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Compassion Quality Innovation Accountability

臺中榮民總醫院
Taichung Veterans General Hospital

Prone position ventilation – from theory to practice

July 3, 2022

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臺中榮總重症醫學部

俯臥通氣治療健保異動規定(111.04.01)

1. 申報代碼47104B，支付點數**5,114**點/每一療程。

2. 每一療程:係指仰臥→俯臥→仰臥

3. 適應症：

(1)成人(19歲以上)，入住加護病房且插管使用呼吸器之急性呼吸窘迫症候群病人（J80），並同時符合下列各項條件	(2)兒童(未滿19歲)，入住加護病房且插管使用呼吸器，並同時符合下列各項條件之一者
A. 氧合指數(PaO2/FiO2ratio)≤150 B. 七日內急性發作 C. 沒有心因性肺水腫的證據 D. CXR顯示兩側肺野浸潤	A. 氧合指數(PaO2/FiO2ratio)≤150 B. OI>16 C. OSI>12.3

3.禁忌症：心胸及腹腔主要手術、脊椎與骨盆不穩定、懷孕第二及第三期、頭部外傷、腦壓或眼壓過高之病人、正在發作之癲癇患者。

4.限內科、外科、麻醉科、兒科、急診醫學科、神經科、神經外科專科醫師執行

5.不得同時申報47045C。

Outline

1. Prone ventilation till 2013 [PROSEVA]

2. Prone ventilation evidence ~2014-2019

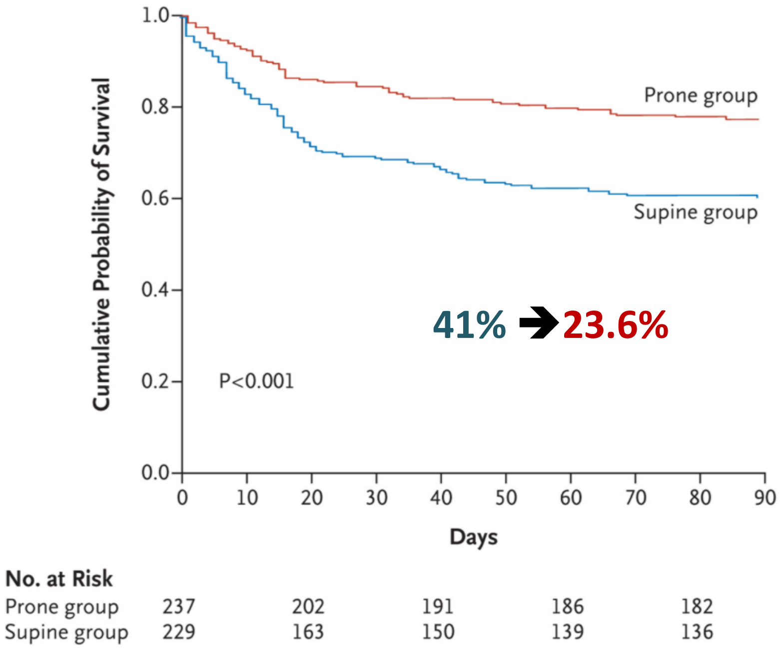
   [LUNG-SAFE, TSIRC, APRONET]

3. Prone positioning in COVID-19 era

4. Prone ventilation on ECMO

Prone Positioning in Severe Acute Respiratory Distress Syndrome

PF ratio <150



12-24 hour stabilization period of supine ventilation Then initiating prone ventilation early (up to 36 hours)

Mean duration of time in the prone position was **17 hours/day** with an average of **4 sessions**.

Protective ventilation strategies are typically concurrently employed.

NMBAs in prone and supine ventilation (91% vs. 82%)

PROSEVA Study Group

Claude Guérin et al. PMID: 23688302
N Engl J Med. 2013 Jun 6;368(23):2159-68.

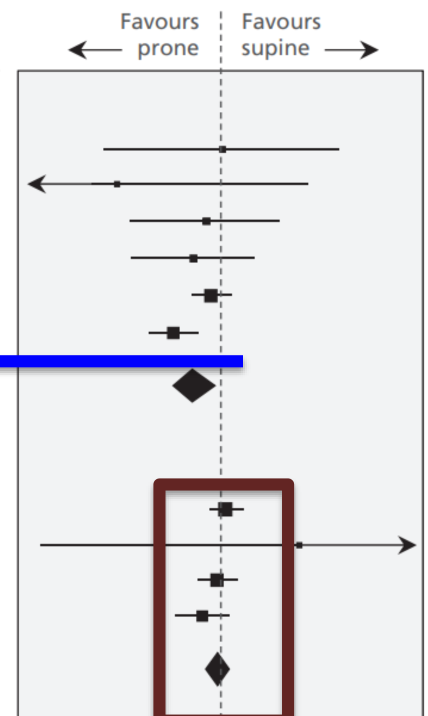
Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome : a systematic review and meta-analysis

- The fundamental role of protective lung ventilation

Protective lung ventilation (+)

Protective lung ventilation (-)

Study	Deaths, n/N: Prone	Supine	RR (95% CI)
Protective lung ventilation mandated			
Curley et al.,[37] 2005	4/51	4/51	1.00 (0.26–3.78)
Voggenreiter et al.,[38] 2005	1/21	3/19	0.30 (0.03–2.66)
Chan et al.,[35] 2007	5/11	6/11	0.83 (0.36–1.94)
Fernandez et al.,[34] 2008	8/21	10/19	0.72 (0.36–1.45)
Taccone et al.,[14] 2009	79/166	91/172	0.90 (0.73–1.11)
Guerin et al.,[17] 2013	57/240	95/234	0.58 (0.44–0.77)
Subtotal	154/510	209/506	0.74 (0.59–0.95)
Heterogeneity: I^2 = 29%			
Protective lung ventilation not mandated			
Gattinoni et al.,[15]* 2001	92/148	87/149	1.06 (0.88–1.28)
Beuret et al.,[39] 2002	1/4	0/3	2.40 (0.13–44.41)
Guerin et al.,[16] 2004	98/230	81/183	0.96 (0.77–1.20)
Mancebo et al.,[36] 2006	38/76	37/60	0.81 (0.60–1.10)
Subtotal	229/458	205/395	0.98 (0.86–1.12)
Heterogeneity: I^2 = 0%			

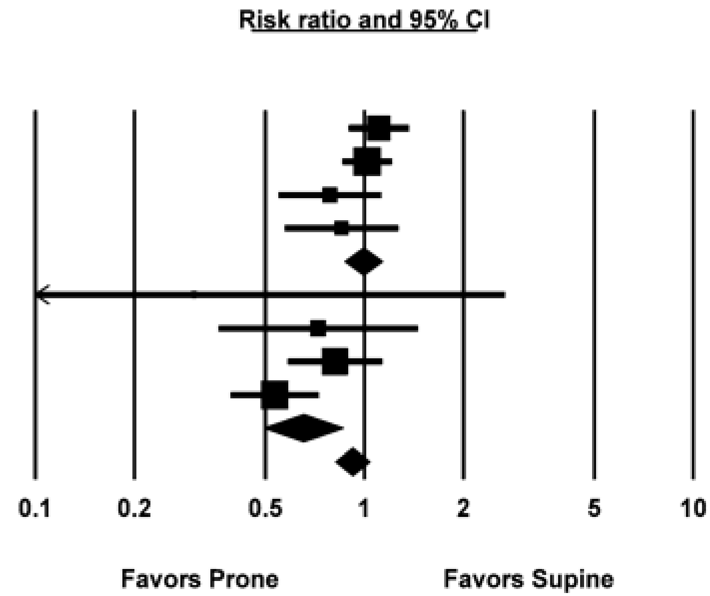


Sachin Sud et al. PMID: 24863923
CMAJ. 2014 Jul 8;186(10):E381-90.

Prone positioning reduces mortality from acute respiratory distress syndrome in the low tidal volume era: a meta-analysis

Group by High vs Low Vt	Study name	Risk ratio	Lower limit	Upper limit	p-Value	Relative weight
High	Gattinoni, 2001	1.106	0.900	1.360	0.337	32.46
High	Guerin, 2004	1.020	0.862	1.207	0.819	45.08
High	Mancebo, 2006	0.786	0.551	1.120	0.183	12.30
High	Taccone, 2009 (mod)	0.852	0.575	1.262	0.424	10.15
High		0.996	0.876	1.132	0.949	
Low	Voggenreiter, 2005	0.304	0.035	2.659	0.282	1.56
Low	Fernandez, 2008	0.724	0.362	1.446	0.360	13.40
Low	Taccone, 2009 (sev)	0.814	0.588	1.128	0.216	40.82
Low	Guerin, 2013	0.534	0.394	0.724	0.000	44.23
Low		0.655	0.499	0.860	0.002	
Overall		0.834	0.683	1.017	0.073	

(Statistics for each study)



Jeremy R. Beitler et al. PMID: 24435203
Intensive Care Med. 2014 Mar; 40(3): 332–341.

Mechanisms for prone response

Mechanisms for prone response

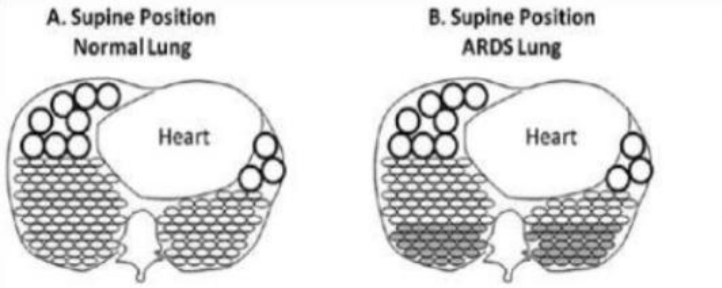
Proposed mechanisms for prone response

	Physiologic effect	Clinical result
Improved configuration between lung and thorax		
Heart is dependent	More homogeneous Ppl gradient in ventrodorsal and cephalocaudal planes	Improved ventilation distribution
Smaller volume of dependent lung		Increased FRC (↓ shunt)
Abdomen is unsupported*		
Secretion mobilization	Improved bronchial drainage	Improved ventilation
Improved aerosol delivery	Improved effect of aerosolized meds	Improved ventilation
More homogeneous perfusion	Less dependent perfusion	Improved V/Q matching (↓ shunt)

- More homogenous Ppleural and perfusion
- Improved bronchial drainage

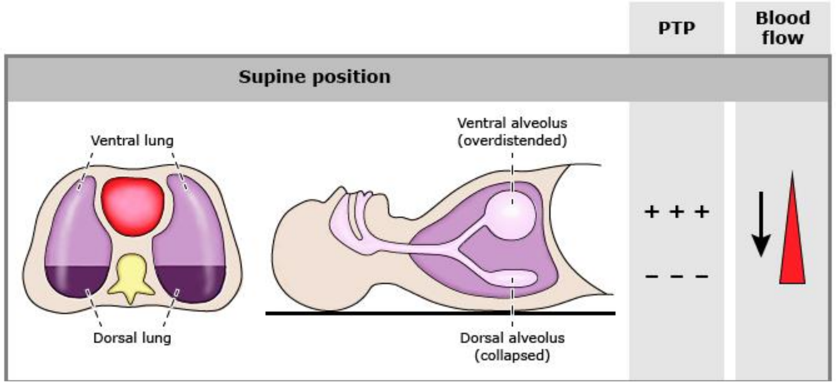
V/Q in supine and prone ventilation

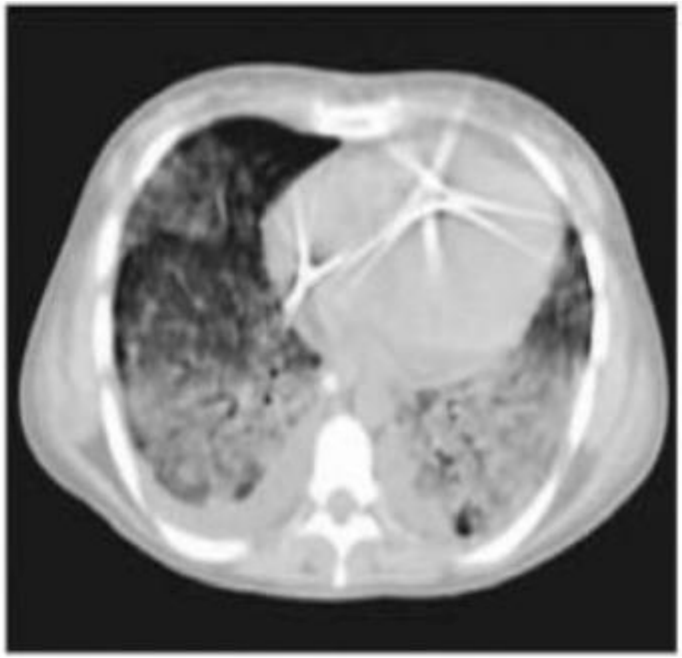
Ventilation



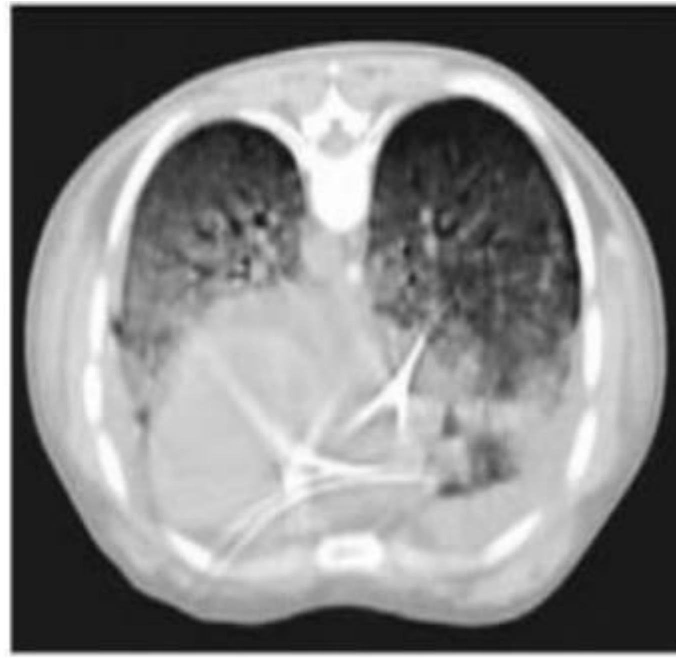
1. *Gravity*
2. *Shape of chest wall*
3. *Heart and diaphragm*

Perfusion





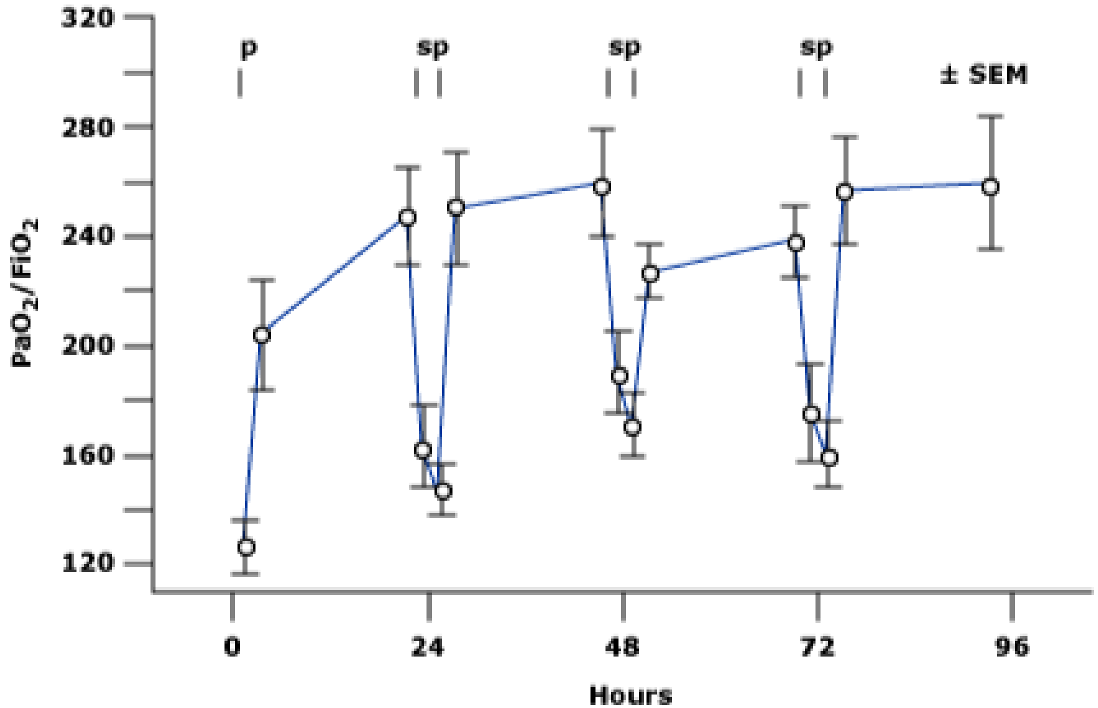
SUPINE



PRONE

Prone positioning
Effect and duration on P/F ratio

Course of PaO_2/FiO_2 during four consecutive 24-hour periods of prone positioning



Fridrich, P, Krafft, P, Hochleuthner, H, et al., Anesth Analg 1996; 83:1206.

Prone positioning evidence ~2014-2019

(Taiwan 2016 influenza epidemic)

Epidemic: 2016-Spring influenza in Taiwan

已無葉克膜救人 流感延燒 衛福部擺爛不調度

壯男早上騎車 下午加護病房 流感發病快又猛 已奪84命

2016年03月04日 G+1 33

流感疫情發燒，[redacted]因急診待床患者暴增，只能暫時將部分病床安排在電梯口。詹智淵攝

【綜合報導】流感疫情大爆炸，急重症病患發病又快又猛，救命的葉克膜卻告急，台大、馬偕、中國醫藥大學附設醫院、彰化基督教醫院、高雄長庚等醫院的葉克膜體外循環器已全數滿機，陷入零空機困境，第一線醫師心急如焚，表示「已沒有武器（指葉克膜）可救人」，要求衛福部統籌調度。但衛福部無視人命關天，昨仍被動地說，現無法得知哪些醫院葉克膜不足，呼籲醫院有需要可告知衛福部介入協助。民眾則痛罵衛福部「根本是草菅人命」！

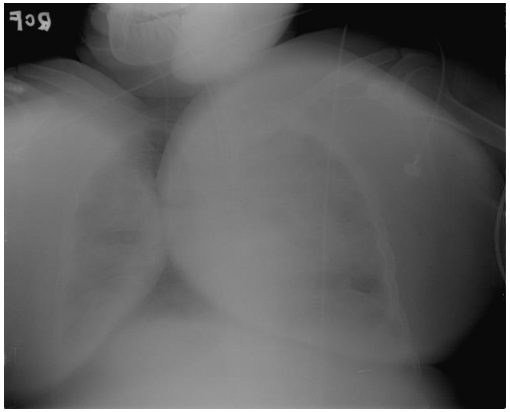
- 已無ECMO救人?
- 擺爛不調度?
- …….

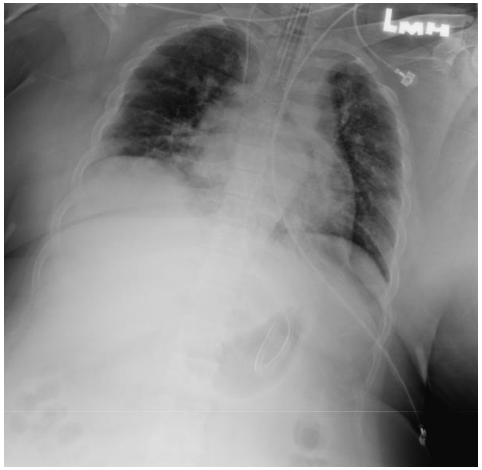
2016-03-04

Rapid recovery under early treatment

Early tamiflu, early protective ventilation strategy,
early prone position, early dry-lung strategy

Influenza A /c severe ARDS





Day 1
FiO2 70%, P/F ratio: 98
PEEP: 16, TV: 300 (IBW: 52)
Tamiflu, EGDT,
protective ventilation strategy

Prone →

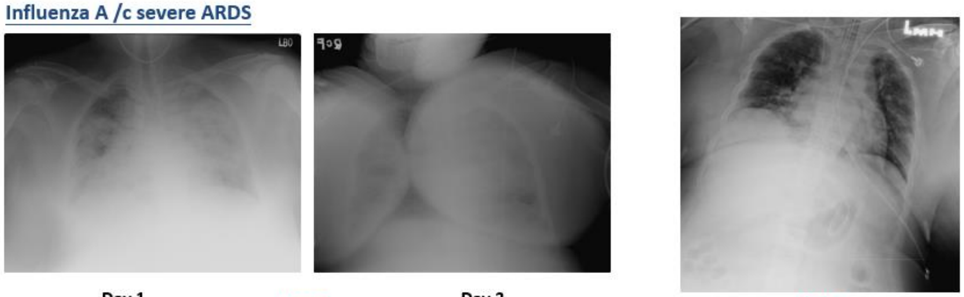
Day 2
FiO2 45%, P/F ratio: 155
PEEP: 16, TV: 300 (IBW: 52)
Toward dry-lung strategy

Day 6
FiO2 35%, extubation with
HFNC (High-flow nasal cannula)

Case report ➔ Case series ➔ Nationwide study

Case report

Influenza A /c severe ARDS



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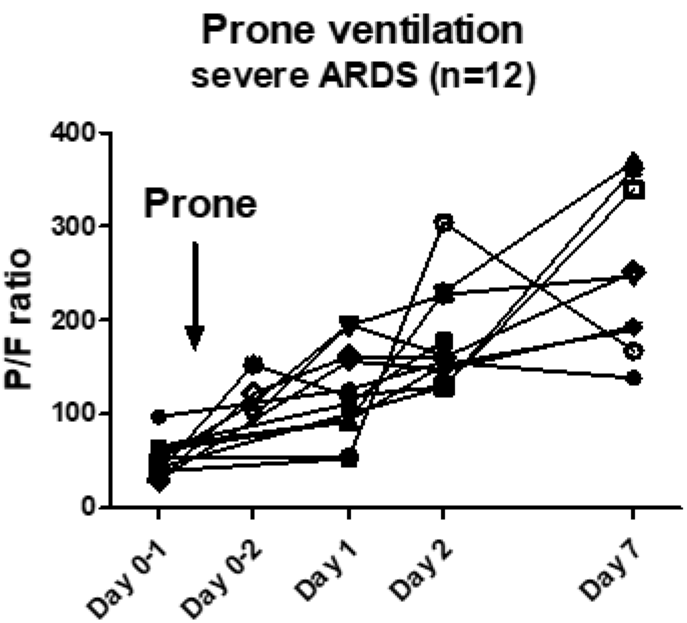
Case series



Taiwan Severe Influenza Research Consortium (TSIRC)

2016/03/12

Taiwan Severe Influenza Research Consortium (TSIRC)

1. First tidal volume greater than 8 mL/kg is associated with increased mortality in complicated influenza infection with acute respiratory distress syndrome.

Chan MC et al. **Taiwan Severe Influenza Research Consortium TSIRC (Taiwan Severe Influenza Research Consortium).**.
J Formos Med Assoc. 2018. PMID: 30041997

2. Association of day 4 cumulative fluid balance with mortality in critically ill patients with influenza: A multicenter retrospective cohort study in Taiwan.

Chao WC et al. **TSIRC (Taiwan Severe Influenza Research Consortium).**
PLoS One. 2018 Jan 9;13(1):e0190952. PMID: 29315320

3. Predictors of survival in patients with influenza pneumonia-related severe acute respiratory distress syndrome treated with prone positioning.

Kao KC et **al.TSIRC (Taiwan Severe Influenza Research Consortium).**
Ann Intensive Care. 2018 Sep 24;8(1):94. doi: 10.1186/s13613-018-0440-4

4. Impact of corticosteroid treatment on clinical outcomes of influenza-associated ARDS: a nationwide multicenter study.

Tsai MJ et a. **Taiwan Severe Influenza Research Consortium (TSIRC) Investigators.**
Ann Intensive Care. 2020 Feb 27;10(1):26.

5. Risk factor analysis of nosocomial lower respiratory tract infection in influenza-related acute respiratory distress syndrome.

Chen WC et al. **TSIRC (Taiwan Severe Influenza Research Consortium).**
Ther Adv Respir Dis. 2020 Jan-Dec;14:1753466620942417.

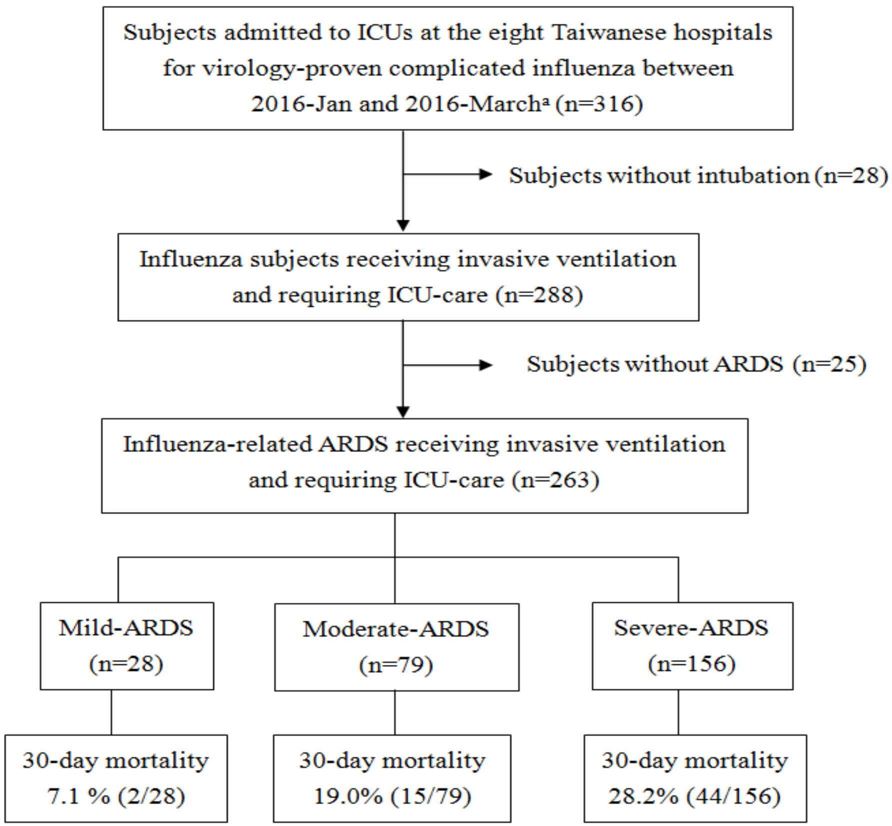
6. Using a machine learning approach to predict mortality in critically ill influenza patients: a cross-sectional retrospective multicentre study in Taiwan.

Hu CA et **al.TSIRC (Taiwan Severe Influenza Research Consortium).**
BMJ Open. 2020 Feb 25;10(2):e033898.

7. Comparison of prone positioning and extracorporeal membrane oxygenation in acute respiratory distress syndrome: A multicenter cohort study and propensity-matched analysis

Chang KW et al. TSIRC (Taiwan Severe Influenza Research Consortium)..
J Formos Med Assoc . 2021 Oct 16;S0929-6646(21)00479-4

Flow chart of enrollment of participants



a Virology proofs include RIDT, RT-PCR, and viral culture.

Abbreviations: ICU: Intensive care unit; RIDT: Rapid influenza diagnostic test; ARDS: Acute respiratory distress syndrome (Berlin definition)

Figure 1. Flow chart of subjects enrollment.

316 virology-proven cases in 2016-epidemic

263 ARDS

Severe ARDS (59.3%, 156/263)

Mortality 23.1% (61/263)

Table 1. Characteristics of the 263 subjects with influenza-related ARDS categorized by 30-day mortality

	All (N=263)	Survivor (N=202)	Non-survivor (N=61)	*P* value
Basic data				
Age (years)	59.8±14.6	59.2±14.7	61.7±14.4	0.25
Male %	166 (63.1%)	126 (62.4%)	40 (65.6%)	0.76
....				
Subtypes of influenza				
Type A (%)	**205 (77.9%)**	**159 (78.7%)**	**46 (75.4%)**	0.69
Type B (%)	23 (8.7%)	16 (7.9%)	7 (11.5%)	
Positive, unknown subtype (%)	35 (13.3%)	27 (13.4%)	8 (13.1%)	
Laboratory data				
....				
Serum C-reactive protein (mg/dL)	15.3±10.2	14.5±9.9	17.8±11.0	0.03
Serum lactate level (mg/dL)	29.6±36.6	23.8±23.4	47.4±58.1	<0.01
Severity scores				
Pneumonia Severity Index	**119.9±46**	**112±42.3**	**145.5±48.7**	<0.01
APACHE II	**23.6±8.6**	**22.1±8**	**28.9±8.4**	<0.01
SOFA score				
Day-1	10.6±4	9.9±3.8	12.8±4	<0.01
Day-3	9.9±4.4	9±4.1	13±4.1	<0.01
Day-7	8.4±4.3	7.5±3.7	12.1±4.8	<0.01
PaO2/FiO2	106.8±62.2	112.3±65.2	88.5±47.5	<0.01
Management and outcomes				
ICU-wait[c] (days)	0.9±1.8	0.9±1.7	1.1±2.2	0.33
Prone-ventilation (%)	**65 (23.2%)**	**45 (21.8%)**	**20 (27.9%)**	**0.39**
ECMO (%)	50 (19%)	30 (14.9%)	20 (32.8%)	<0.01
Renal replacement therapy[d] (%)	31 (11.8%)	15 (7.4%)	16 (26.2%)	<0.01

Prone-positioning (23.2%)

Predictors of survival in patients with influenza pneumonia-related severe acute respiratory distress syndrome treated with prone positioning.

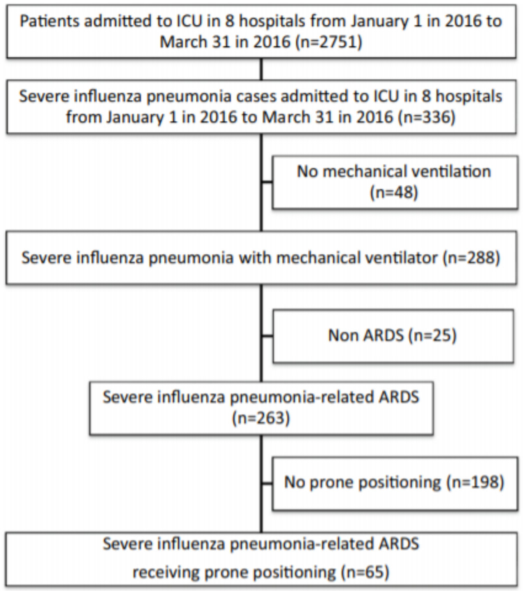


Table 3 Cox regression analysis of clinical variables associated with 60-day mortality in influenza pneumonia-relate ARDS with prone positioning

Clinical variables	Univariate		Multivariate	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
APACHE II score	1.089 (1.035–1.147)	0.001*	1.042 (0.982–1.106)	0.178
PSI	1.015 (1.005–1.026)	0.003*	1.020 (1.009–1.032)	<0.001
Renal replacement therapy	5.355 (2.159–13.281)	0.000*	6.248 (2.245–17.389)	<0.001
Δ Peak airway pressure (cm H_2O)	1.143 (1.019–1.282)	0.022*	0.996 (0.822–1.208)	0.969
Δ Dynamic driving pressure (cm H_2O)	1.147 (1.008–1.305)	0.037*	1.372 (1.095–1.718)	0.006
Δ Dynamic compliance (ml/cm H_2O)	0.925 (0.871–0.983)	0.011*	0.941 (0.872–1.015)	0.117

ARDS acute respiratory distress syndrome, *CI* confidence interval, *APACHE II* Acute Physical and Chronic Health Evaluation, *PSI* pneumonia severity index, *Δ* difference between before and after prone positioning 1 day

*$p < 0.05$

- 65 patients receiving prone ventilation: Survivors (n=45); Non-survivors (n=20).
- An increase in dynamic driving pressure were associated with 60-day mortality in patients with infuenza pneumonia-related ARDS receiving prone positioning

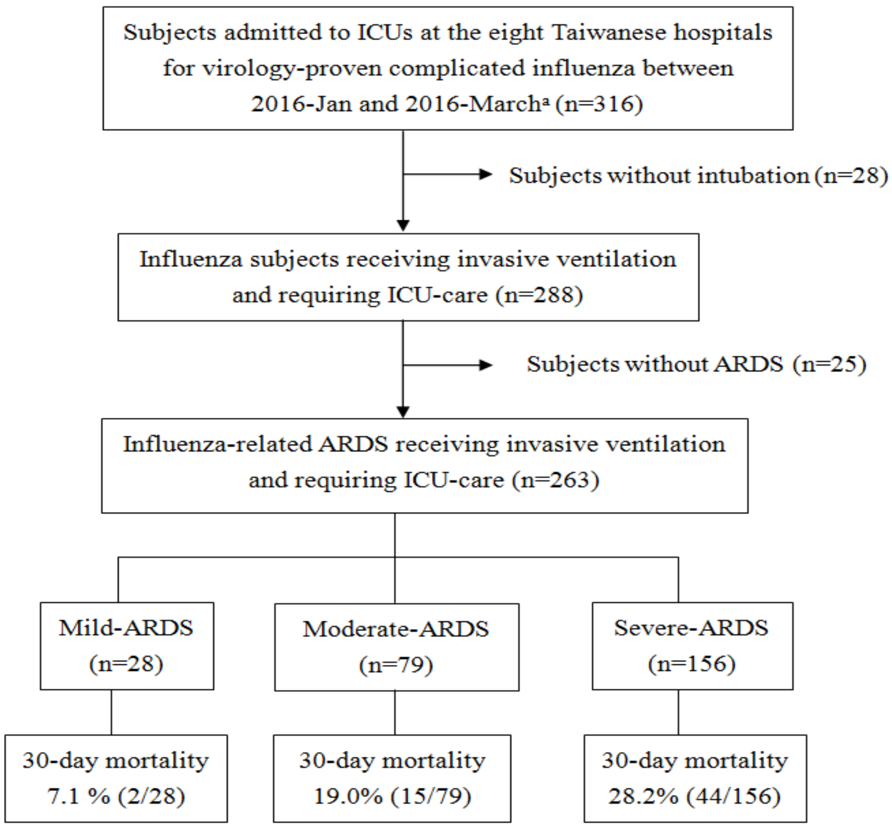
Kuo-Chin Kao, et al. PMID: 30251181
Ann Intensive Care. 2018 Sep 24;8(1):94.

知易行難

ARDS-Protective ventilation

ARDS-Prone positioning

Flow chart of enrollment of participants



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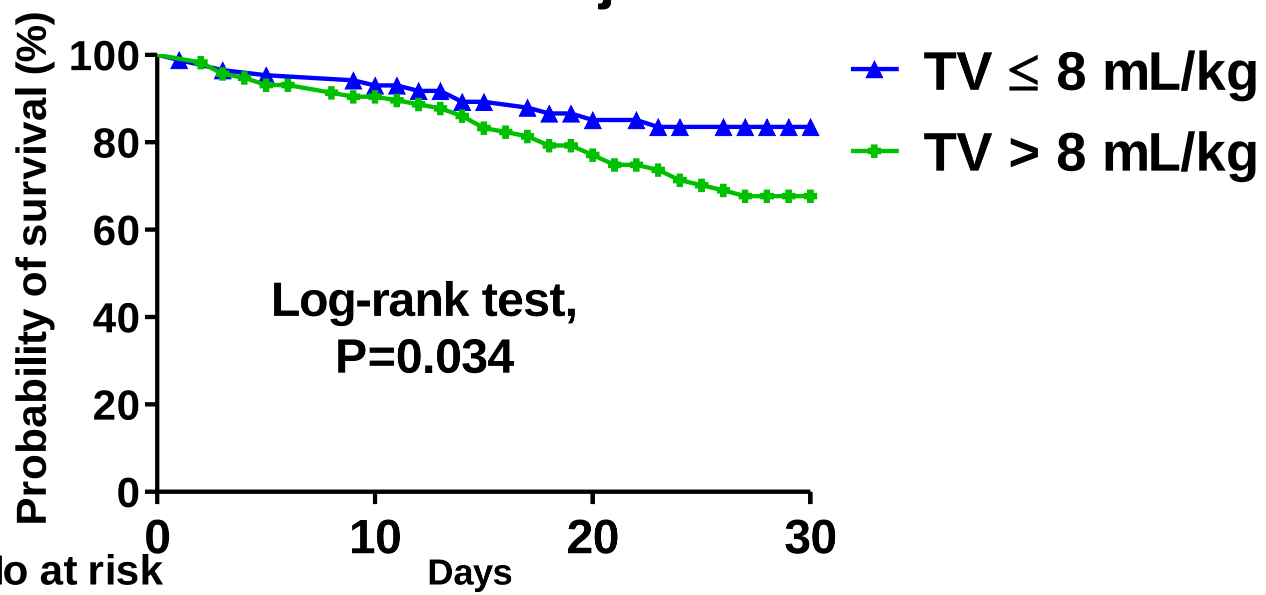
Mortality 23.1% (61/263)

Table 2. Respiratory parameters of subjects with influenza-related ARDS categorized by 30-day mortality

	All (N=263)	Survivor (N=202)	Non-survivor (N=61)	*P* value
Day-intubation (N=222)				
FiO_2 (%)	80.7±22	78.1±22.7	89.3±16.8	<0.01
PEEP	10.6±3.8	**10.9±4**	**9.6±3**	0.01
V_T/PBW	8.5±2	**8.2±1.9**	**9.3±2.2**	<0.01
P_{peak}	29.3±4.9	29.2±4.9	29.7±4.9	0.52
Day 1 (N=233)				
FiO_2 (%)	63.4±22.5	59.4±21.2	77.2±21.4	<0.01
PEEP	11.7±3.7	11.6±3.7	12.1±3.6	0.38
V_T/PBW	8.3±2	**8.3±2**	**8.1±2.1**	0.44
P_{peak}	28.5±4.7	28.3±4.8	29.5±4	0.10
Day 2 (N=233)				
FiO_2 (%)	54.5±20.2	51.7±18.5	65.5±22.8	<0.01
PEEP	11.5±3.7	11.3±3.8	12.6±3.3	0.03
V_T/PBW	8.1±2	**8.2±2**	**7.7±1.9**	0.09
P_{peak}	28±5.2	27.5±5.3	29.8±4.1	0.01

Early low tidal volume ventilation is associated with 30-day mortality

All subjects



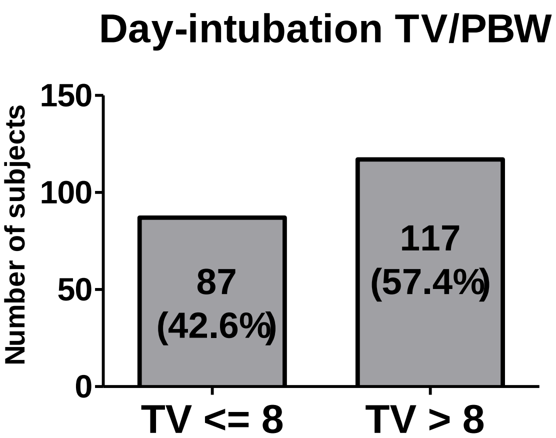
No at risk

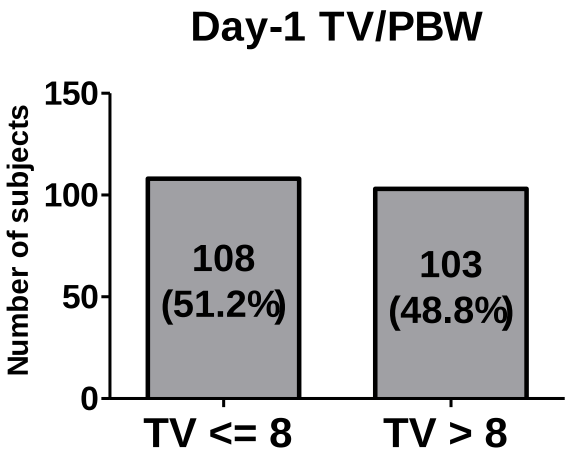
TV ≤ 8	87	80	58	38
TV > 8	117	102	71	46

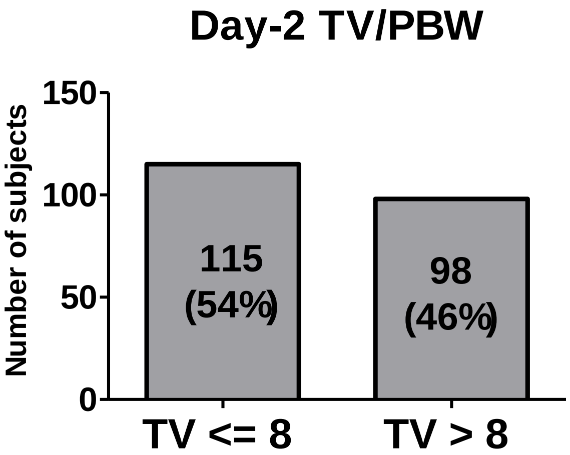
A surprisingly low proportion of implementation of low tidal volume ventilation

$V_T/PBW \leqq 8$

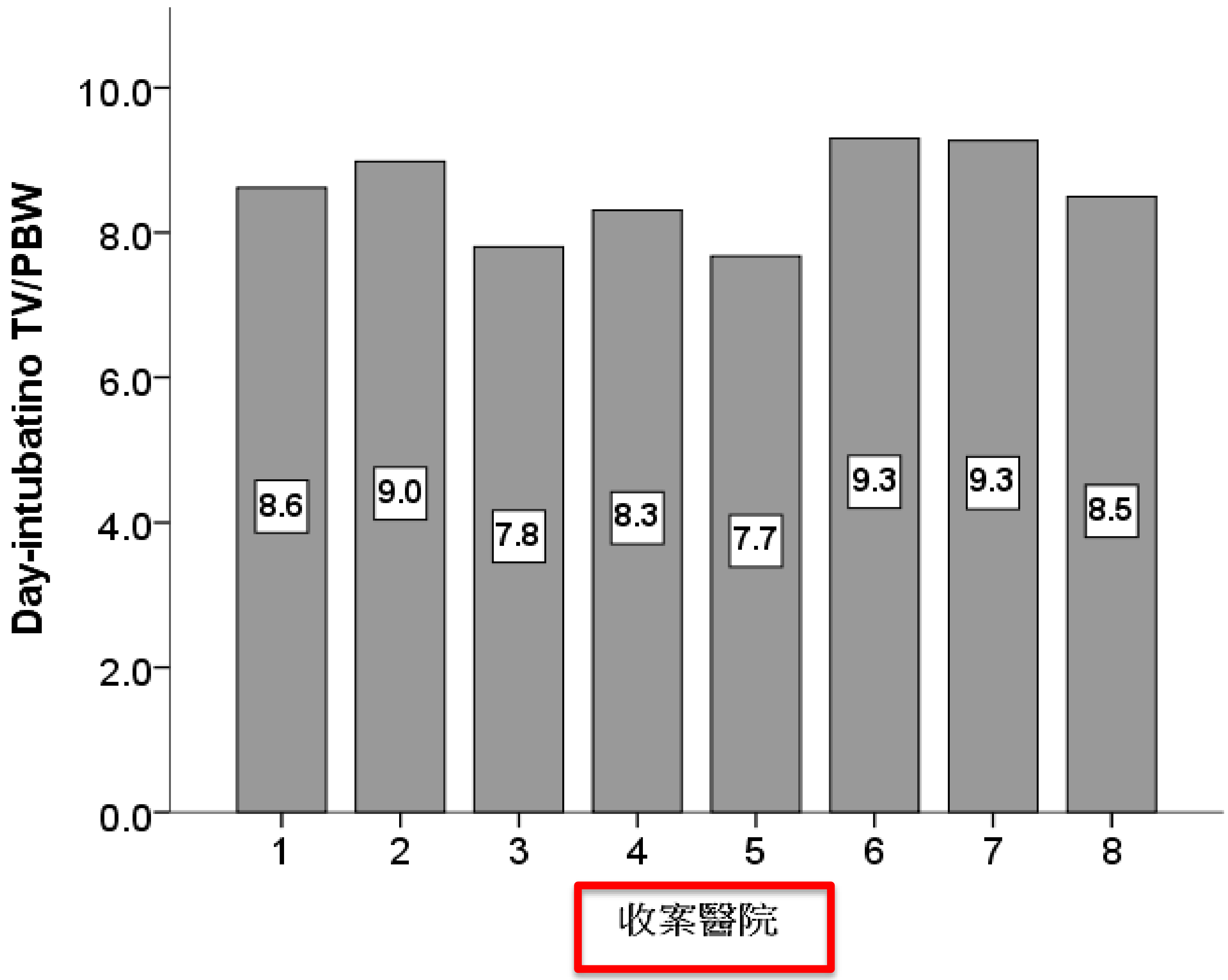
42.6% **51.2%** **54.0%**







The real-world application of the early low tidal volume ventilation



Real-world practice in countries other than Taiwan

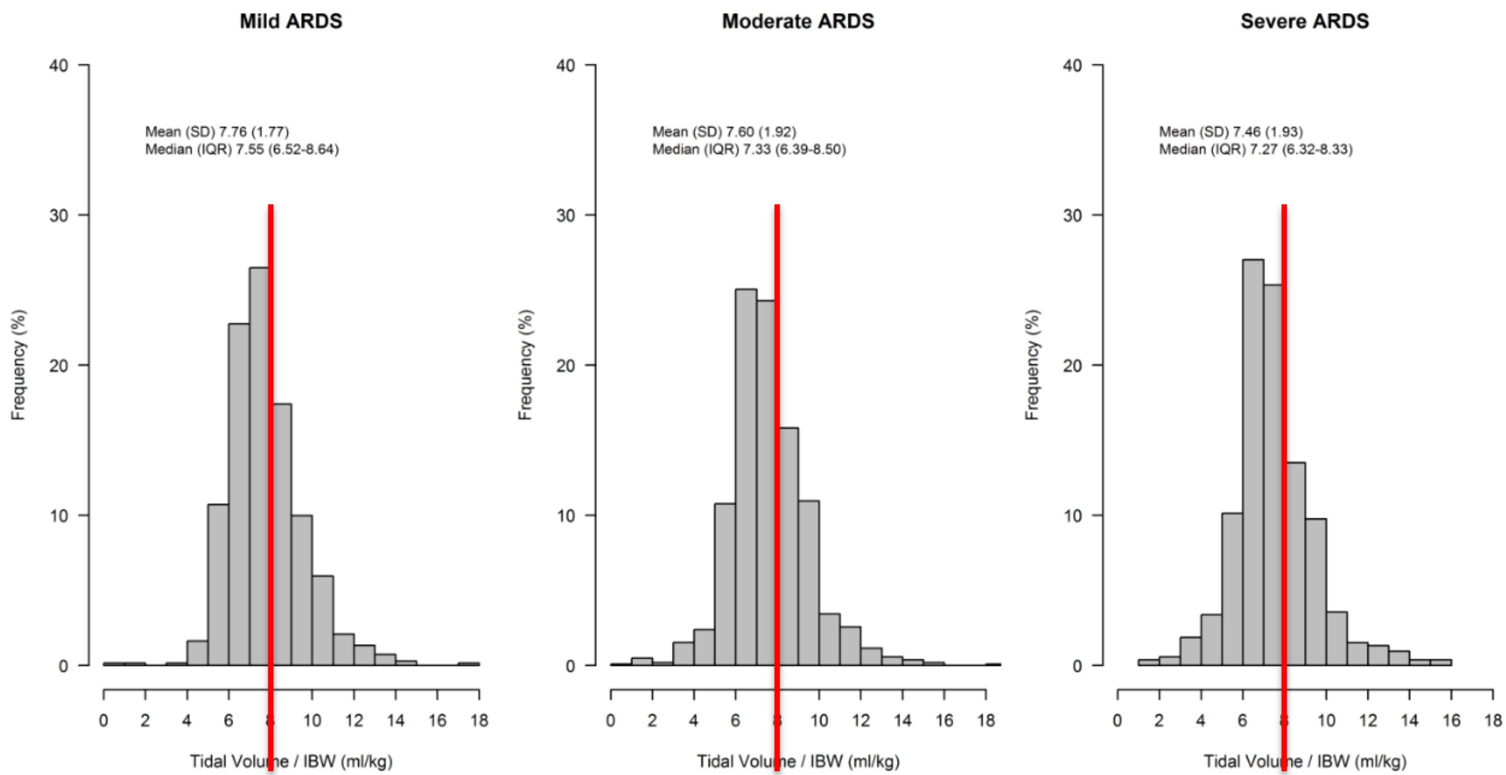
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

- 4 consecutive weeks in the winter of 2014 in a convenience sample of 459 ICUs from 50 countries across 5 continents.
- Of 29,144 patients admitted to participating ICUs, 3022 (10.4%) fulfilled ARDS criteria.
- Mild, moderate and severe ARDS was 30.0%, 46.6% and 23.4%, respectively.

LUNG SAFE Investigators

Giacomo Bellani et al. PMID: 26903337
JAMA. 2016 Feb 23;315(8):788-800

Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study



Intensive Care Med. 2016 Dec;42(12):1865-1876

Real-world poor adherence for LTVV

➢**Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries**

✓**LUNG SAFE study** (50 countries)

✓**Less than two-thirds** of patients with ARDS received a TV/PBW≦8 mL/kg

Giacomo Bellani et al.* *JAMA. 2016 Feb 23;315(8):788-800.

➢**Low Tidal Volume Ventilation Use in Acute Respiratory Distress Syndrome**

✓**Using electronic health records (EHRs)** to assess the real-world practical compliance of LTVV in four American hospitals

✓**Only 54%** of ARDS patients received a TV/PBW≦8 mL/kg

Weiss CH et al.* *Crit Care Med 2016; 44:1515-1522

Real-world application of prone position

The rate of use of prone position has been found as low as [ ] in severe ARDS patients in the recent large prospective epidemiologic Lung safe study.

LUNG SAFE Investigators

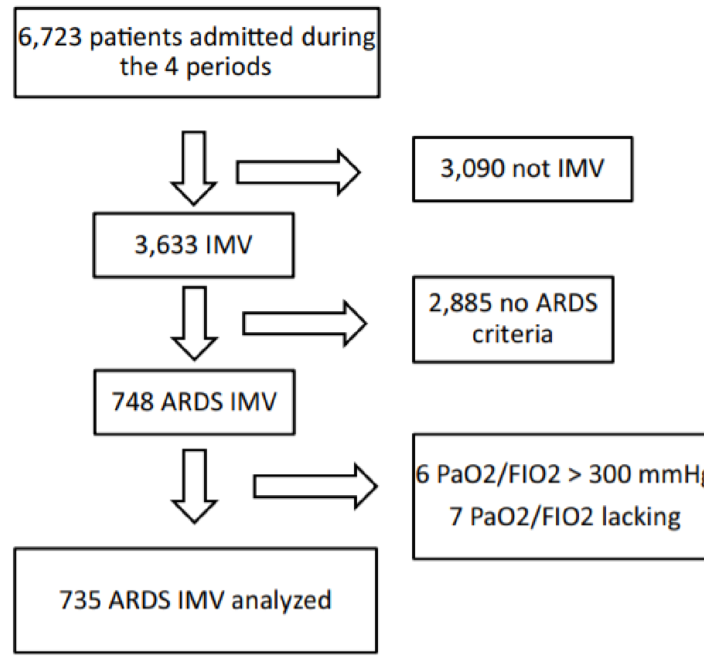
Giacomo Bellani et al. PMID: 26903337
JAMA. 2016 Feb 23;315(8):788-800

Hallmark studies of prone positioning

- PROSEVA in 2013
- LUNG-SAFE in 2014
- TSIRC in 2016
- **APRONET in 2017**

A prospective international observational prevalence study on prone positioning of ARDS patients

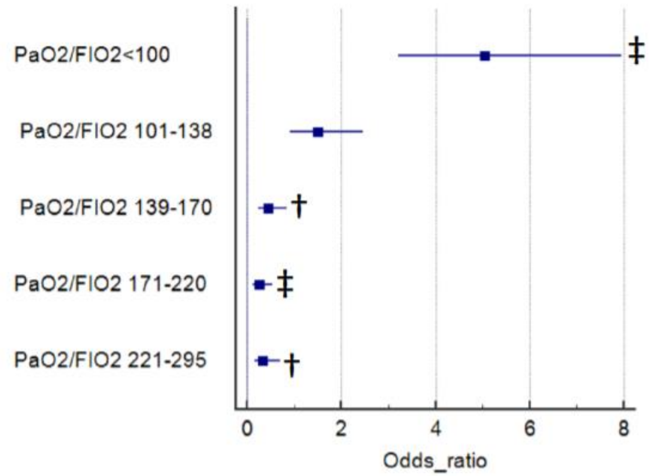
- Prospective international 1-day prevalence study performed four times in April, July, and October 2016 and January 2017.
- 6723 patients were screened in 141 ICUs from 20 countries
- 735 had ARDS and were analyzed.
- 101 ARDS patients had at least one session of PP (13.7%)



APRONET (ARDS Prone Position Network) study

Claude Guérin et al. PMID: 29218379
Intensive Care Med . 2018 Jan;44(1):22-37.

A prospective international observational prevalence study on prone positioning of ARDS patients



N patients (% total)	N patients in prone (% prone)*
149 (20.3)	49 (48.5)
145 (19.7)	28 (25.7)
150 (20.4)	11 (10.9)
153 (20.8)	7 (6.9)
138 (18.8)	8 (7.9)

- The rate of PP use was 5.9% (11/187), 10.3% (41/399) and 32.9% (49/149) in mild, moderate and severe ARDS,

APRONET (ARDS Prone Position Network) study

Claude Guérin et al. PMID: 29218379
Intensive Care Med . 2018 Jan;44(1):22-37.

A prospective international observational prevalence study on prone positioning of ARDS patients

- **Duration**

➔ 18 (16-23) hours.

- **Efficacy of 1st prone**

➔PaO2/FIO2 increased from 101 (76-136) to 171 (118-220) mmHg;

➔Driving pressure decreased from 14 [11-17] to 13 [10-16] cmH2O

➔Pplat decreased from 26 [23-29] to 25 [23-28] cmH2O (P = 0.04).

APRONET (ARDS Prone Position Network) study

Claude Guérin et al. PMID: 29218379
Intensive Care Med . 2018 Jan;44(1):22-37.

A prospective international observational prevalence study on prone positioning of ARDS patients

- Reason for not using PP

➔(64.3%) was that hypoxemia was not considered sufficiently severe.

- Complications

➔were reported in 12 patients (11.9%)

➔Pressure sores in five, hypoxemia in two, endotracheal tube-related in two, ocular in two, and a transient increase in intracranial pressure in one).

APRONET (ARDS Prone Position Network) study

Claude Guérin et al. PMID: 29218379
Intensive Care Med . 2018 Jan;44(1):22-37.

Prone position

1. Contraindications
2. Complications

Prone positioning
Absolute contraindication

1. Shock (hemodynamic cannot be stabilized)
2. Life-threatening arrhythmias
3. Acute bleeding (bronchial bleeding, ….)
4. Multiple fractures or trauma (eg, unstable fractures of femur, pelvis, face)
5. Spinal instability (trauma, RA)
6. Pregnancy
7. Raised intracranial pressure
8. Tracheal surgery or sternotomy within two weeks

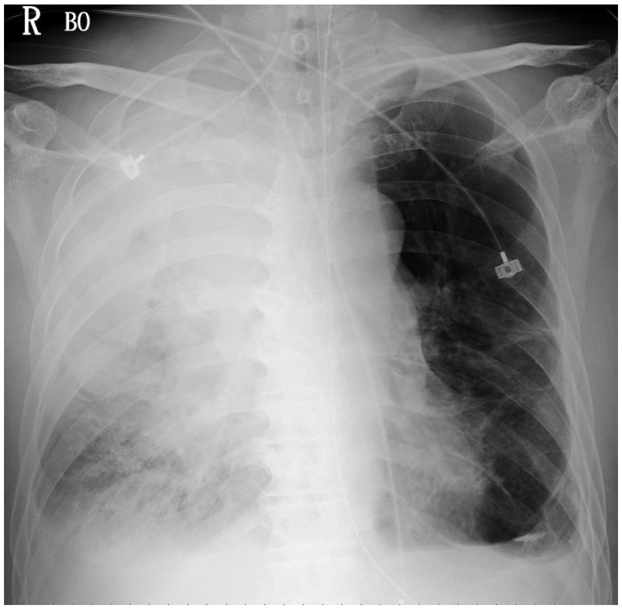
Prone positioning
Relative contraindication

1. Recent DVT treated for <2 days*
2. Anterior chest tube(s) with air leaks*
3. Major abdominal surgery
4. Recent pacemaker*
5. Clinical conditions limiting life expectancy*
6. Severe burns*
7. Lung transplant recipient*
8. Prior use of rescue therapies (NO, ECMO..)

NO

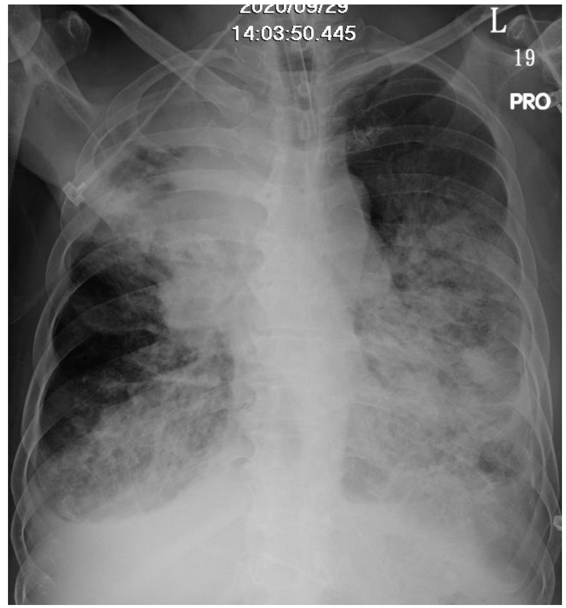
1. **One lung ventilation**
2. **Obesity**

Prone positioning case-sharing

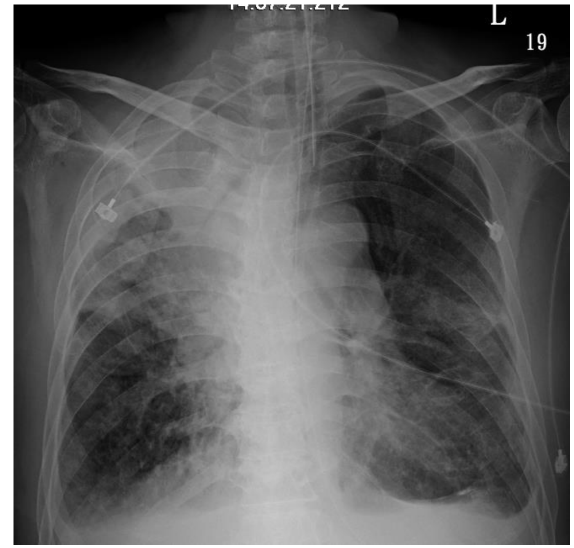


- SCLC /c RUL collapse
- (FiO2 60%, PEEP 10, P/F 133

==>Cisplatin+VP-16



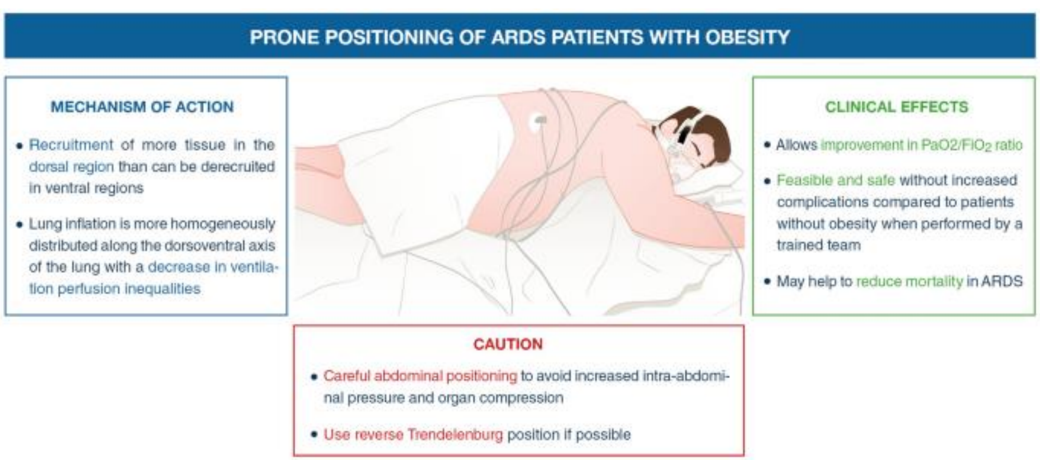
- Day-7 after Cisplatin+VP-16
- FiO2 90%, PEEP 14, P/F ratio80
- Prone ventilation



- Day-12 after Cisplatin+VP-16
- Supine ventilation
- FiO2 50%, PEEP 10, P/F ratio 180

Prone positioning in obese patients

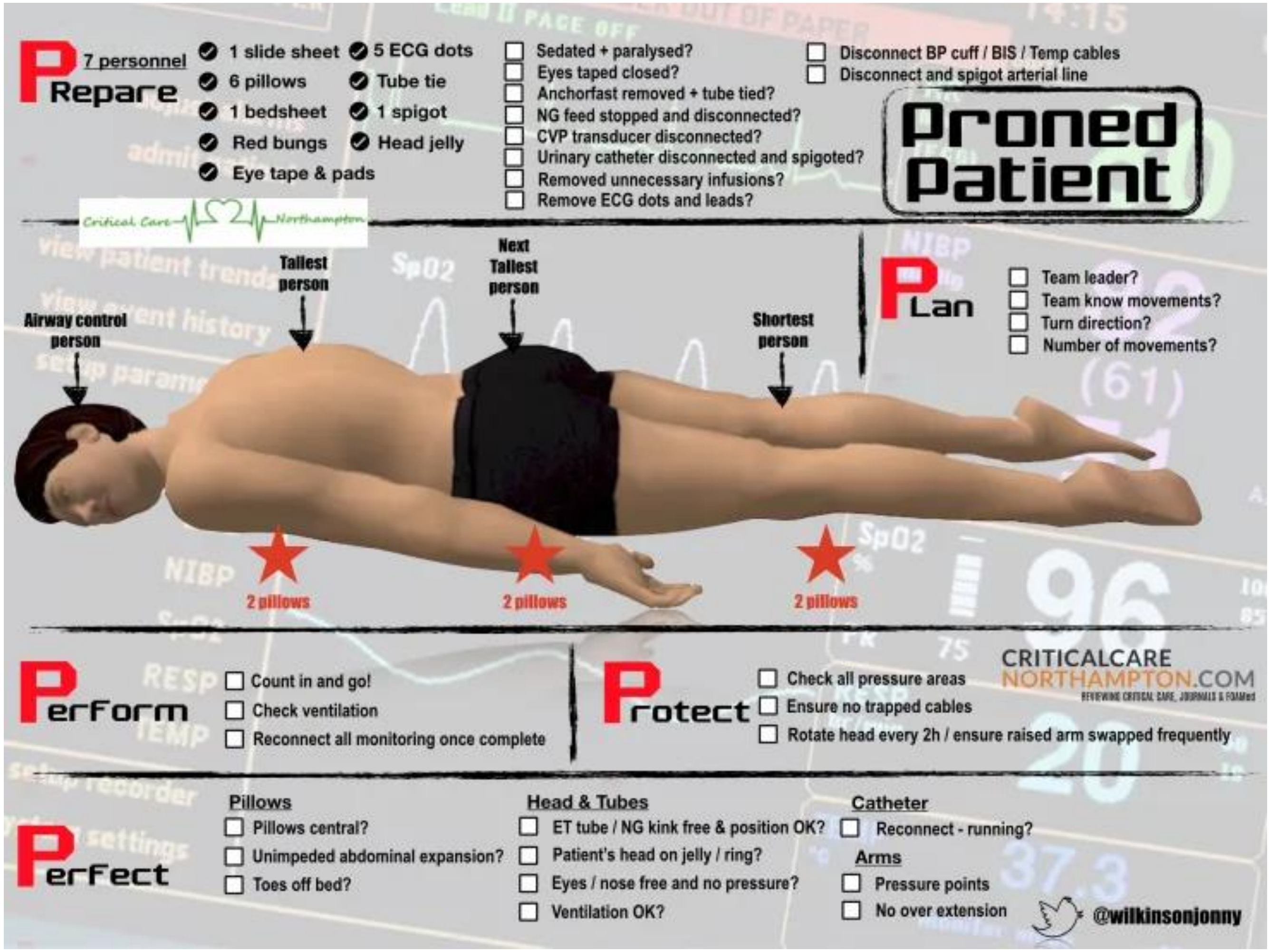
1. Obesity is NOT generally considered a contraindication.
2. In PROSEVA trial, the median body mass index was 28, ranging from 21 to 36.
3. However, turning patients with massive obesity may pose more procedural challenges



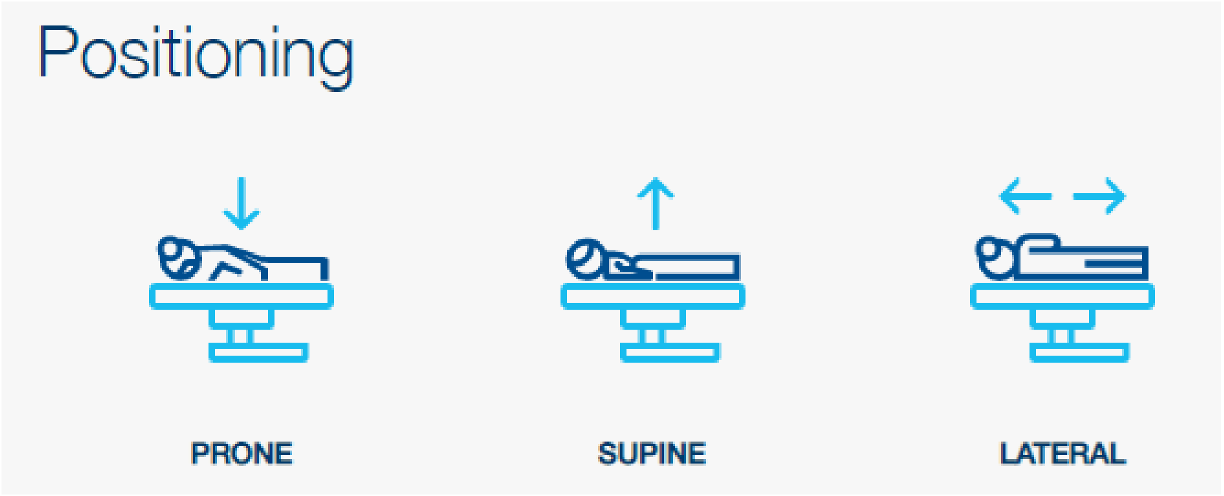
Prone positioning: complication

- Nerve compression (eg, brachial plexus injury)
- Venous stasis (eg, facial edema)
- Dislodging endotracheal tube
- Pressure sores (eg, facial)
- Dislodging vascular catheters or drainage tubes
- Retinal damage
- Vomiting
- Transient arrhythmias

Checklist of prone positioning



Modular Table System (MTS)



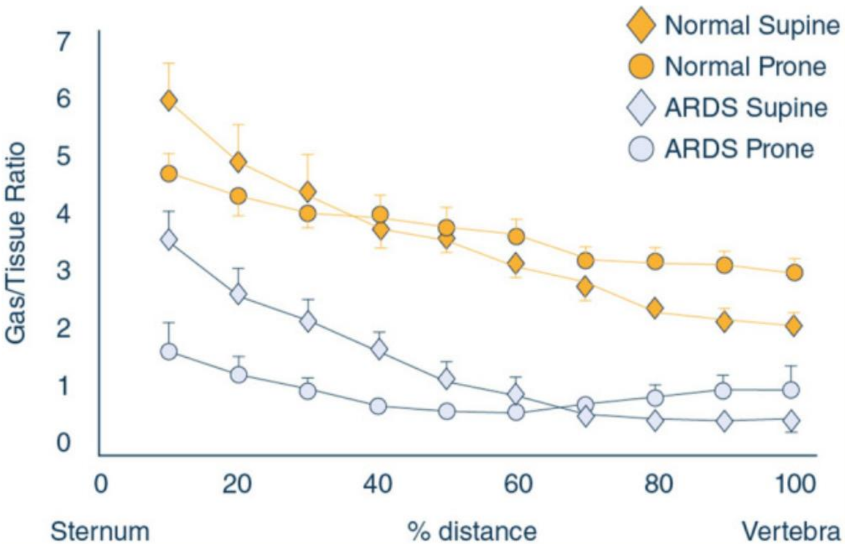

ADAC

Prone positioning

in 2020[COVID-19 era]

Prone position in ARDS patients: why, when, how and for whom

Gas/Tissue ratio

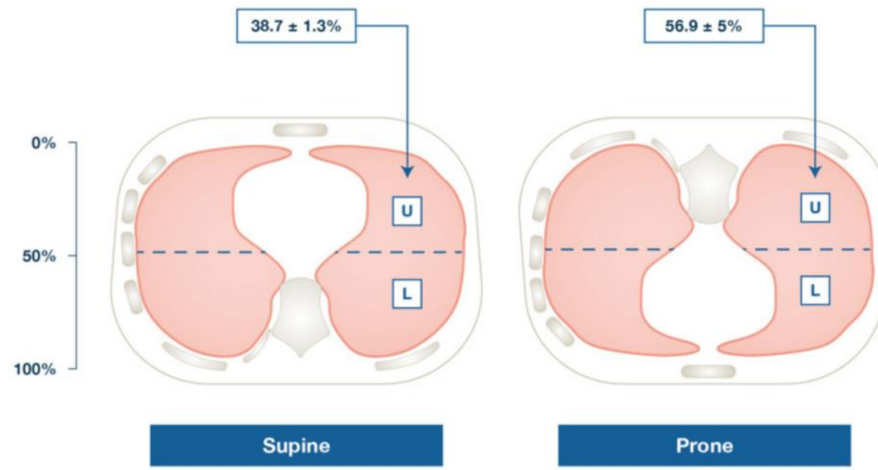


Open lung mass

Recruitability

38.7 +/- 1.3

56.9 +/- 5



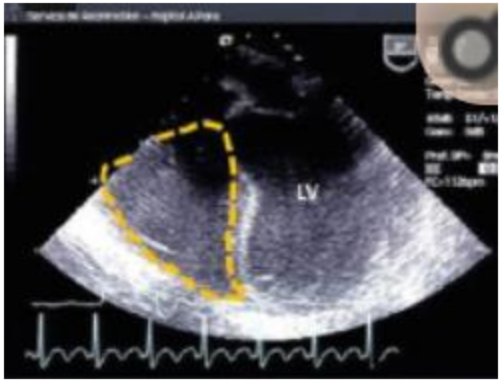
***Claude Guérin* et al. PMID: 33169218**

Intensive Care Med. 2020 Nov 10 : 1–12.

Prone position in ARDS patients: why, when, how and for whom

Supine Position before proning

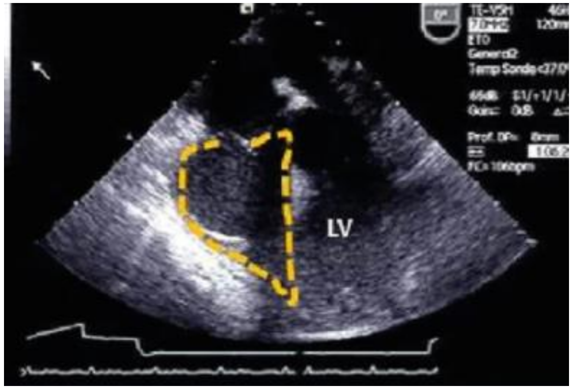
PaO_2/FiO_2 (mmHg)	$PaCO_2$ (mmHg)	P_{plat} (cmH_2O)	DrivingP (cmH_2O)
74	54	27	21



Proning for 18 hours

Supine position after 18 hours of proninig

PaO_2/FiO_2 (mmHg)	$PaCO_2$ (mmHg)	P_{plat} (cmH_2O)	DrivingP (cmH_2O)
115	50	25	19



Claude Guérin et al. PMID: 33169218
Intensive Care Med. 2020 Nov 10 : 1–12.

Prone position in ARDS patients: why, when, how and for whom

Unanswered questions

- Underutilized of prone ventilation

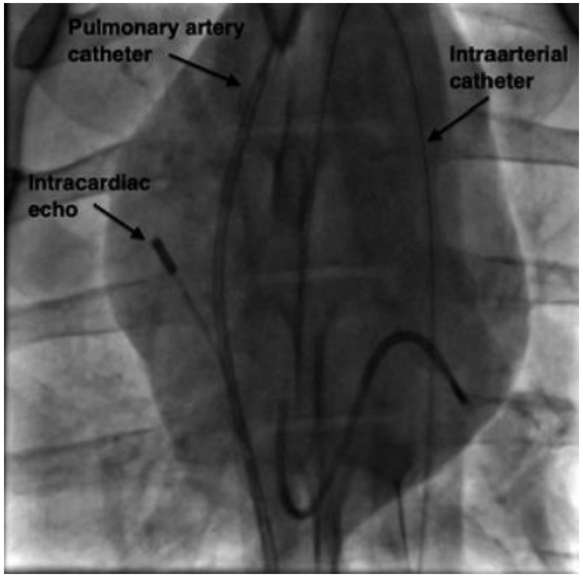
  (improved in COVID-19, 76% of 735 COVID-19 ARDS in Spain)

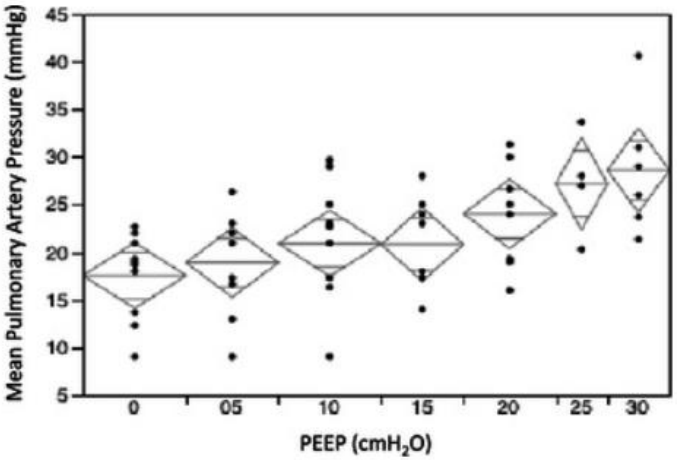
- Optimal duration is not definitely determined
- How ventilator settings (PEEP/FiO_2) should be adjusted in prone position is an unanswered issue.
- Awaken prone position in non-intubated patients

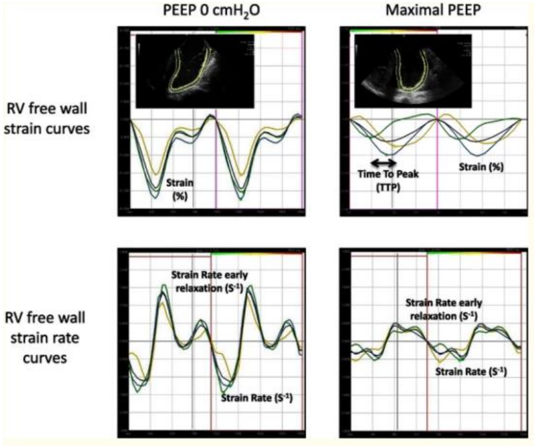
Claude Guérin et al. PMID: 33169218
Intensive Care Med. 2020 Nov 10 : 1–12.

Optimal PEEP in ARDS

Effect of positive end-expiratory pressure on porcine right ventricle function assessed by speckle tracking echocardiography



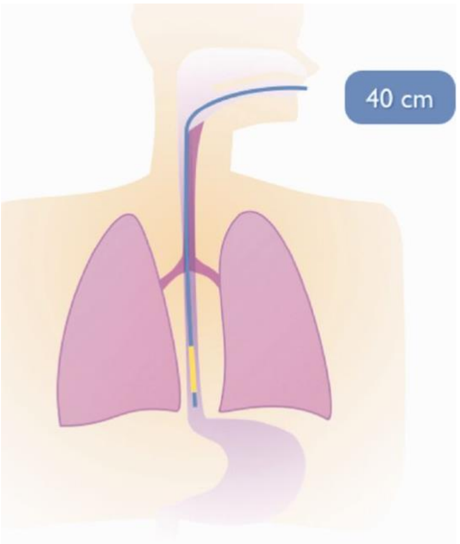




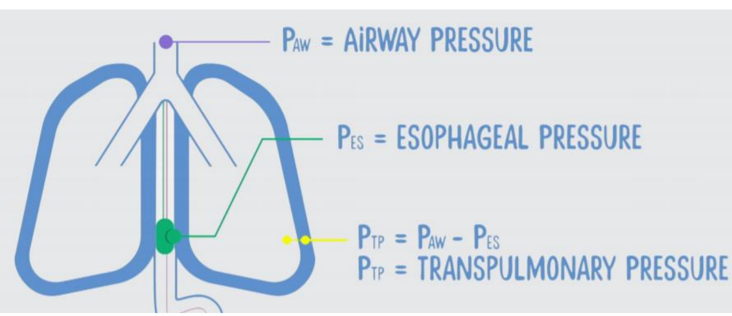
Intracardiac echocardiography (ICE), pulmonary artery and arterial catheters

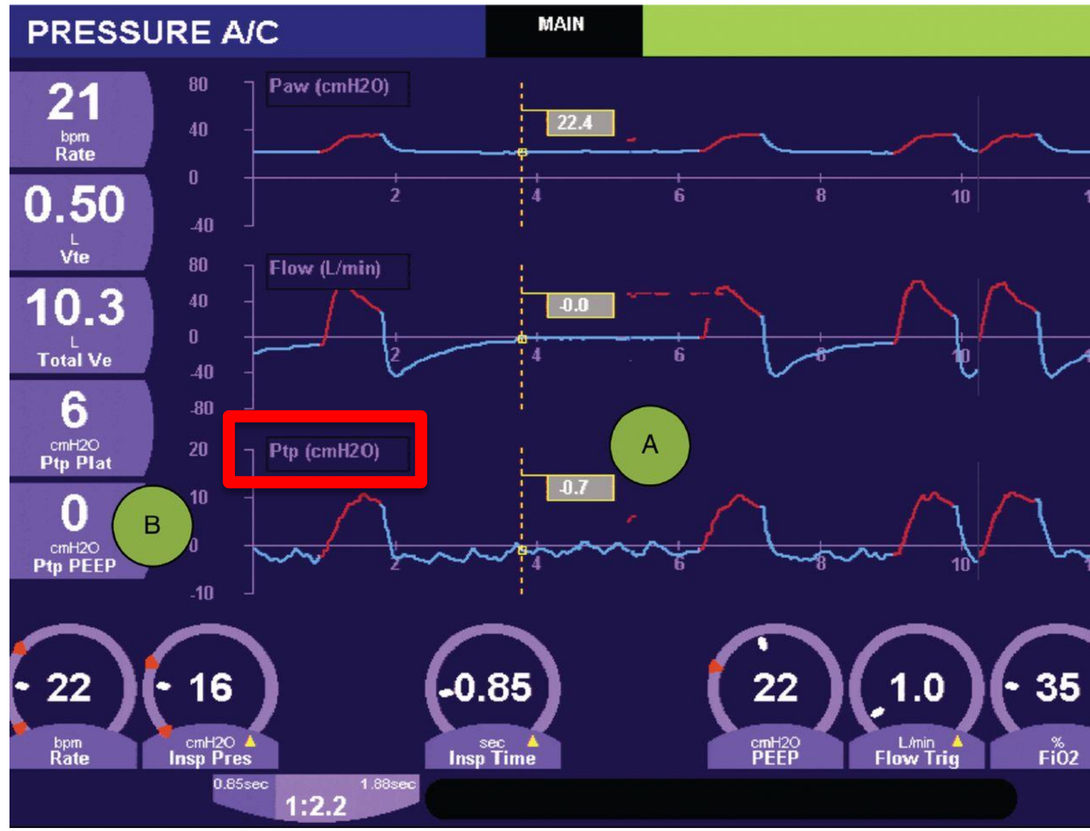
Sam R Orde et al. PMID: 25873786
BMC Anesthesiol. 2015; 15: 49.

Optimal PEEP Guided by Esophageal Balloon Manometry



Look for cardiac oscillations





Tom Piraino and Deborah J Cook.
Respiratory Care April 2011, 56 (4) 510-513

Optimal PEEP in prone position?

- 參照PEEP table，是否一定要higher PEEP 目前無定論
- Obesity/腹壓高須考慮higher PEEP

Lower PEEP/higher FiO2

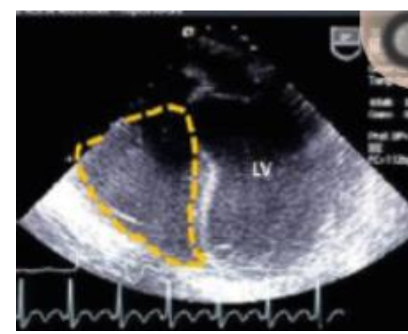
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

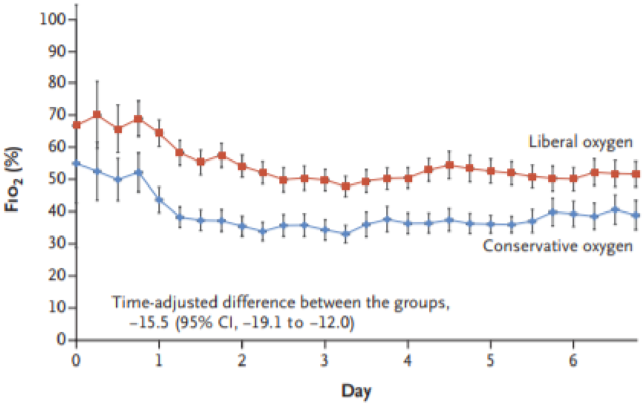
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

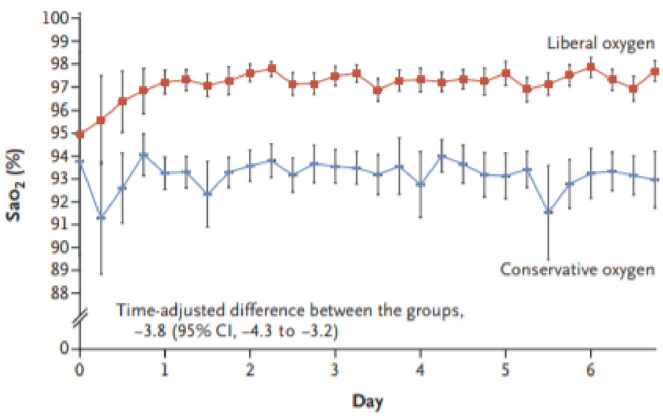
FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

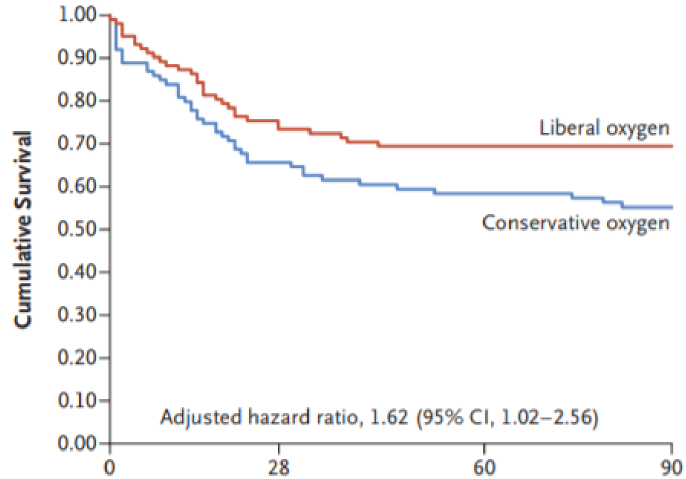


Optimal FiO_2 in ARDS

Liberal or Conservative Oxygen Therapy for Acute Respiratory Distress Syndrome







Mesenteric ischemia →

Arrhythmia →

Variable	Conservative Oxygen (N=99)		Liberal Oxygen (N=102)	
	no./total no.	*% (95% CI)*	*no./total no.*	*% (95% CI)*
Mesenteric ischemia	5/99	5.1 (1.7–11.4)	0/102	
Cardiac adverse events				
Arrhythmia	23/99	23.2 (14.9–31.6)	16/102	15.7 (8.6–22.7)
New-onset atrial fibrillation	21/99	21.2 (13.2–29.3)	13/102	12.7 (6.3–19.2)
Events leading to treatment	23/99	23.2 (14.9–31.6)	14/102	13.7 (7.0–20.4)

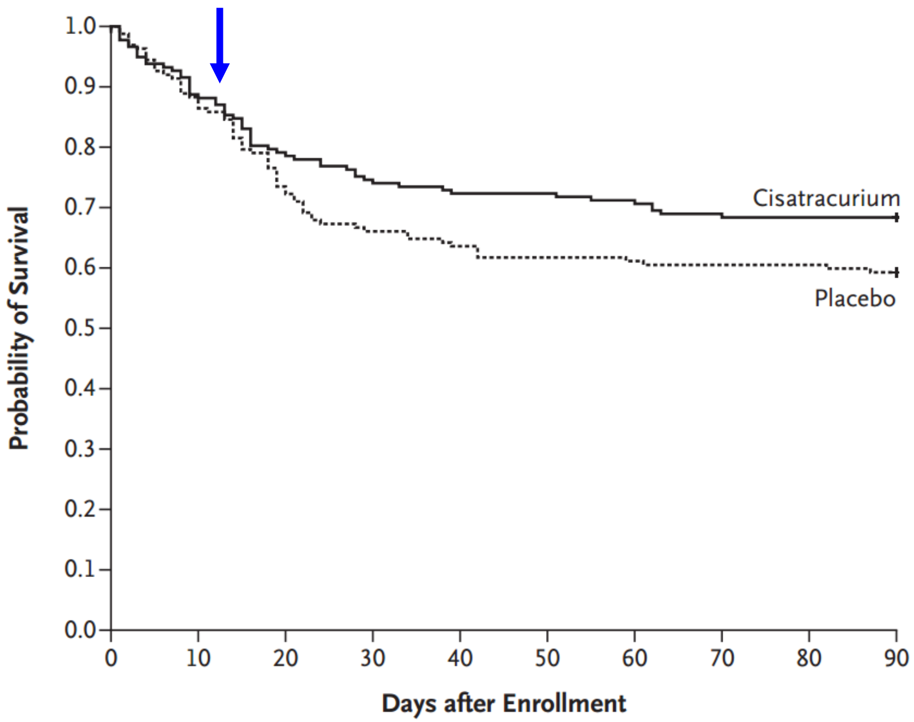
A relatively high oxygenation (SaO2 96%) might be feasible in those with risk for mesenteric ischemia or arrhythmia.

Loic Barrot et al. PMID: 32160661
N Engl J Med. 2020 Mar 12;382(11):999-1008.

Is NMBAs always required in ARDS without and with prone positioning?

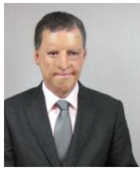
Neuromuscular blockers in early acute respiratory distress syndrome

ACURASYS



- **2 days of Cisatracurium**
- **Patients with severe ARDS. (P/F ratio < 150)**
- The impact of **VILI** appeared to be prominent after day-15

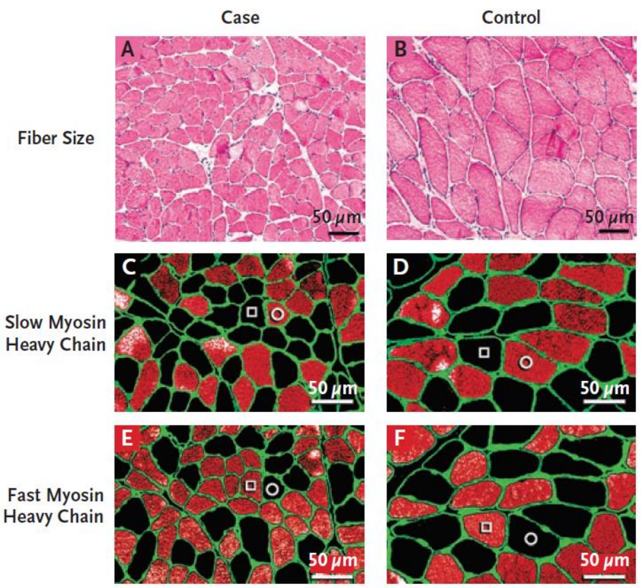
(Baseline mortality: 45%)



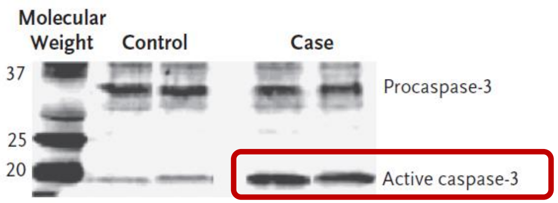
Papazian L. et al. ACURASYS Study Investigators. N Engl J Med. 2010 Sep 16;363(12):1107-16.

Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans

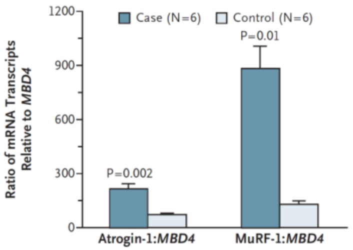
- **Background**: Diaphragm inactivity post mechanical ventilation for **18 hours in animals.**
- **Study-design**:
  - ✓ Case: Costal diaphragms of **14 brain-dead organ donors**. (**MV: 18-69 hours**)
  - ✓ Control**: Intraoperative diaphragm-biopsy** of 8 patients. (**MV: 2-3 hours).**



Active caspase-3 (protein degradation)



Atrogin-1/MuRF-1 (ubiquitin ligases)

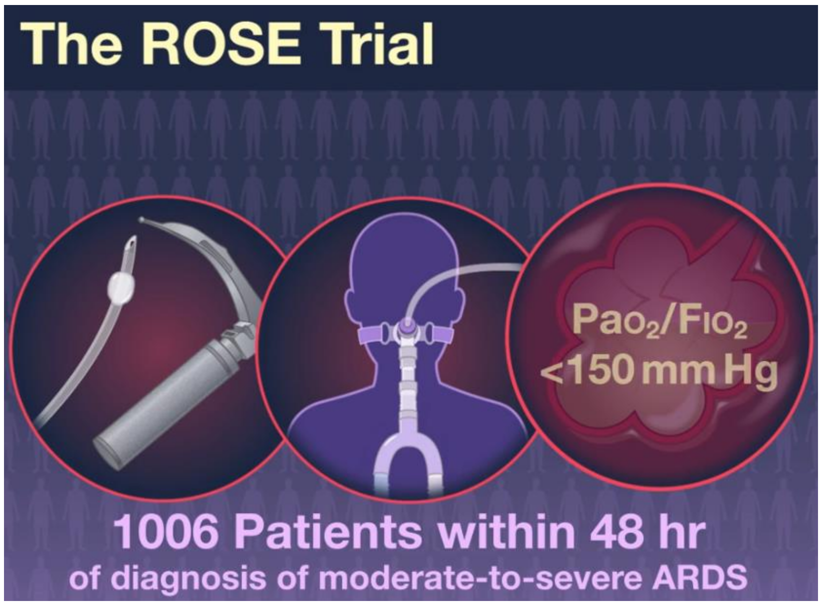


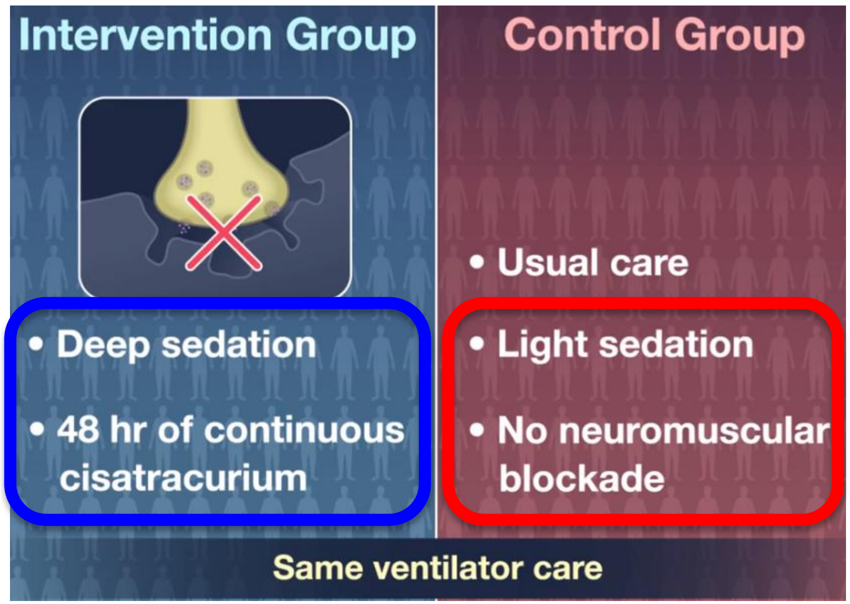
Levine S. et al.
N Engl J Med. 2008 Mar 27;358(13):1327-35.

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

ROSE trial

lightly sedated **(RASS 0 to -1)**





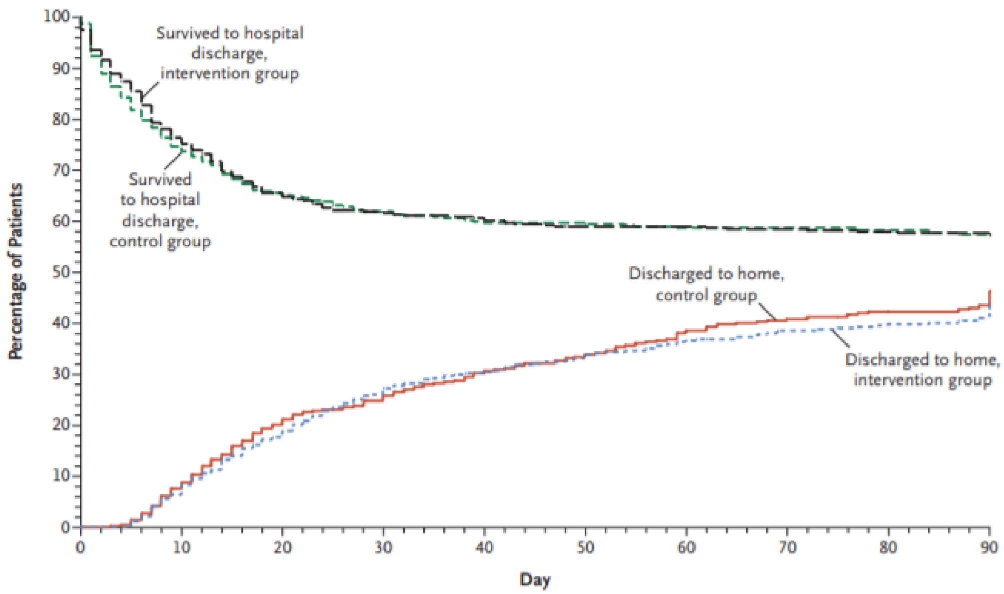
PEEP of ≥8 cm

1,408 ➔ early stopped

PETAL Clinical Trials Network. PMID: 31112383
Prevention and Early Treatment of Acute Lung Injury (PETAL)
N Engl J Med. 2019 May 23;380(21):1997-2008.

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

ROSE trial



PETAL Clinical Trials Network. PMID: 31112383
Prevention and Early Treatment of Acute Lung Injury (PETAL)
N Engl J Med. 2019 May 23;380(21):1997-2008.

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

ROSE trial

1,408 ➔ 1006 early stopped

Adverse Events

ICU-acquired weakness

- **At Day 7**: 41.0% vs. 31.3% (Difference -9.7, 95% CI -21.5 to 2.1)
- **At Day 28**: 46.8% vs. 27.5% (Difference -19.4, 95% CI -38.2 to -0.6)

Serious adverse events

- 35 events vs. 22 events (P=0.09)
- **Barotrauma**: 4.0% vs. 6.3% (P=0.12)
- **Serious adverse cardiovascular events**: 14 events vs. 4 events (P = 0.02)

Cardiac arrest

System/disorder	Event	Severity	Intervention	Control
Blood/lymphatic	Methemoglobinemia	Serious	2	0
Cardiac	Complete atrioventricular block	Serious	1	0
	Atrial fibrillation (paroxysmal)	Non-Serious	1	0
	Atrial fibrillation w/ rapid vent response	Serious	1	0
	Bradycardia	Serious	1	0
		Non-Serious	1	0
	Cardiac arrest	Serious	6	2
		Non-Serious	0	2
	Cardiac arrhythmia (NOS)	Non-Serious	1	0
	3rd degree atrioventricular block	Serious	0	1
	Myocardial infarction	Serious	1	1
	Serious prolonged bradycardia	Non-Serious	1	0
	Tachycardia	Non-Serious	1	0
	Supraventricular tachycardia	Serious	1	0
	Torsades De Pointe	Serious	1	0
	Vasovagal reaction	Non-Serious	0	1
	Ventricular tachycardia	Serious	2	0

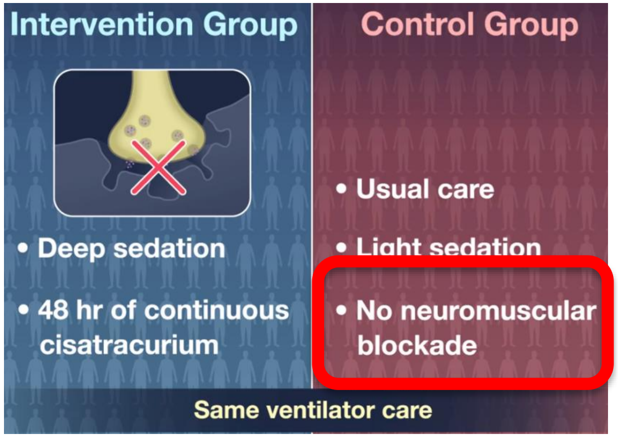
PETAL Clinical Trials Network. PMID: 31112383
Prevention and Early Treatment of Acute Lung Injury (PETAL)
N Engl J Med. 2019 May 23;380(21):1997-2008.

Is NMBAs always required in ARDS without and with prone positioning?

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

ROSE trial

lightly sedated **(RASS 0 to -1)**



- **Prone positioning** was used in **15.8%** of patients (**159**/1006), with **similar use in the two groups**.
- **Most (56%, 42/75 patients)** of patients who underwent prone positioning in the control group

did not receive concomitant NMBAs

PETAL Clinical Trials Network. PMID: 31112383
N Engl J Med. 2019 May 23;380(21):1997-2008.

GUIDELINES SURVIVING SEPSIS CAMPAIGN SEPSIS

Surviving Sepsis Campaign Guidelines 2021

For adults with sepsis induced moderate-severe ARDS, we suggest using intermittent NMBA boluses, over NMBA continuous infusion.

Quality of evidence: Moderate

Ventilation Weak Neuro Muscular Blockade

Intermittent NMBA boluses, over NMBA continuous infusion

Is NMBAs always required in ARDS without and with prone positioning?

↓

Real-world use of NMBAs among patients with ARDS in Taiwan

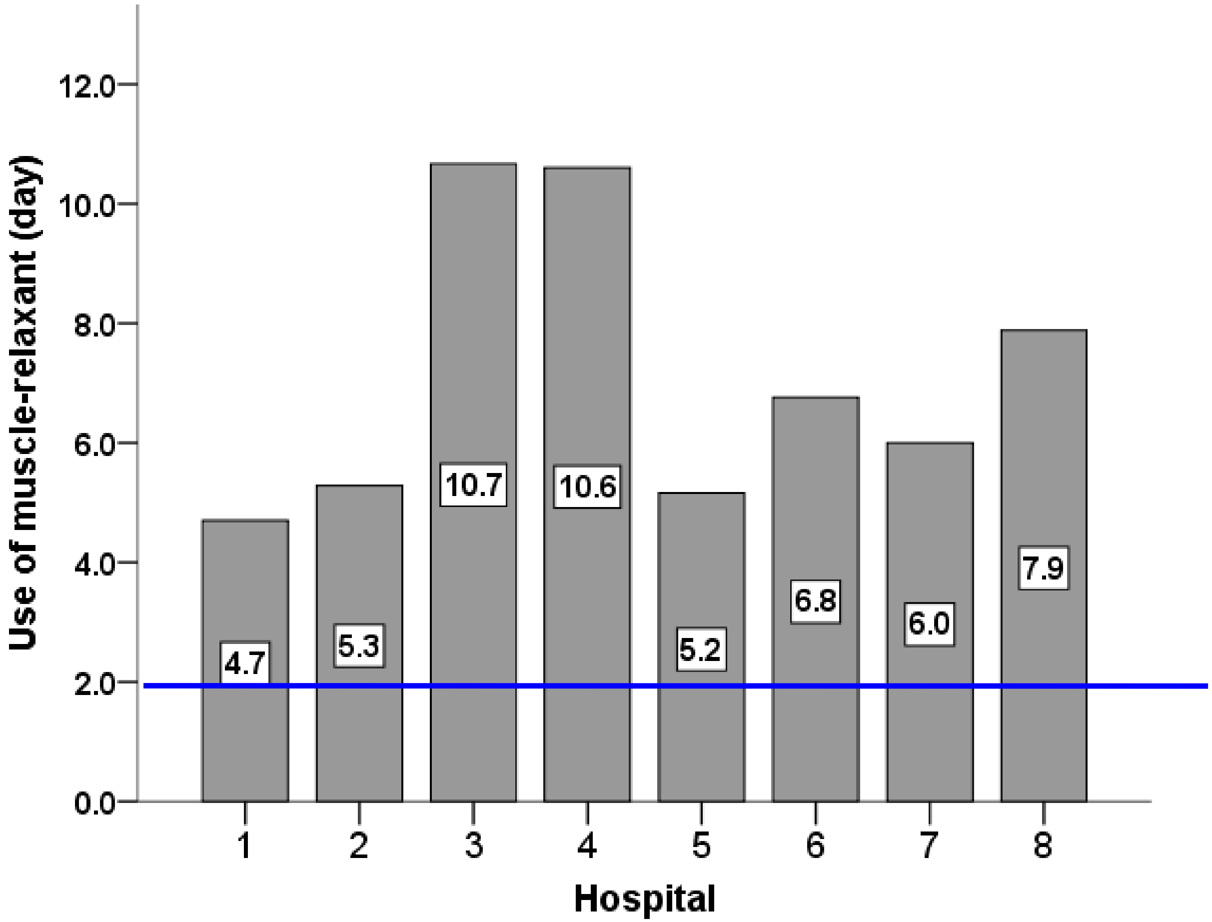
Usage of sedative agents and neuromuscular blockade of subjects with influenza-related ARDS during 2016 influenza epidemic in Taiwan

Administration-day of sedative agents and neuromuscular blockade in influenza-related ARDS

	All	Severe-ARDS	Moderate-ARDS	Mild-ARDS
	N=216	N=135	N=60	N=21
Sedative agent (days)	10.6±9.6	11.7±9.8	9.6±10.1	6.5±4.8
Neuromuscular blockade (days)	6.2±5.5	7.4±5.4	5±5.4	2±3.6

Taiwan Severe Influenza Research Consortium (TSIRC) investigators.

Administered-day of NMBA in subjects with influenza-related **severe ARDS** by participating **hospital**



Taiwan Severe Influenza Research Consortium (TSIRC) investigators.

Prone position in ARDS patients: why, when, how and for whom

Unanswered questions

1.Underutilized of prone ventilation.

2.Optimal duration is not definitely determined.

3. Ventilator settings (PEEP/FiO2) in prone should be addressed.

4. NMBAs may not be always required .

5. Awaken prone position in non-intubated patients

Claude Guérin et al. PMID: 33169218

Intensive Care Med. 2020 Nov 10 : 1–12.

Awake Proning without ventilator

Anand Swaminathan et al.

https://rebelem.com/covid-19-awake-proning/

Intubation rate of patients with hypoxia due to COVID-19 treated with awake proning: A meta-analysis

- 16 studies with 364 patients
- The intubation rate was 28% (95% CI 20%-38%, I2 = 63%).
- The mortality rate among patients who underwent awake PP was 14% (95% CI 7.4%-24.4%).

Stephanie Cardona et al. PMID: 33550104
Am J Emerg Med . 2021 Jan 27;43:88-96

Intubation rate of patients with hypoxia due to COVID-19 treated with awake proning: A meta-analysis

16 studies with 364 patients ➔High heterogeneity

Delta ROX index might potentially a predictor for intubation

Table 3B
Results from meta-regression measuring the associations between continuous variables and outcome of any intubation during hospital stay

Moderator variables	Number of studies	Correlation coefficient	95% CI	*P* value	R^2	I^2
Age - years	17	0.06	−0.02, 0.14	0.14	0	66%
Percent of male patients	17	1.7	−1.3, 5.01	0.3	0	65%
BMI	6	0.15	−0.13, 0.43	0.29	0.1	81%
Initial P/F ratio[a]	12	0	−0.01, −0.85	0.4	0	66%
Delta P/F ratio[a]	12	0.01	−0.01, 0.03	0.36		
Initial ROX index[b]		−0.07			0.51	67%
	11		−0.2, 0.08	0.45		
Delta ROX index[b]	9	0.1	−0.01, 0.2	0.06		
Proning duration per day (hours)	8	0.04	−0.19, 0.26	0.76	0	1%
Total duration of proning (hours)	9	−0.04	−0.09, 0.01	0.12	0.47	31%

[a,b]Multivariable meta-regressions included both continuous variables.
95% CI, 95% confidence interval; BMI, body mass index; Delta, change between initial and repeat values of ROX index or P/F ratio; P/F ratio, PaO2 (partial pressure of oxygen)/FiO2 (fraction of inspired oxygen) ratio; ROX index, respiratory oxygen index.

Stephanie Cardona et al. PMID: 33550104
Am J Emerg Med . 2021 Jan 27;43:88-96

High Flow Nasal Cannula

- HFNC使用之後，何時決定換BiPAP或插管

➔ROX index < 4.88

ROX Index = (SpO2/FiO2)/RR

➔ROX index不考慮PaCO2, pH, HCO3

(HFNC主要提升氧合功能，RR變快就表示只靠提升氧合已經撐不住)

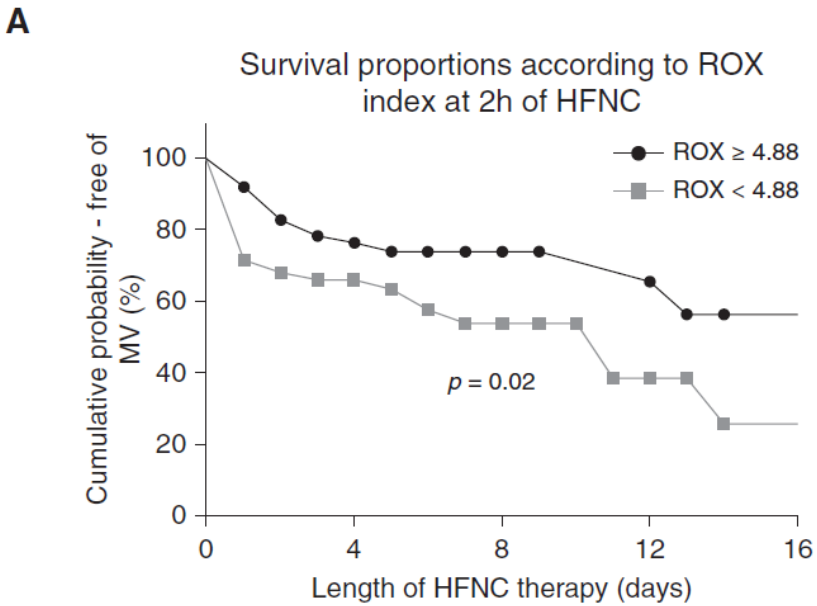
➔ROX 4.88➔FiO2 60%, SpO2 94%, RR:32

An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy

pneumonia with acute respiratory failure

ROX index ➔ [SpO2/FIO2] / RR

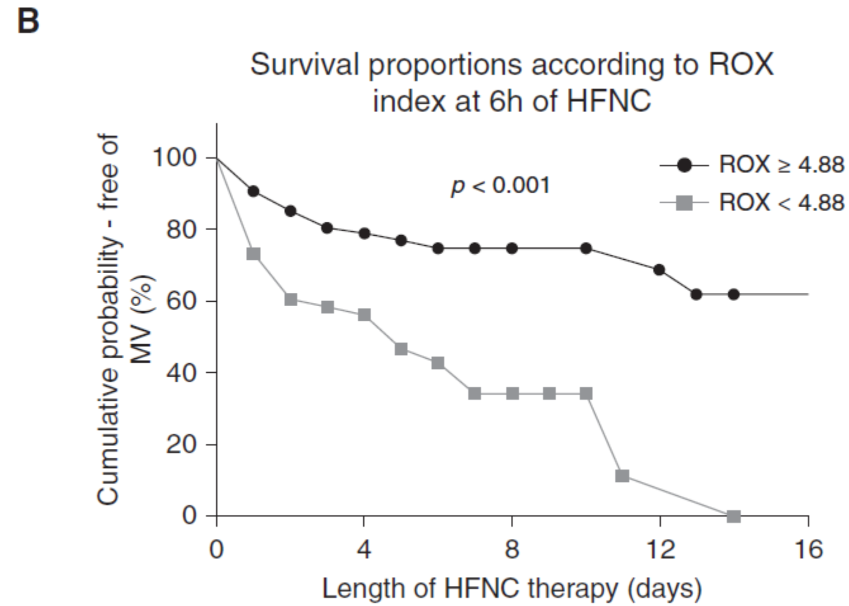
2h after HFNC



Number at risk

ROX ≥ 4.88	105	40	11	8	1
ROX < 4.88	74	26	11	4	1

6h after HFNC



Number at risk

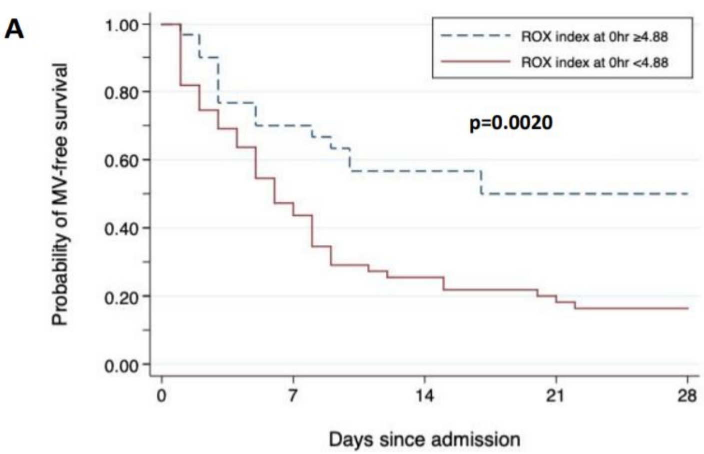
ROX ≥ 4.88	127	53	17	12	3
ROX < 4.88	49	16	8	1	0

Roca O et al. PMID: 30576221
Am J Respir Crit Care Med. 2019 Jun 1;199(11):1368-1376.

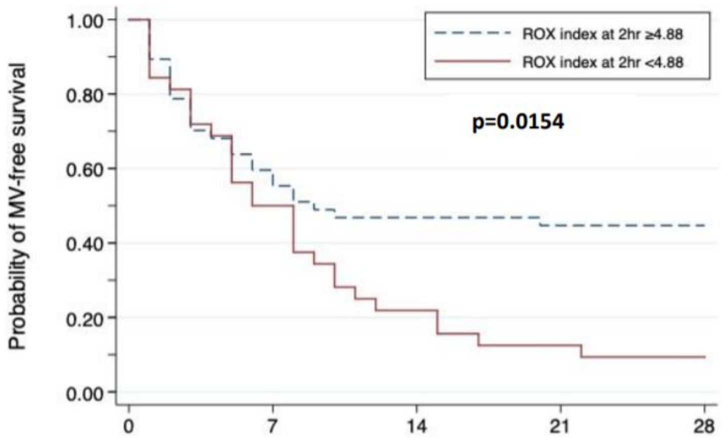
ROX Index to Guide Management of COVID-19 Pneumonia

ROX index → [SpO2/FIO2] / RR

ROX 4.88 at 0-hr



ROX 4.88 at 2-hr

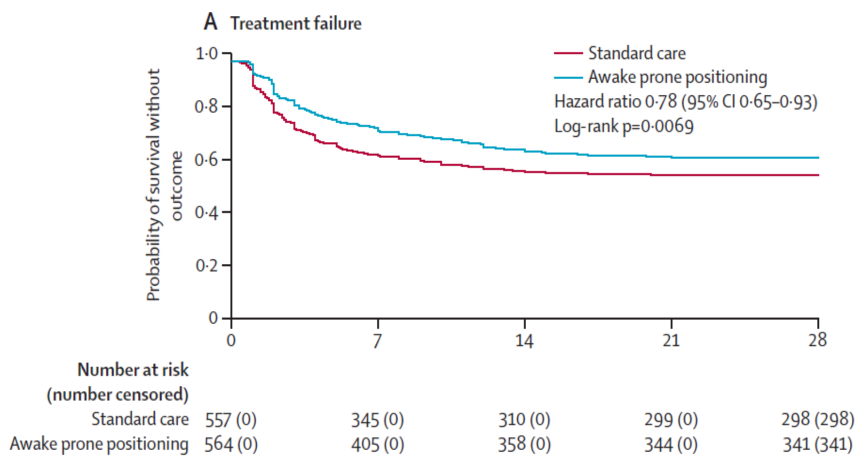


Douglas L Fink et al. PMID: 33636094
Ann Am Thorac Soc. 2021 Feb 26.

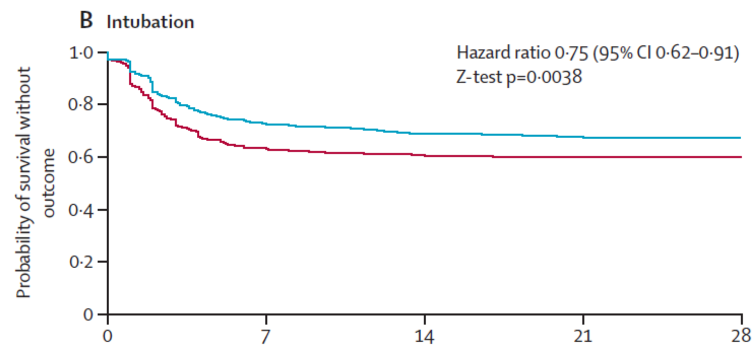
Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

N=1126

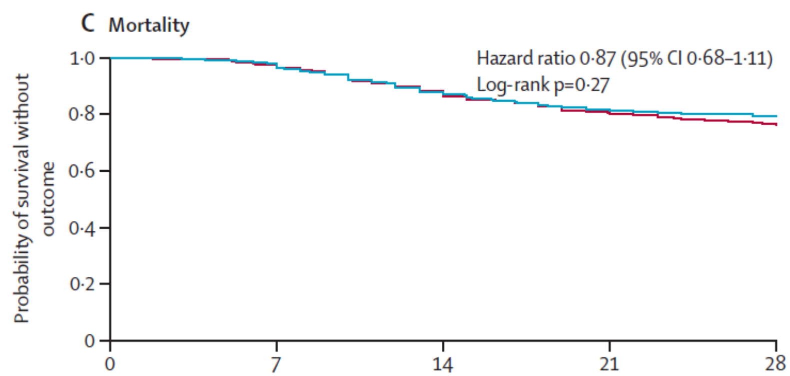
Treatment failure (intubation or death).



Intubation



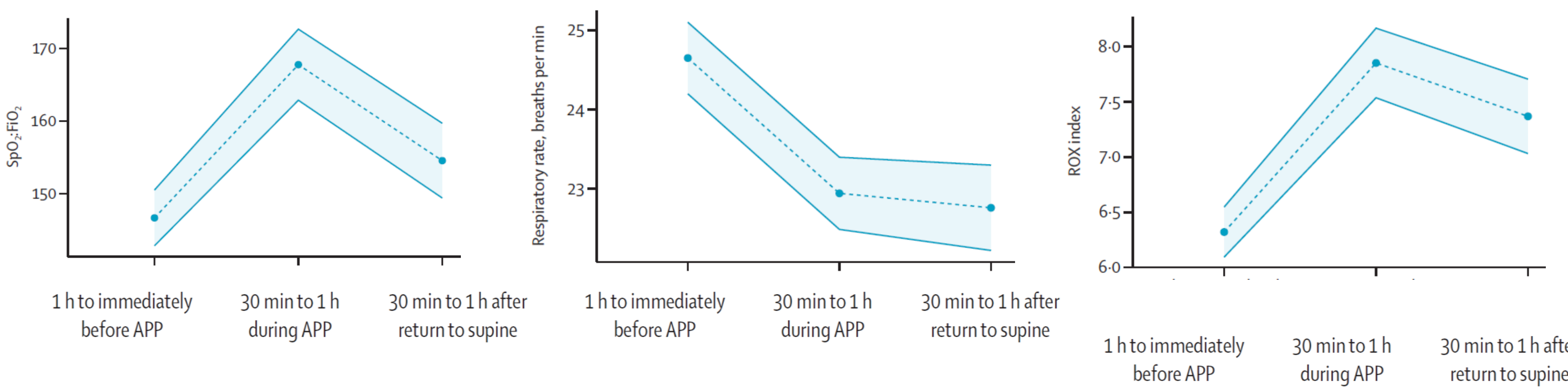
Death



Stephan Ehrmann et al. Awake Prone Positioning Meta-Trial Group
Lancet Respir Med. 2021 Dec;9(12):1387-1395. PMID: 34425070

Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

SpO2/FiO2 **Respiratory rate** **ROX index**



Conclusions

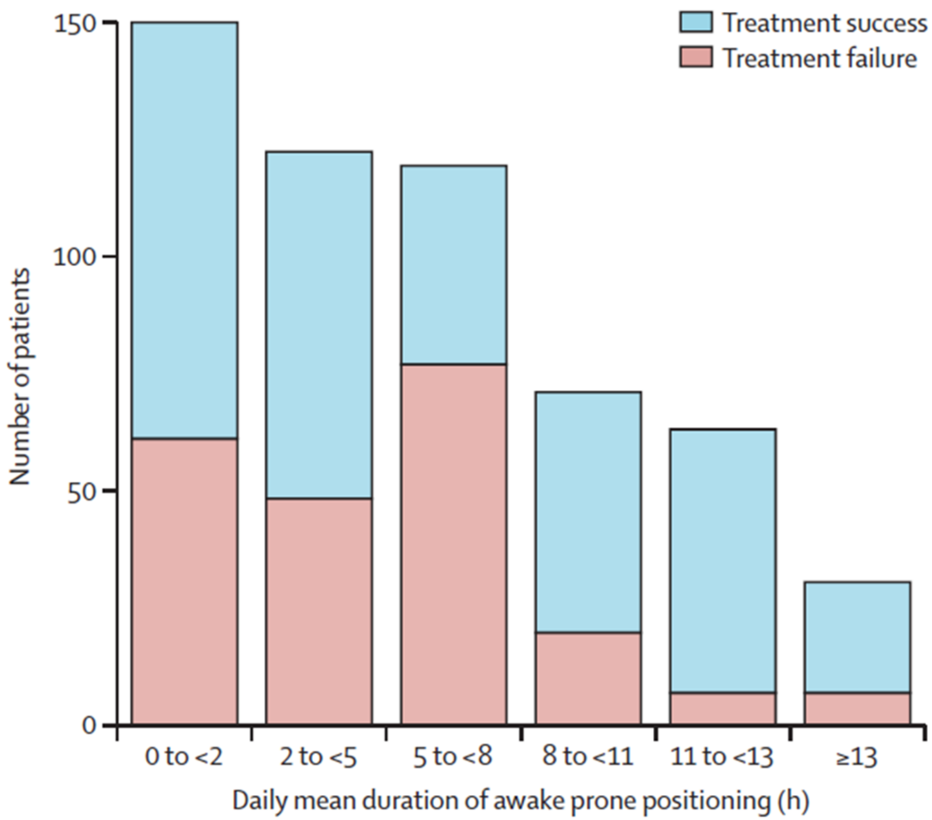
1.Awake prone positioning of patients with hypoxaemic respiratory failure due to **COVID-19 reduces the incidence of treatment failure and the need for intubation** without any signal of harm.

2.These results **support routine awake prone positioning** of patients with COVID-19 who **require support with high-flow nasal cannula.**

Stephan Ehrmann et al. Awake Prone Positioning Meta-Trial Group
Lancet Respir Med. 2021 Dec;9(12):1387-1395. PMID: 34425070

Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

The optimal/feasible duration of awake prone positioning remains unclear.



Stephan Ehrmann et al. Awake Prone Positioning Meta-Trial Group
Lancet Respir Med. 2021 Dec;9(12):1387-1395. PMID: 34425070

Outline

1. Prone ventilation till 2013 [PROSEVA]

2. Prone ventilation evidence ~2014-2019

   [LUNG-SAFE, TSIRC, APRONET]

3. Prone positioning in COVID-19 era

4. Prone ventilation on ECMO

Prone on ECMO

- **Effect of prone positioning on survival in adult patients receiving venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis.**

  Papazian L et al. PMID: 35037993
  Intensive Care Med. 2022 Mar;48(3):270-280.

- **Prone positioning during venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a pooled individual patient data analysis.**

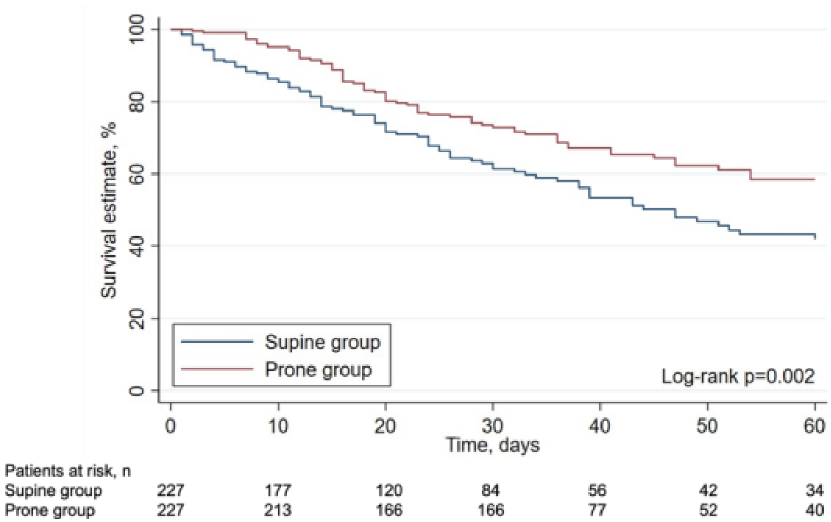
  Giani M et al. (EuroPronECMO Investigators.)
  Crit Care. 2022 Jan 6;26(1):8. PMID: 34986895

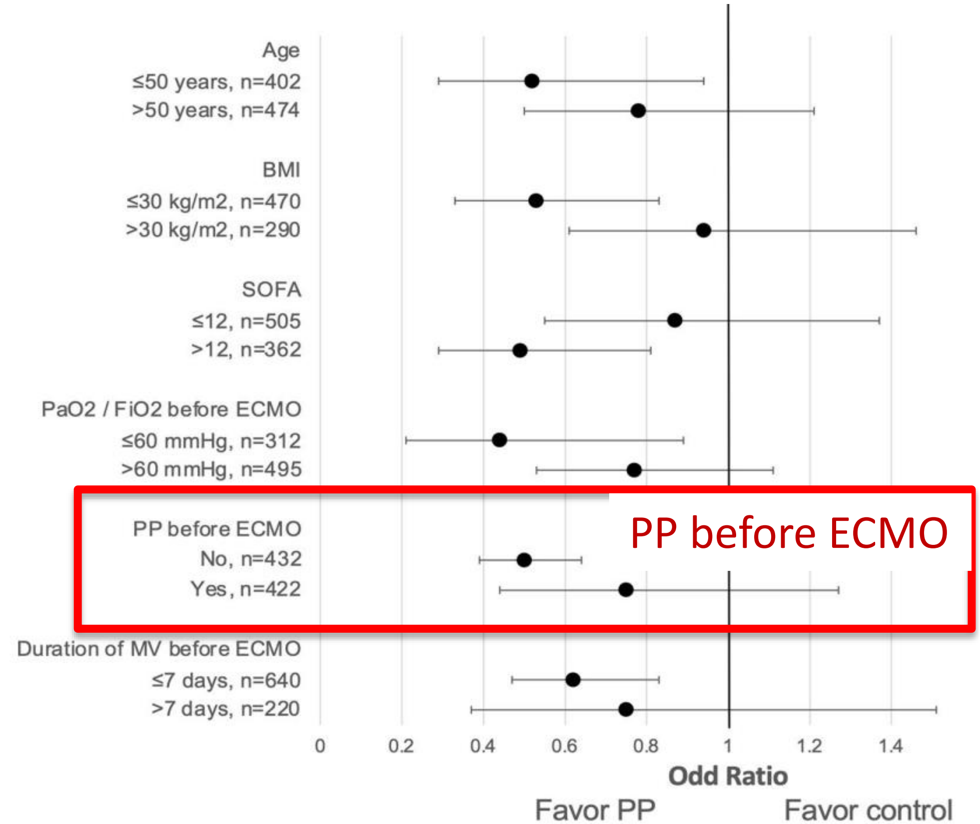
- **Beneficial Effect of Prone Positioning During Venovenous Extracorporeal Membrane Oxygenation for Coronavirus Disease 2019.**

  Zaaqoq AM et al. COVID-19 Critical Care Consortium (COVID Critical).
  Crit Care Med. 2022 Feb 1;50(2):275-285. PMID: 34582415

Prone positioning during venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a pooled individual patient data analysis. [n=889]

Matched groups of patients





Conclusions:

In a large population of ARDS patients receiving venovenous extracorporeal support, the use of prone positioning during ECMO was **not** significantly associated with reduced ICU mortality.

Giani M et al. (EuroPronECMO Investigators.)
Crit Care. 2022 Jan 6;26(1):8. PMID: 34986895

Take home message

1. Prone positioning improves mortality in ARDS (P/F <150) under concurrent protective ventilation strategy.
2. Prone positioning is relatively underutilized and increasingly applied in COVID-19 era.
3. Optimal duration, PEEP, FiO2, and use of NMBAs remains to be elaborated.
4. Awake prone position is feasible and may be standard of care among patients with COVID and require HFNC in the near future.
5. Prone position might be feasible in ARDS patients receiving ECMO.
6. More Taiwanese data are urgently needed.

中榮官網 中榮FB

臺中榮民總醫院
Taichung Veterans General Hospital

感謝您的聆聽！

Thank you !

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Compassion Quality Innovation Accountability