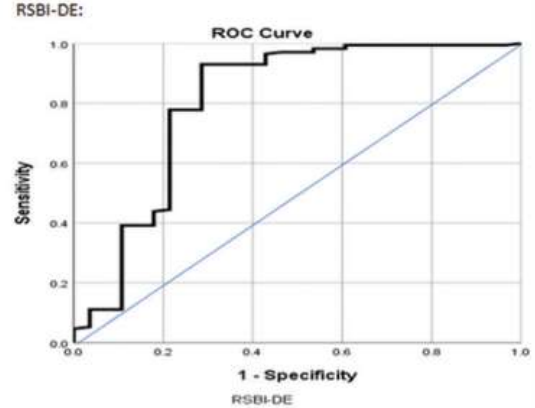


Table 3 Strategies to prevent and to treat diaphragm weakness in mechanically ventilated patients

Preventive strategies	Level of evidence	Clinical recommendations
Prevention of disuse atrophy		
Maintaining inspiratory efforts	High (experimental and clinical data)	Spontaneous breathing should be preferred (except in case of high drive)
Phrenic nerve pacing	Low (experimental data)	Not in routine practice
Inspiratory muscles training		
Progressive threshold loading	Moderate (clinical data)	Can be implemented in specific populations (long-term ventilation)
Pharmacological approach		
Antioxidants (*N*-acetylcysteine)	Low (experimental and clinical data)	Not recommended
Curatives or rescue techniques		
Phrenic nerve pacing		
Restoring progressively diaphragm function	Low (only experimental data)	Not in routine practice
Pharmacological approach		
Anabolics	Low (experimental data)	Not in routine practice
Optimization of muscle contractility		
Theophylline	Moderate (experimental and clinical data)	Not in routine practice
Levosimendan	Moderate (experimental and clinical data)	Not in routine practice

Martin Dres et al ICM 2017

Neuromuscular weakness – Prevention

- Intensive glucose control – Lower incidence of CIP/CIM and duration of MV
- Early mobilization –
- NMES/EMS may reduce the CIPM and improve the MRCS score

Study (place/year)	TEAM study (12 ICU in Australia and Newzelands/2015)
Population	ICU patients who were functionally independent and expected to be ventilated for >48 hrs
Method	Mobilization during first 14 days or extubation/ ICUAW at ICU discharge/ 90 day mortality and return to work at 6 month were measured.
outcome	Of 1288 planned early mobilization episode no mobilization occurred in 1079. the maximum levels of mobilization were exercises in bed (N = 94, 7%), standing at the bed side (N = 11, 0.9%) or walking (N = 26, 2%). In 94 of the 156 ICU survivors, 48 (52%) had ICU-AW. The MRC-SS score was higher in those patients who mobilized while mechanically ventilated (50.0 ± 11.2 versus 42.0 ± 10.8, P = 0.003). Patients who survived to ICU discharge but who had died by day 90 had a mean MRC score of 28.9 ± 13.2 compared with 44.9 ± 11.4 for day-90 survivors (P <0.0001).

Finfer et al NEJM 2009
Routsi et al Crit Care 2010
Abukhabar et al 2013

Psychological dysfunction

- Delirium – disturbance of the level of cognition and arousal
- Delirium has been associated with many modifiable risk factors in ICU such as untreated pain, hypoxemia, anemia, sepsis, psychoactive drugs, and sleep deprivation
- Delirium can occur in up to 80% of patients in ICU

Goldberg et al JAMA 2020
Kotfis K et al 2018

- Anxiety and depression –
- Many patients suffer significant anxiety during their icu stay
- Contributors are dyspnea, inability to communicate and sleep disturbances
- Prevalence of anxiety reported to be 30-75%
- Polysomnography showed frequent arousal and sleep fragmentation
- These patients are associated with longer ICU and hospital length of stay

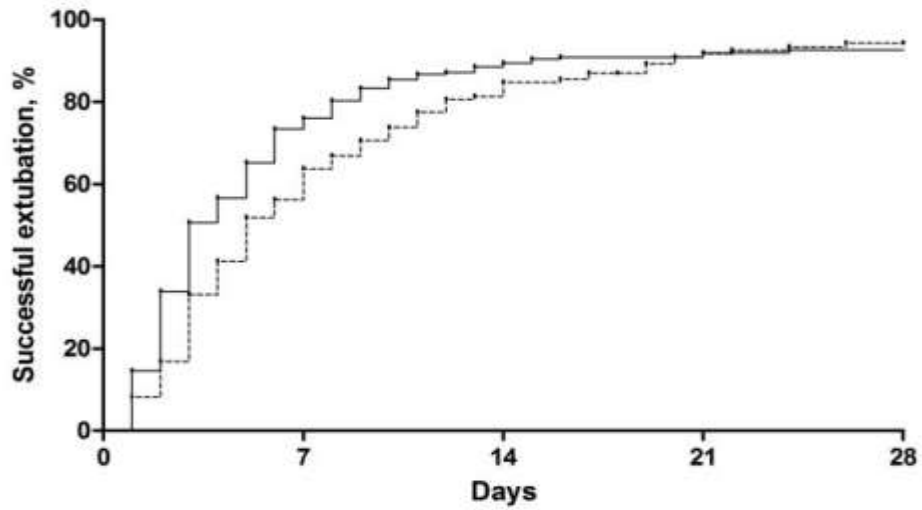
Andrew May et al ICM 2021
Alireza et al JCCM 2021
Brijesh et al JCCM 2021

Impact of delirium on weaning from mechanical ventilation in medical patients

KYEONGMAN JEON,[1,2]* BYEONG-HO JEONG,[2]* MYEONG GYUN KO,[3] JIMYOUNG NAM,[3] HONGSEOK YOO,[2] CHI RYANG CHUNG[1] AND GEE YOUNG SUH[1,2]

- Cohort study
- Delirium was assessed by using the Confusion Assessment Method for the ICU (CAM-ICU)
- 393 patients with MV support underwent a SBT
- Mean age 70 yrs (CAM ICU+), 61 yrs in (CAM ICU -)
- Mean SOFA score on ICU admission 6 vs 9 in CAM ICU +
- 160 (40.7%) were diagnosed with delirium on the day of the first SBT

	Total (n = 393)	CAM-ICU (–) (n = 233)	CAM-ICU (+) (n = 160)	P-value
Extubation	301 (76.6)	190 (81.5)	111 (69.4)	0.005
Extubation failure within 48 h	92/301 (30.6)	48/190 (25.3)	44/111 (39.6)	0.009
Reintubation	71/301 (23.6)	32/190 (16.8)	39/111 (35.1)	<0.001
Classification of weaning				
Simple weaning	251 (63.9)	165 (70.8)	86 (53.8)	0.001
Difficult weaning	89 (22.6)	44 (18.9)	45 (28.1)	0.032
Prolonged weaning	53 (13.5)	24 (10.3)	29 (18.1)	0.026
Tracheostomy after the first weaning trial	90 (22.6)	35 (15.0)	55 (34.4)	<0.001
ICU mortality	44 (11.2)	26 (11.2)	18 (11.3)	0.978
Length of stay in ICU, days	8 (4–14)	6 (4–12)	10 (6–16)	<0.001
Hospital mortality	117 (29.9)	62 (26.6)	55 (34.8)	0.082
Length of stay in hospital, days	29 (16–52)	25 (15–49)	33 (18–59)	0.022



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Haloperidol for the Treatment of Delirium in ICU Patients

N.C. Andersen-Ranberg, L.M. Poulsen, A. Perner, J. Wetterslev, S. Estrup,

- Multicentre, blinded, placebo-controlled, RCT
- Patients with positive results on a screening test for delirium according to either CAM-ICU or the ICDSC were assessed for eligibility
- N = 1000, 1:1, 510 – Haloperidol, 490 – placebo
- Median age 70/71 yrs
- 447 patients had hyperactive delirium and 540 patients had hypoactive delirium

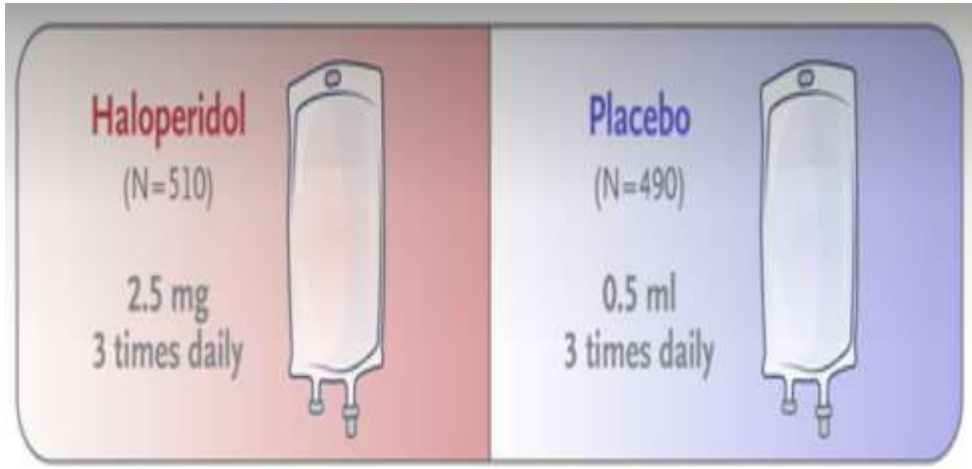
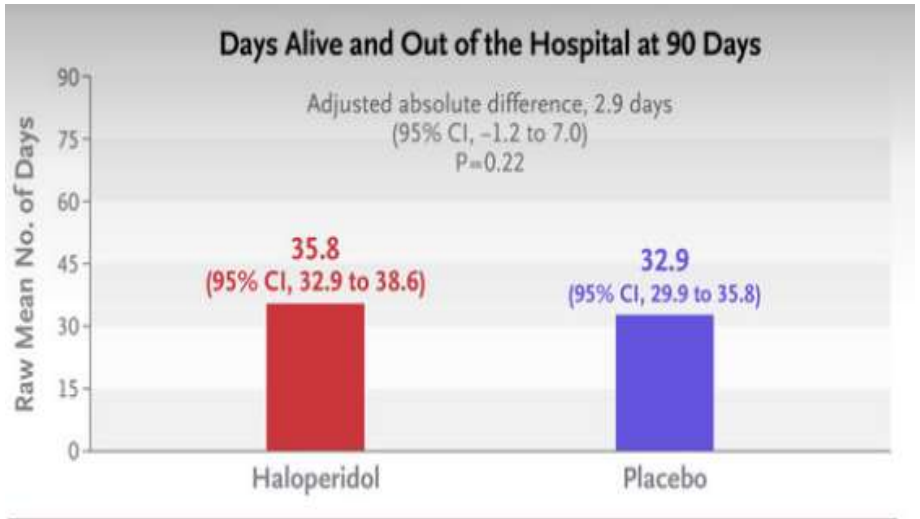
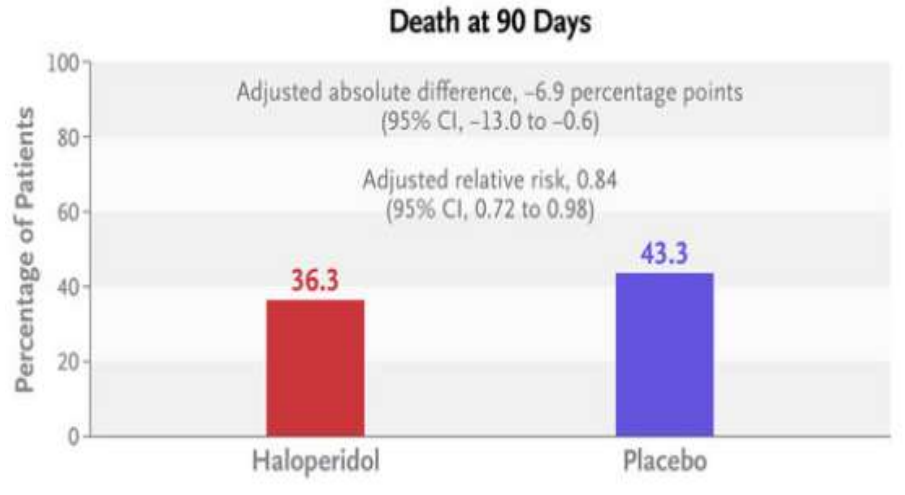


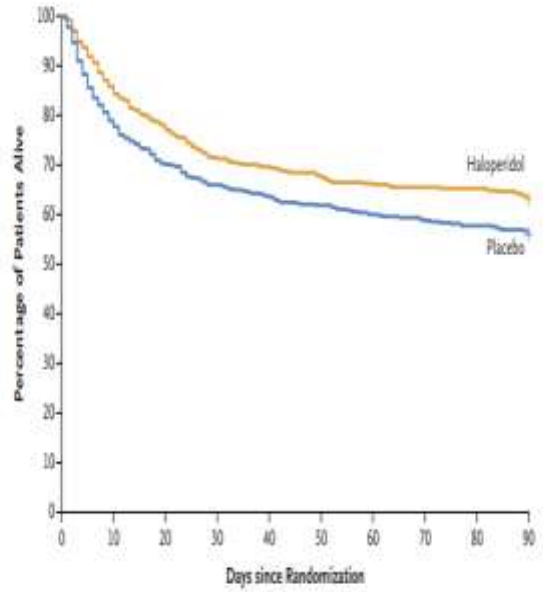
Table 3. Primary and Secondary Outcomes.*

Outcome	Haloperidol	Placebo	Adjusted Absolute Difference (95% or 99% CI)†	Adjusted Relative Risk (95% or 99% CI)†	P Value
Primary outcome					
Days alive and out of hospital at 90 days — raw mean no. (95% CI)‡	35.8 (32.9 to 38.6)	32.9 (29.9 to 35.8)	2.9 (–1.2 to 7.0)§	NC	0.22¶
Death — no./total no. (%)‖	182/501 (36.3)	210/485 (43.3)	–6.9 (–13.0 to –0.6)**	0.84 (0.72 to 0.98)	
Length of hospital stay — raw mean no. of days (95% CI)††	28.8 (26.7 to 30.8)	26.4 (24.4 to 28.5)	2.3 (–0.6 to 5.1)§	NC	
Secondary outcomes					
Days alive without delirium or coma — raw mean no. (99% CI)‡‡	57.7 (53.4 to 62.0)	52.6 (48.0 to 57.1)	5.1 (–1.2 to 11.3)§	NC	
Days alive without mechanical ventilation — raw mean no. (99% CI)	57.9 (53.7 to 62.2)	53.9 (49.5 to 58.3)	4.0 (–2.2 to 10.1)§	NC	
Serious adverse reaction in ICU — no./total no. (%)	11/501 (2.2)	9/486 (1.9)	0.4 (–1.9 to 2.7)**	1.20 (0.33 to 5.45)	
Use of rescue medication — no./total no. (%)§§	288/501 (57.5)	302/486 (62.1)	–4.0 (–11.8 to 3.6)**	0.93 (0.82 to 1.06)	
Days with use of rescue medication per patient — raw mean no. (99% CI)	2.9 (2.3 to 3.5)	2.9 (2.3 to 3.4)	0.1 (–0.7 to 0.9)	NC	





A Overall Survival

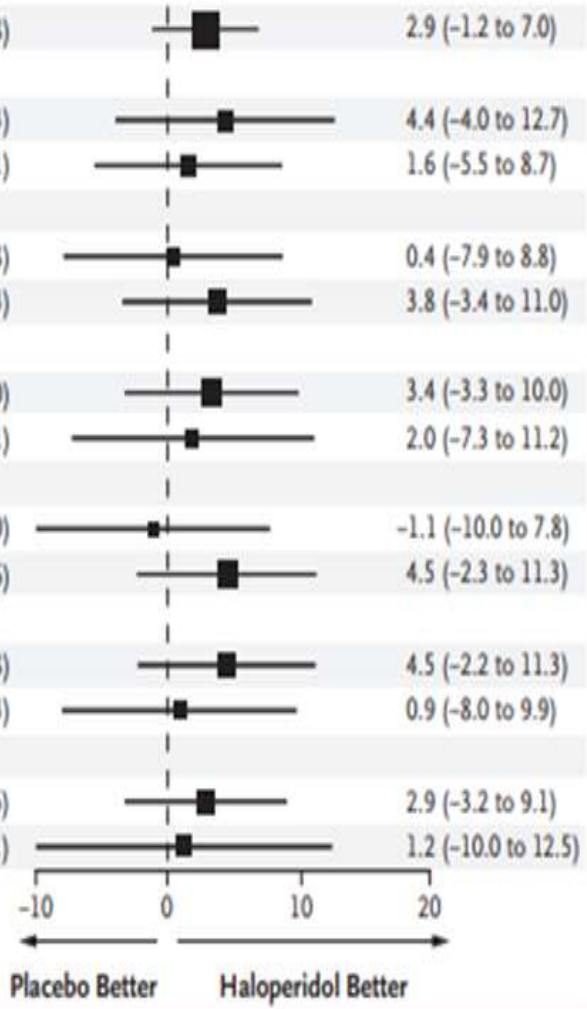


No. at Risk

Haloperidol	501	430	391	358	349	340	332	328	327	319
Placebo	485	383	341	320	309	300	291	286	280	275

B Main and Subgroup Analyses of the Primary Outcome

Subgroup	No. of Patients		Mean No. of Days Alive and Out of Hospital (95% CI)		Adjusted Mean Difference (95% or 99% CI)
	Haloperidol	Placebo	Haloperidol	Placebo	
All patients	501	486	35.8 (32.9 to 38.7)	32.9 (29.9 to 35.8)	2.9 (−1.2 to 7.0)
Motor subtype of delirium					
Hyperactive	217	216	39.3 (34.9 to 43.7)	34.9 (30.4 to 39.3)	4.4 (−4.0 to 12.7)
Hypoactive	274	256	33.0 (29.3 to 36.8)	31.2 (27.3 to 35.1)	1.6 (−5.5 to 8.7)
Age					
<69 yr	221	189	39.3 (35.2 to 43.4)	39.1 (34.5 to 43.8)	0.4 (−7.9 to 8.8)
≥69 yr	270	283	32.9 (29.0 to 36.9)	28.7 (24.9 to 32.4)	3.8 (−3.4 to 11.0)
Sex					
Male	319	314	35.6 (32.1 to 39.1)	32.4 (28.8 to 36.0)	3.4 (−3.3 to 10.0)
Female	172	158	36.2 (31.2 to 41.2)	33.8 (28.6 to 39.1)	2.0 (−7.3 to 11.2)
Admission type					
Surgical	178	149	36.9 (32.4 to 41.5)	36.9 (31.9 to 42.0)	−1.1 (−10.0 to 7.8)
Medical	313	323	35.2 (31.5 to 38.8)	31.0 (27.4 to 34.6)	4.5 (−2.3 to 11.3)
Risk factors for delirium					
Yes	308	279	37.5 (33.9 to 41.1)	33.0 (29.2 to 36.8)	4.5 (−2.2 to 11.3)
No	183	193	32.9 (28.2 to 37.6)	32.7 (27.9 to 37.4)	0.9 (−8.0 to 9.9)
SMS-ICU					
<25	383	361	38.5 (35.3 to 41.7)	35.3 (32.0 to 38.6)	2.9 (−3.2 to 9.1)
≥25	108	111	26.3 (20.3 to 32.3)	25.1 (19.0 to 31.1)	1.2 (−10.0 to 12.5)



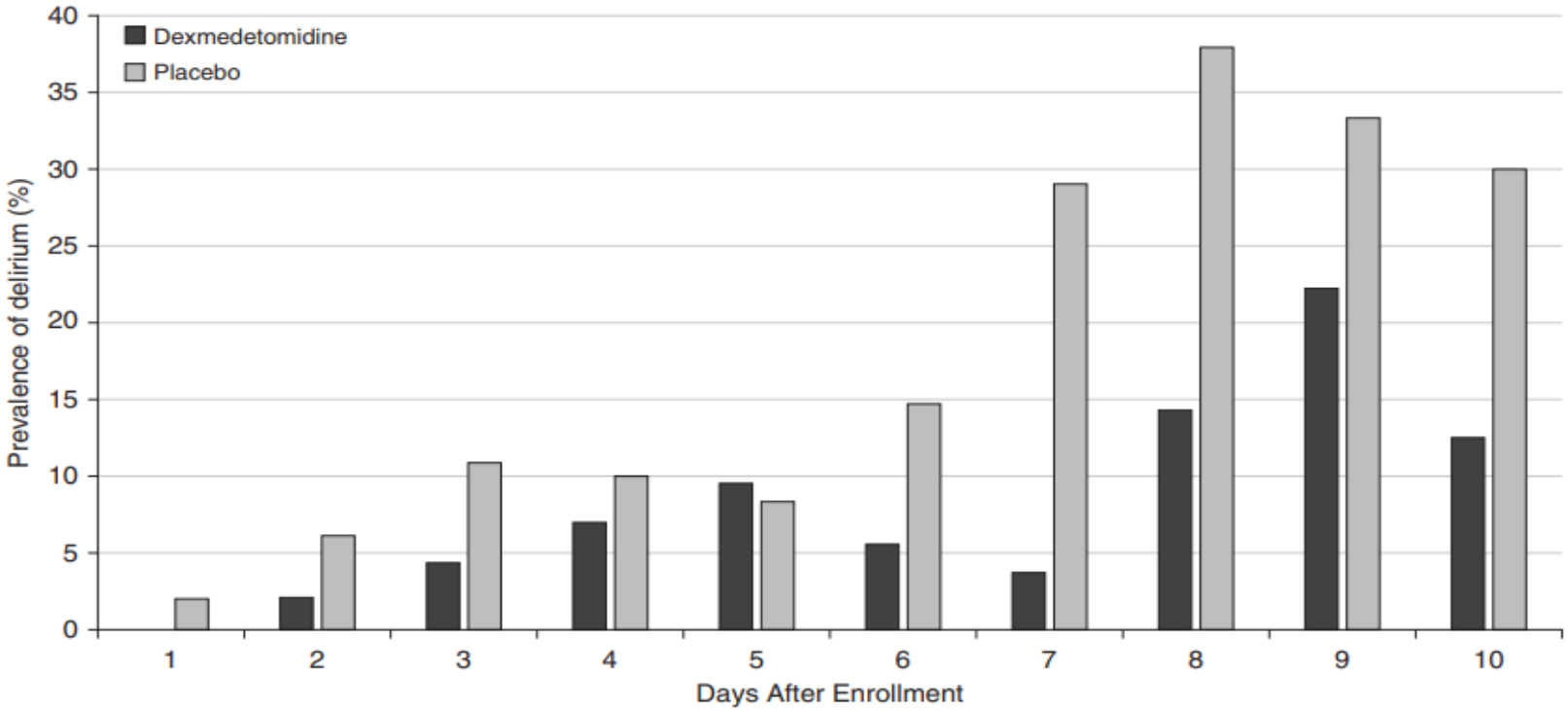
Low-Dose Nocturnal Dexmedetomidine Prevents ICU Delirium

A Randomized, Placebo-controlled Trial

Yoanna Skrobik[1,2], Matthew S. Duprey[3,4], Nicholas S. Hill[4], and John W. Devlin[3,4]

[1]Department of Medicine, McGill University, Montreal, Quebec, Canada; [2]Regroupement de Soins Critiques Respiratoires, Réseau de Santé Respiratoire, Fonds de Recherche du Québec-Santé, Montréal, Québec, Canada; [3]School of Pharmacy, Northeastern University, Boston, Massachusetts; and [4]Department of Pulmonary, Critical Care, and Sleep Medicine, Tufts Medical Center, Boston, Massachusetts

- Two-center, double-blind, placebo-controlled trial
- Randomized 100 delirium-free critically ill adults receiving sedatives to receive nocturnal (9:30 P.M. to 6:15 A.M.) iv dexmedetomidine (0.2 mg/kg/h, titrated by 0.1 mg /kg/h every 15 min until a goal RASS score of -1 or maximum rate of 0.7 mg/kg/h was reached) or placebo until ICU discharge
- During study infusions, all sedatives were halved; opioids were unchanged
- Delirium was assessed using the Intensive Care Delirium Screening Checklist every 12 hours throughout the ICU admission



40 (80%) of 50 patients] vs. placebo [27 (54%) of 50 patients]; relative risk, 0.44; 95% confidence interval, 0.23–0.82; P = 0.006

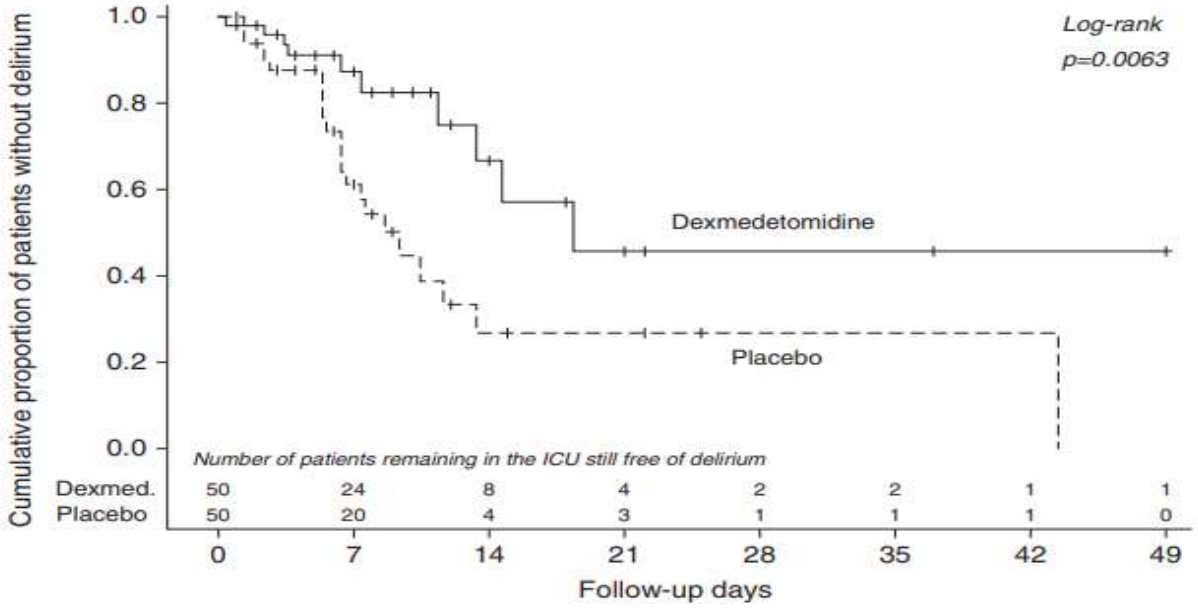
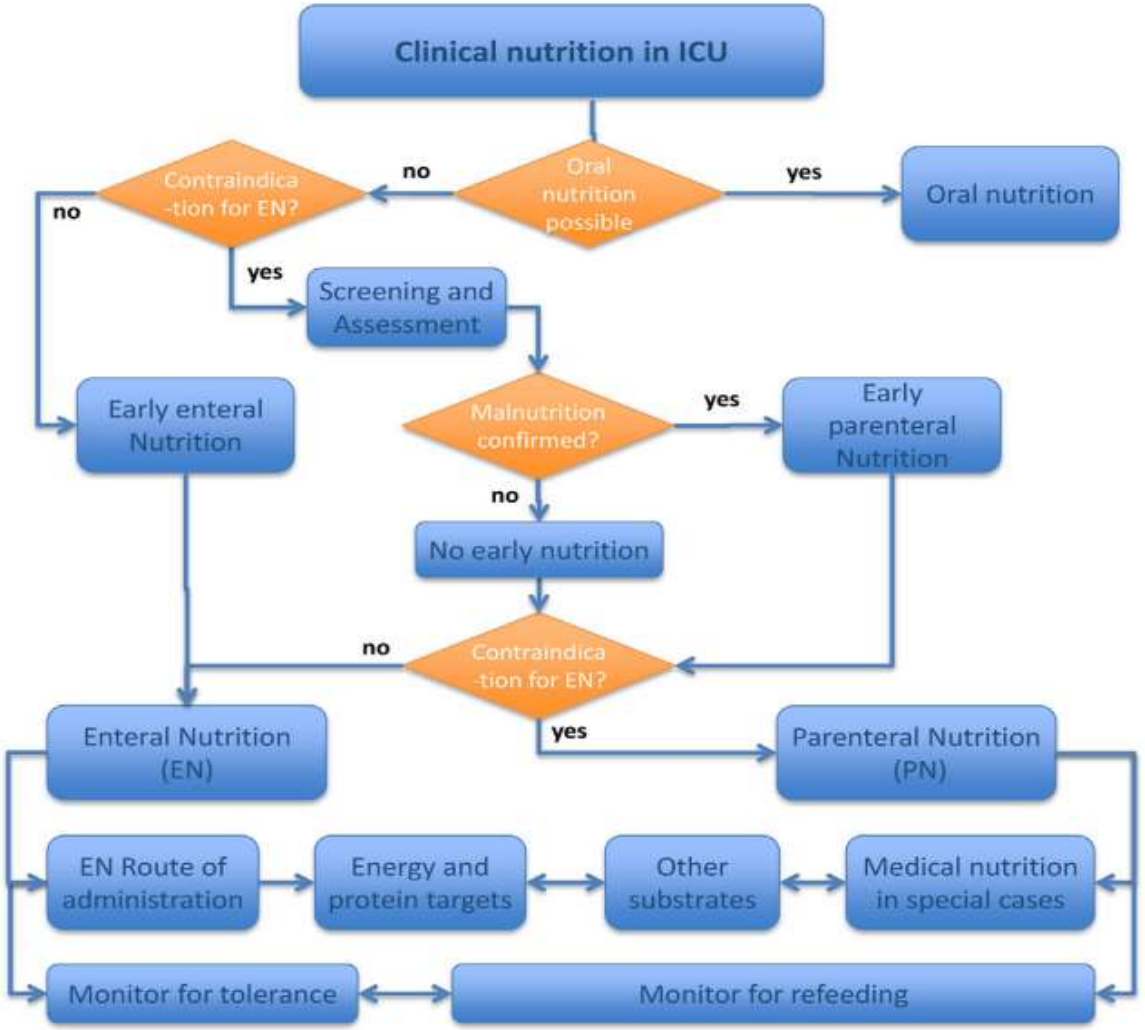


Table 5. Clinical Outcomes during and after the Period of ICU Admission

Variable	Dexmedetomidine (*n* = 50)	Placebo (*n* = 50)	*P* Value
Duration of mechanical ventilation, d, median (IQR)	3 (2–9)	4 (2–10)	0.94
Duration of ICU stay, d, median (IQR)	10 (4–20)	9 (3–19)	0.56
ICU mortality, *n* (%)	9 (18)	6 (12)	0.22
Duration of hospital stay, d, median (IQR)	27 (5–45)	29 (17–41)	0.48
Hospital mortality, *n* (%)	13 (26)	11 (22)	0.64

Nutrition in ICU

- Nutritional status monitoring, time to initial EN, calories, and target requirements are associated with positive effects on the duration of mechanical ventilation
- ESPEN guidelines suggest an energy requirement of 20-25 kcal/kg/day and 1.3 g/kg protein equivalents/day



ESPEN guidelines 2023
Koontalay A et al 2021

Nutritional support for successful weaning in patients undergoing prolonged mechanical ventilation

Shih-Ching Lo[1,2,3], Kevin Sheng-Kai Ma[4,5,6], Yen-Ru Li[7], Zi-Yue Li[8], Cheng-Hung Lin[9], Hsing-Chun Lin[2,3,10] & Shun-Fa Yang[1,10]✉

- Retrospective study
- Aim – To study the association between nutritional provision and successful ventilator weaning
- Primary outcome – Optimal nutrition intake
- Clinical outcomes – Length of stay, mortality, disease severity and hospital cost
- N = 326, 161 were extubation success, 161 – extubation failure

- The successful extubation group consisted of patients who tended towards IBW during the weaning process (BMI 23.9 ± 5.0 versus 22.7 ± 4.8 kg/m2, $p < 0.001$)
- Patients of successful extubation received significantly more calories and protein after weaning (23.8± 7.8 kcal versus 27.8 ± 9.1 kcal, $p < 0.001$ and 0.97 ± 0.36 g versus 1.14 ± 0.42 g, $p < 0.001$)
- Successful weaning was associated with a higher survival rate ($p = 0.016$), shortened hospital stay ($p = 0.001$), and reduced medical costs ($p < 0.001$)

Post extubation

- Laryngeal edema can lead to stridor and post-extubation respiratory failure
- Risk factors include high cuff pressure, duration of ET intubation, excess ET secretions, difficult intubation, h/o self-extubation etc
- Studies showed the role of corticosteroids (MPS) 4-12 hrs before extubation in at-risk patients
- Doing cuff leak test for at-risk patients can be helpful

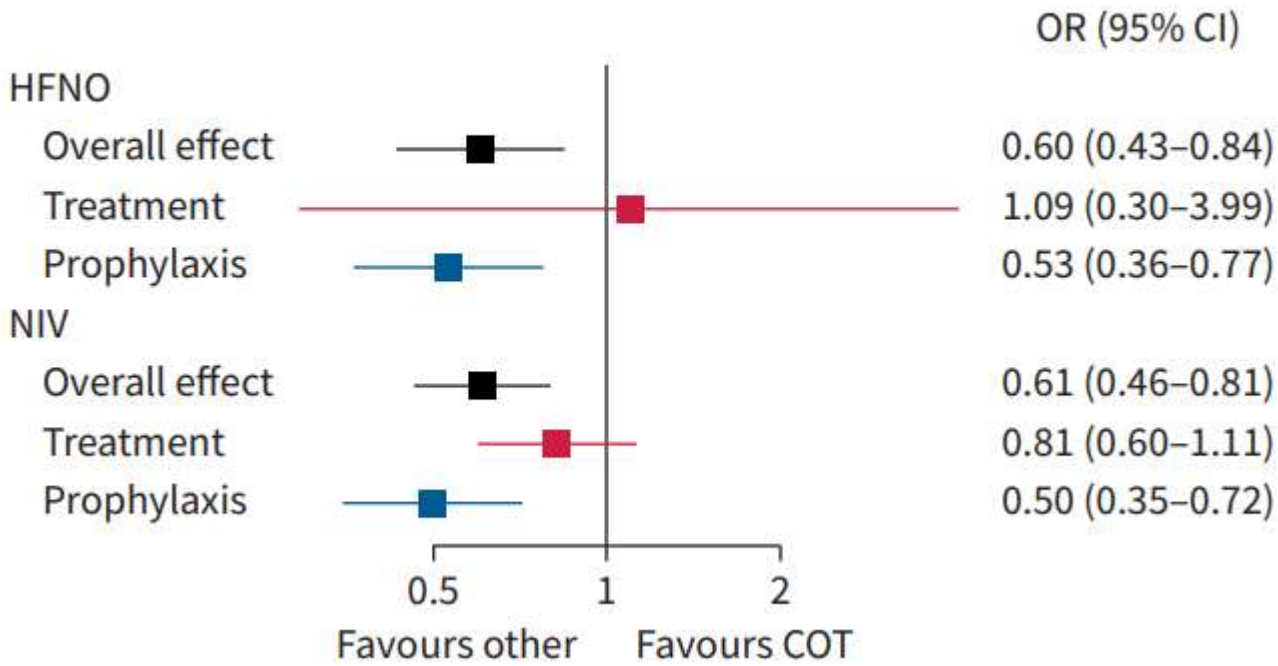
Wouter A et al Crit Care 2015
Francis et al
Cheng et al

	Effect of post extubation HFNC vs NIV on reintubation and postextubation RF in high risk patients – Hernandez et al JAMA 2016	Effect of post extubation NIV with active humidification vs HFNC on reintubation in patients at very high risk for extubation failure – Hernandez et al ICM 2022
Study	Multicentre RCT, 3 ICU in spain	RCT in 2 ICUs in spain
Population	N = 604	N = 182
Intervention & Comparison	NIV – 314, HFNC - 290 SBT with either t-tube or PSV 7/0 for 30-120 min (**Low HF, high surgical pts in HFNC**) spo2 target <92%	NIV – 92, HFNC – 90 SBT with PSV 7/0 Spo2 target >92%, **Heart disease,copd,pts with >2 comorbidities, more surgical pts in HFNC grp**
Inclusion Criteria	Adult pts receiving MV >12 hrs, ready for scheduled extubation	Pts receiving MV ≥ 24 hrs, ready for scheduled extubation
Primary Outcome	**Reintubation within 72 hrs** – 60(19.1%) in NIV vs 66(22.8%) in HFNC group (Diff -3.7%, CI -9.1 to ∞) **Post extubation RF** – 125(39.8) vs 78(26.9) [diff 6.6 to ∞) reaching noninferiority threshold(10)	Reintubation within 7 days – 21 (22.8%) in NIV vs 35 (38.9%) in HFNC [Diff -16, CI-29.2 to -0.3, p=0.019]
Secondary Outcomes	Median ICU length of stay after randomization – 4 vs 3 days (NIV vs HFNC) p=0.048 Adverse events – more in NIV – 135(43) vs 0 (p=.001) Mortality, VAP, time to reintubation – similar	ICU LOS – 9.5d vs 12.5, D=3,p=0.047 Intolerance to therapy – 19(20.7%) vs 8(8.9), p=0.02 Post extubation RF,VAP, Hospital LOS, ICU and hosp mortality, time to reintubation – Similar

Noninvasive respiratory support after extubation: a systematic review and network meta-analysis

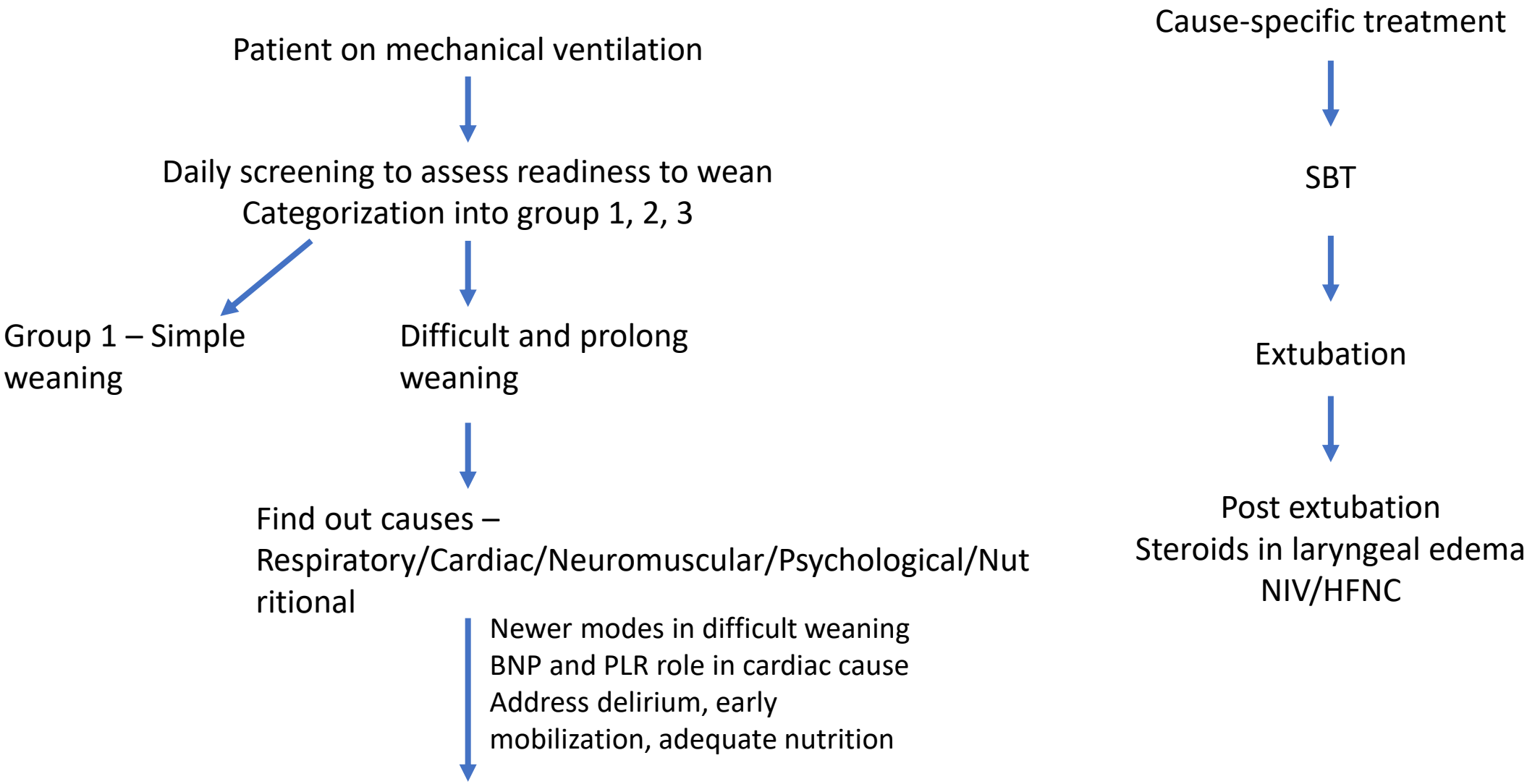
Annalisa Boscolo [1,2,4], Tommaso Pettenuzzo [2,4], Nicolò Sella [2], Matteo Zatta [1], Michele Salvagno [1], Martina Tassone [1], Chiara Pretto [1], Arianna Peralta [2], Luisa Muraro [2], Francesco Zarantonello [2], Andrea Bruni [3], Federico Geraldini [2], Alessandro De Cassai [2] and Paolo Navalesi [1,2]

- 32 RCTs entered the quantitative analysis (5063 patients)
- Extubation failure (primary outcome), as defined by re-intubation secondary to post-extubation RF in a time interval varying from 48 h to 7 days
- Randomisation for COT or one type of NRS (i.e. CPAP, NIV or HFNO)



Comparison	MD or OR (95% CI)	p-value
Re-intubation		
HFNO *versus* COT	0.60 (0.43–0.84)	**0.003**
NIV *versus* COT	0.61 (0.46–0.81)	**<0.001**
NIV *versus* HFNO	0.98 (0.69–1.40)	0.844

Summary


Patient on mechanical ventilation
Daily screening to assess readiness to wean
Categorization into group 1, 2, 3
Group 1 – Simple weaning
Difficult and prolong weaning
Find out causes – Respiratory/Cardiac/Neuromuscular/Psychological/Nutritional
Newer modes in difficult weaning
BNP and PLR role in cardiac cause
Address delirium, early mobilization, adequate nutrition
Cause-specific treatment
SBT
Extubation
Post extubation
Steroids in laryngeal edema
NIV/HFNC

Thank you !