UNIVERSITÀ DEGLI STUDI DI MILANO

Ospedale San Paolo
Polo Universitario

Sistema Socio Sanitario

Regione Lombardia

ASST Santi Paolo e Carlo

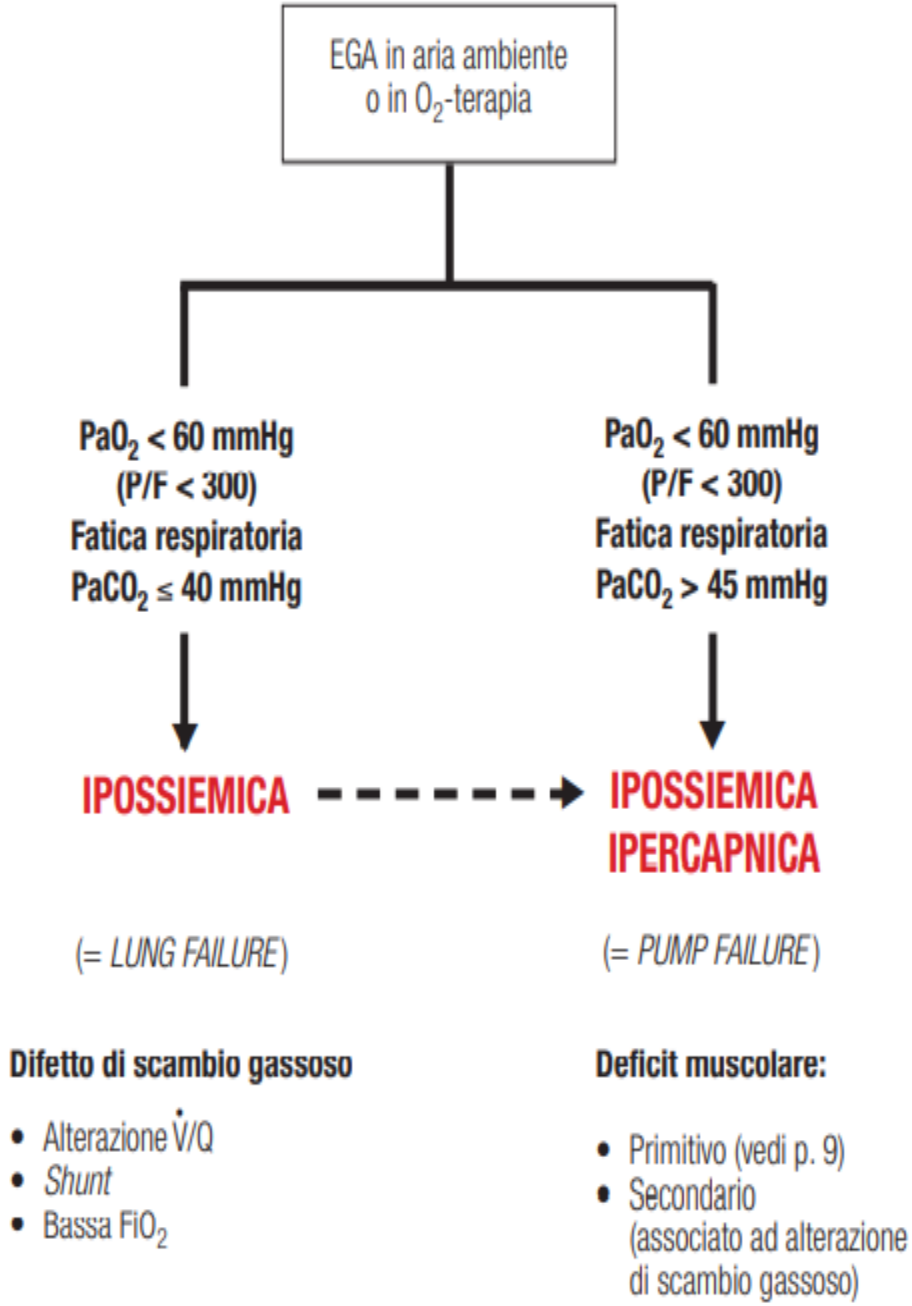
COVID 19
CRITERI DI VENTILAZIONE INVASIVA E NON

DOTT.SSA BARBARA BOVERI
UOC PNEUMOLOGIA
ASST- SANTI PAOLO CARLO
MILANO

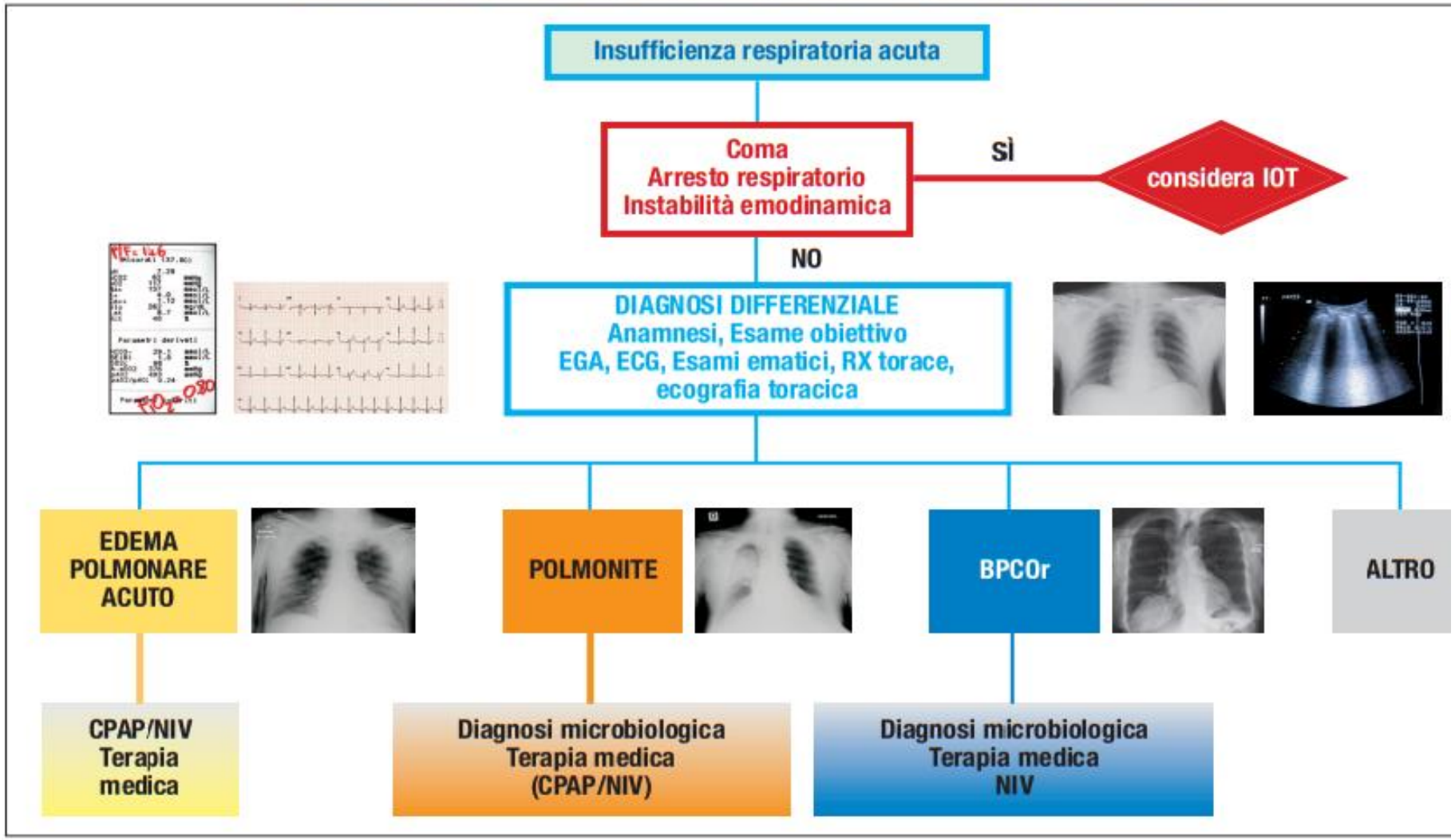
Insufficienza respiratoria acuta

- I valori di $PaCO_2$ e PaO_2 rilevati all'emogasanalisi arteriosa servono per definire la PRESENZA e il TIPO di insufficienza respiratoria acuta

- Il polmone non è in grado di garantire un'adeguata ossigenazione del sangue arterioso e/o eliminare correttamente la CO_2


EGA in aria ambiente
o in O_2-terapia
PaO_2 < 60 mmHg
(P/F < 300)
Fatica respiratoria
$PaCO_2 \leq 40$ mmHg
IPOSSIEMICA
(= *LUNG FAILURE*)
Difetto di scambio gassoso
• Alterazione $\dot{V}/Q$
• *Shunt*
• Bassa FiO_2
PaO_2 < 60 mmHg
(P/F < 300)
Fatica respiratoria
$PaCO_2$ > 45 mmHg
IPOSSIEMICA
IPERCAPNICA
(= *PUMP FAILURE*)
Deficit muscolare:
• Primitivo (vedi p. 9)
• Secondario
(associato ad alterazione
di scambio gassoso)

ALGORITMO DELLA NIV NELL'INSUFFICIENZA RESPIRATORIA ACUTA



Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

Eur Respir J 2017; 50: 1602426

TABLE 2 Recommendations for actionable PICO questions

Clinical indication[#]	Certainty of evidence[¶]	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
***De novo* respiratory failure**		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made

Justification

Despite the lack of any RCTs, the positive data from most of the observational studies and the controversial issue of possible increased risk of passing infection on to caregivers, we consider the prior recommendations against the use of NIV for pandemics as unsupportable. Although a cautious NIV trial in carefully selected patients at experienced centres, in a protected environment (*i.e.* negative pressure rooms), may be reasonable, further research is needed before a recommendation is possible.

Helmet CPAP treatment in patients with COVID-19 pneumonia: a multicenter, cohort study

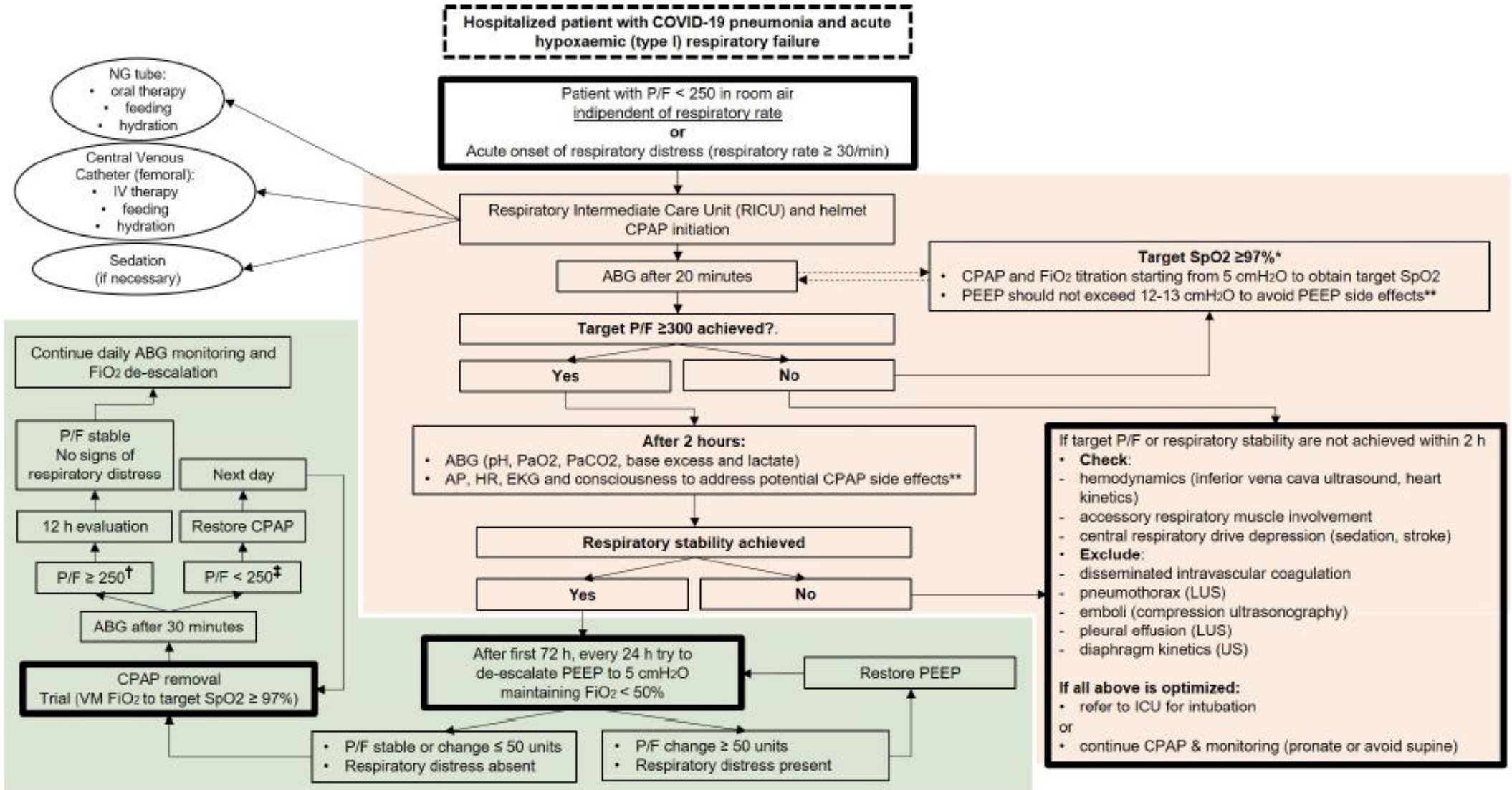
Stefano Aliberti MD[1,2], Dejan Radovanovic MD[3], Filippo Billi MD[4], Giovanni Sotgiu MD, PhD[5], Matteo Costanzo MS[2], Tommaso Pilocane MD[1,2], Laura Saderi BSc[5], Andrea Gramegna MD[1,2], Angelo Rovellini MD[4], Luca Perotto MD[3,6], Valter Monzani MD[4], Pierachille Santus MD, PhD[3,6], Francesco Blasi MD, PhD[1,2]

	CPAP Success (n= 87)	CPAP Failure (n= 70)	p-value
Demographics			
Males, n (%)	60 (69.0)	57 (81.4)	0.08
Median (IQR) age	66 (56-75)	60 (51-72)	0.08
Age > 65 years, n (%)	45 (51.7)	26 (27.1)	0.07
Age > 75 years, n (%)	20 (23.0)	15 (21.4)	0.82
Median (IQR) BMI	27.4 (25.1-30.2)	27.5 (23.7-29.3)	0.39
Obesity (BMI ≥30 kg/m^2), n (%)	16 (25.4)	13 (24.1)	0.87
Current/former smoker, n (%)	17 (19.5)	10 (14.3)	0.39
Comorbidities			
Any cardiovascular disease, n (%)	49 (56.3)	32 (45.7)	0.19
Hypertension, n (%)	41 (47.1)	28 (40.0)	0.37
Diabetes, n (%)	24 (27.6)	12 (17.1)	0.12
Ischemic Cardiac Disease, n (%)	19 (21.8)	8 (11.4)	0.09
Chronic Arrhythmias, n (%)	7 (8.1)	10 (14.3)	0.21
Cerebrovascular disease, n (%)	9 (10.3)	4 (5.7)	0.39
Immunosuppression, n (%)	8 (9.2)	3 (4.3)	0.35
COPD, n (%)	7 (8.1)	3 (4.3)	0.51
Chronic Renal Failure, n (%)	6 (6.9)	3 (4.3)	0.73
Liver disease, n (%)	5 (5.8)	4 (5.7)	1.00
Asthma, n (%)	1 (1.29	2 (2.9)	0.59

Study Outcomes			
Weaning from CPAP to Oxygen therapy, n (%)	84 (96.6)	6 (8.6)	<0.0001
Median (IQR) days from CPAP initiation to weaning to Oxygen therapy (n= 87)	7 (4-12)	7 (1-8)	0.31
Intubation, n (%)	0 (0.0)	34 (48.6)	<0.0001
Median (IQR) days from CPAP initiation to intubation (n= 34)	-	3 (2-5)	-
Mortality in HDU, n (%)	0 (0.0)	36 (51.4)	<0.0001
Median (IQR) days from CPAP initiation to HDU mortality (n= 36)	-	5 (3-10)	-
Median (IQR) length of hospitalization (n= 138)	18 (14-25.5)	8 (4-22)	<0.0001
In-hospital mortality, n (%)	0 (0.0)	45 (64.3)	<0.0001
Median (IQR) days from CPAP initiation to in-hospital mortality (n= 45)	0 (0-0)	6 (4-11)	-

Helmet CPAP to Treat Acute Hypoxemic Respiratory Failure in Patients with COVID-19: A Management Strategy Proposal

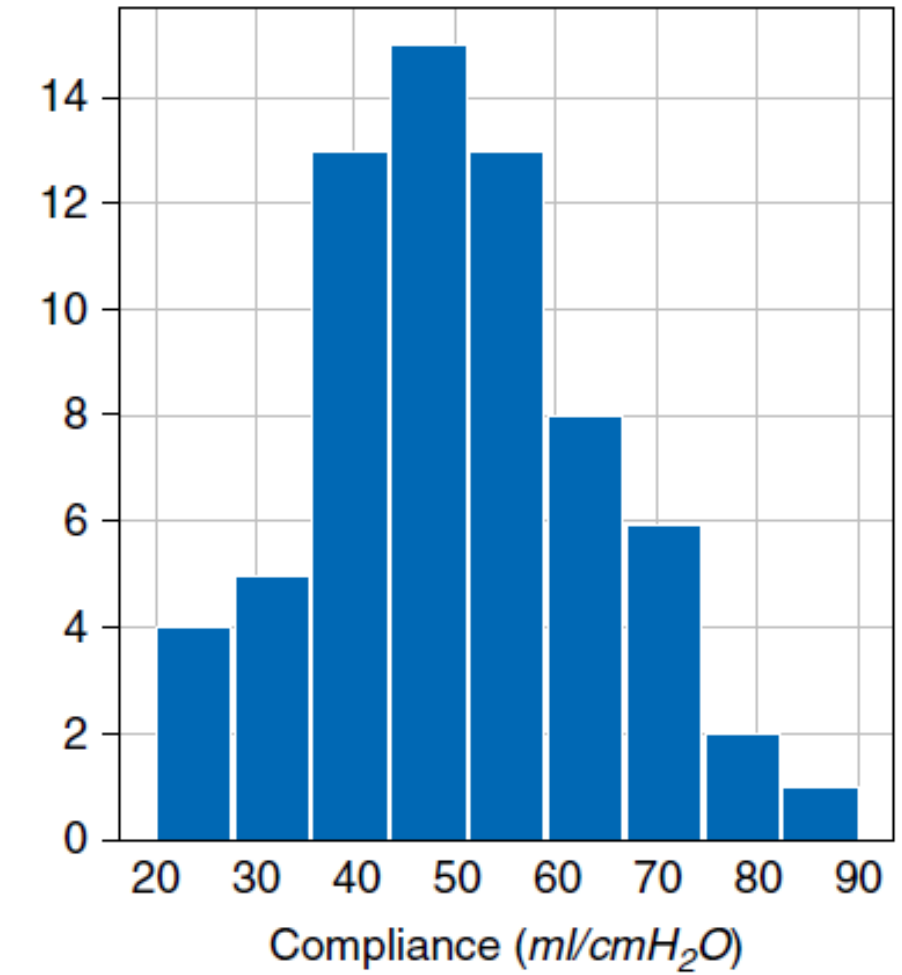
Dejan Radovanovic [1], Maurizio Rizzi [1], Stefano Pini [1], Marina Saad [1], Davide Alberto Chiumello [2,3] and Pierachille Santus [1,*]



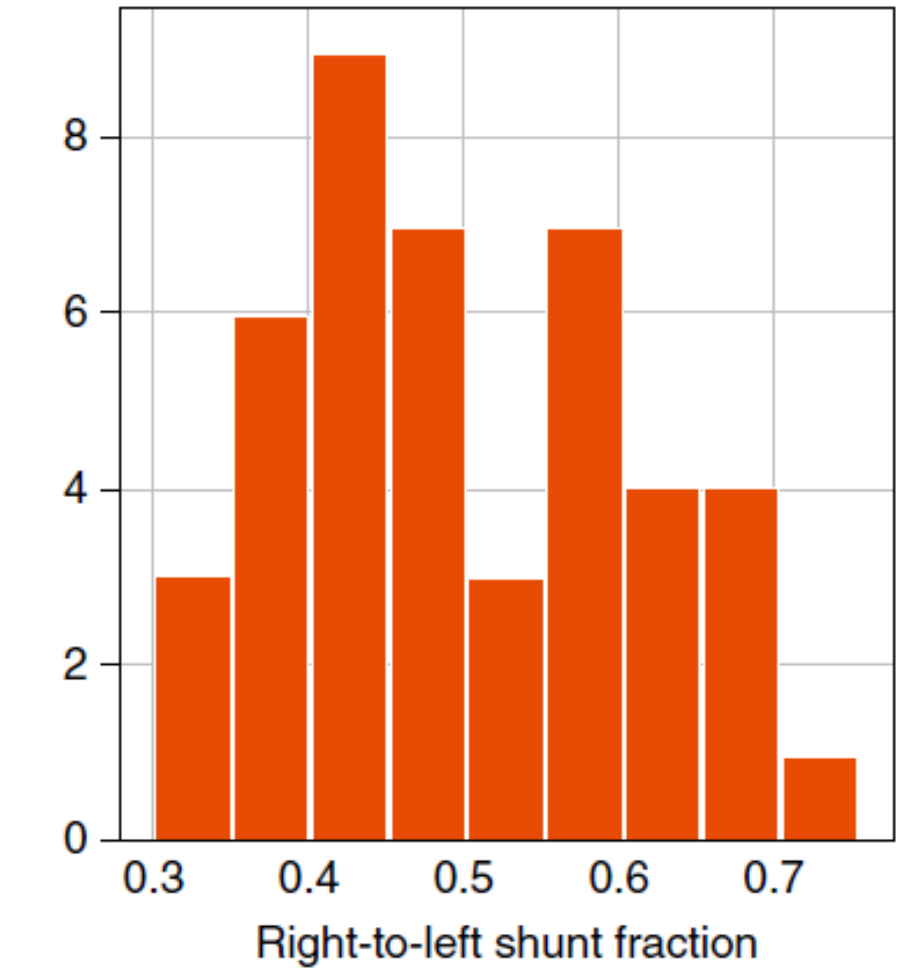
J. Clin. Med. **2020**, *9*, 1191; doi:10.3390/jcm9041191

COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome

Respiratory system **compliance** of **50**±14 ml/cm H_2O



Shunt fraction of **50**±11 %.



American Journal of Respiratory and Critical Care Medicine Volume 201 Number 10 | May 15 2020

Different phenotypes?

"…**COVID-19** pneumonia, despite falling in most of the circumstances under the Berlin **definition** of **ARDS**, is a **specific disease**, whose distinctive features are severe hypoxemia often associated with near normal respiratory system compliance…This remarkable combination is **almost never seen in severe ARDS**."

Type L

- **Low** elastance.
- **Low** ventilation-to-perfusion (VA/Q) ratio. (*loss of hypoxic vasoconstriction?)*
- **Low** lung weight.
- **Low** lung recruitability.

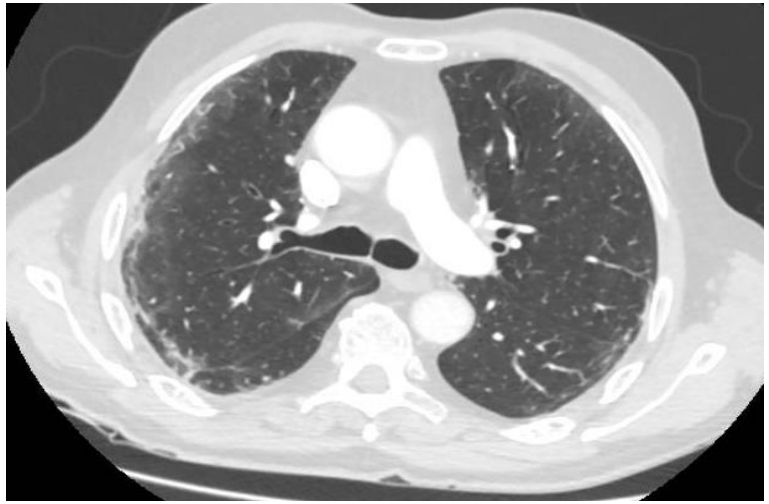
Type H

- **High** elastance.
- **High** right-to-left shunt.
- **High** lung weight.
- **High** lung recruitability.

Gattinoni et al. Intensive Care Med 2020

Different phenotypes of Covid19?

Type L



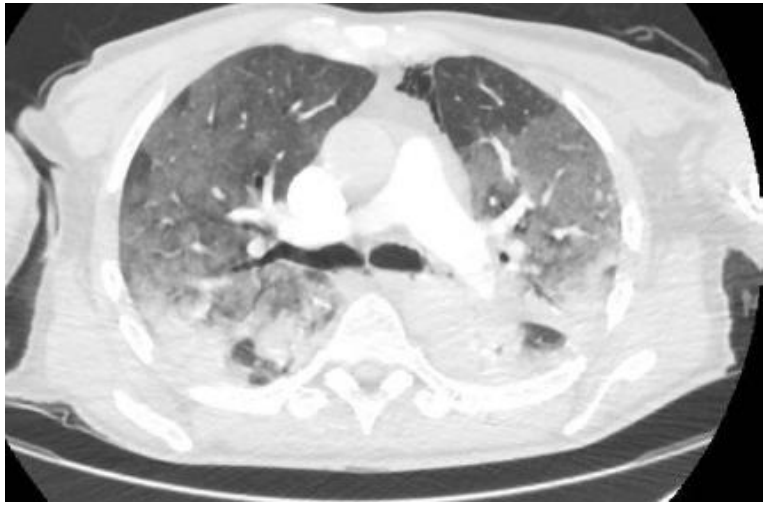
TREATMENT:

- **Increase FiO2:** low flow oxygen nasal cannula, Venturi Mask, Non rebreather mask
- **Non invasive support:** high-fow nasal cannula (HFNC), continuous positive airway pressure (CPAP), noninvasive ventilation (NIV).

P-SILI

COVID-19 Evolution

Type H



TREATMENT:

- **Treat as severe ARDS**, including higher PEEP, if compatible with hemodynamics, prone positioning and extracorporeal support.

Gattinoni et al. Intensive Care Med 2020

Management of COVID-19 Respiratory Distress

John J. Marini, MD; Luciano Gattinoni, MD

Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS

Time period	Objective	Respiratory support options	Rationale
Before intubation	Adequate gas exchange Avoid P-SILI	Supplemental oxygen, CPAP, NIV, HFNC Awake prone positioning, Target nonvigorous breathing	Powerful respiratory effort can cause reinforcing lung and vascular stress, resulting in injury
During mechanical ventilation	Avoid pulmonary deterioration and VILI vortex	Minimize PEEP, frequency and tidal volume Adjust to acceptable gas exchange Maintain fluid balance Reduce O_2 demand Consider ECMO	Minimize transpulmonary and vascular stresses
After intubation	Minimize pulmonary stress Optimize O_2 Avoid VILI vortex	Type L[a]: use lower PEEP (<10 cm H_2O) Use more liberal tidal volume (7-9 mL/kg) as needed Reduce O_2 demand Consider prone positioning	Lower tidal volumes are unnecessary Higher PEEP is ineffective, creates dead space, and adversely redirects blood flow
	Reduce and evenly distribute lung and vascular stresses Optimize O_2 Avoid VILI vortex	Type H[a]: use higher PEEP (<15 cm H_2O) Lower tidal volume (5-7 mL/kg) Reduce O_2 demand Implement prone positioning	More closely behaves and responds like typical ARDS
Weaning phase	Avoid reversion to previously worsened pulmonary state by causing VILI and worsening edema	Make transitions cautiously Avoid abrupt changes Spontaneous trials only at the very end of the weaning process	Strong spontaneous efforts raise O_2 demand, increase edema, and promote P-SILI

Abbreviations: ARDS, acute respiratory distress syndrome; CARDS, COVID-19 with ARDS; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; P-SILI, patient self-inflicted lung injury; PEEP, positive end-expiratory pressure; VILI, ventilator-induced lung injury.

[a] Type L: Scattered ground-glass infiltrates, higher compliance (>50 mL/cm H_2O), not PEEP responsive; less dyspnea.
Type H: Extensive infiltrates of atelectasis and edema, lower compliance, PEEP responsive, overtly dyspneic.

Clinical strategies for implementing lung and diaphragm-protective ventilation: avoiding insufficient and excessive effort

Intensive Care Med (2020) 46:2314–2326

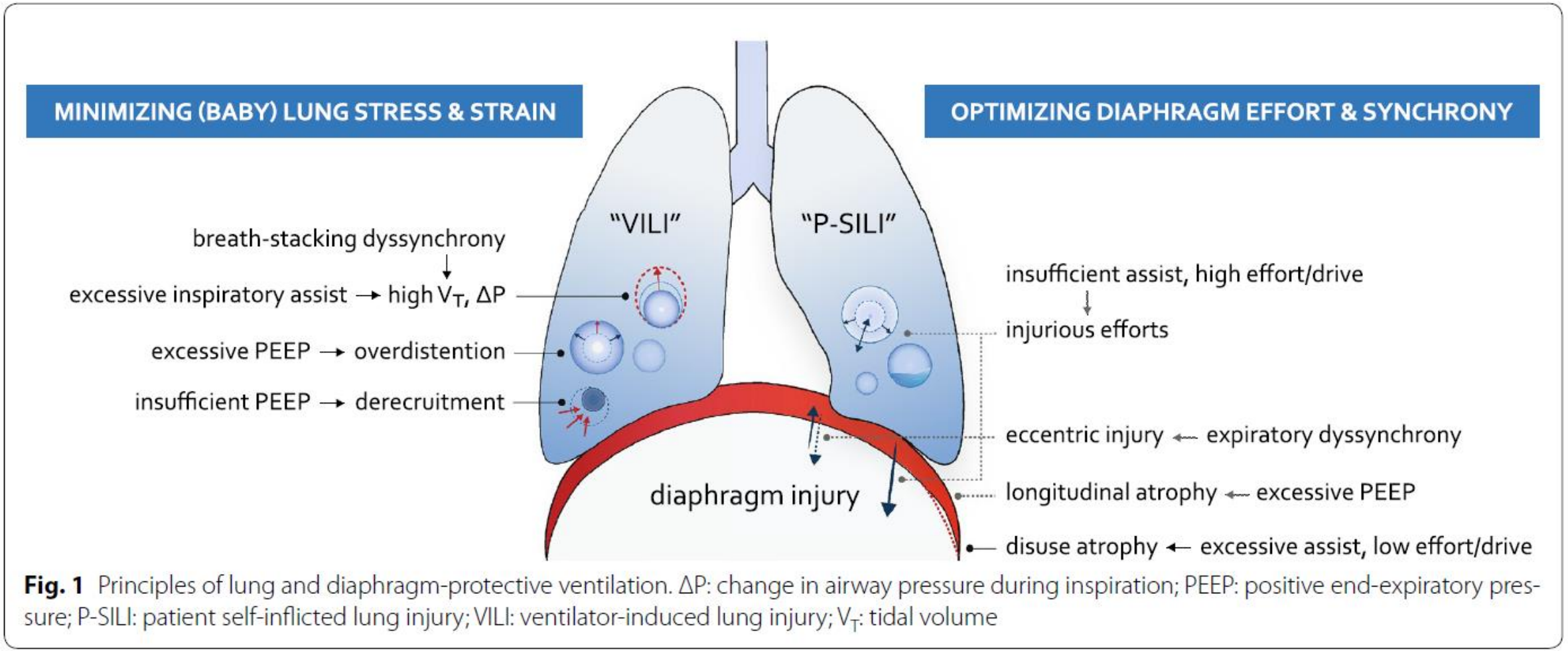
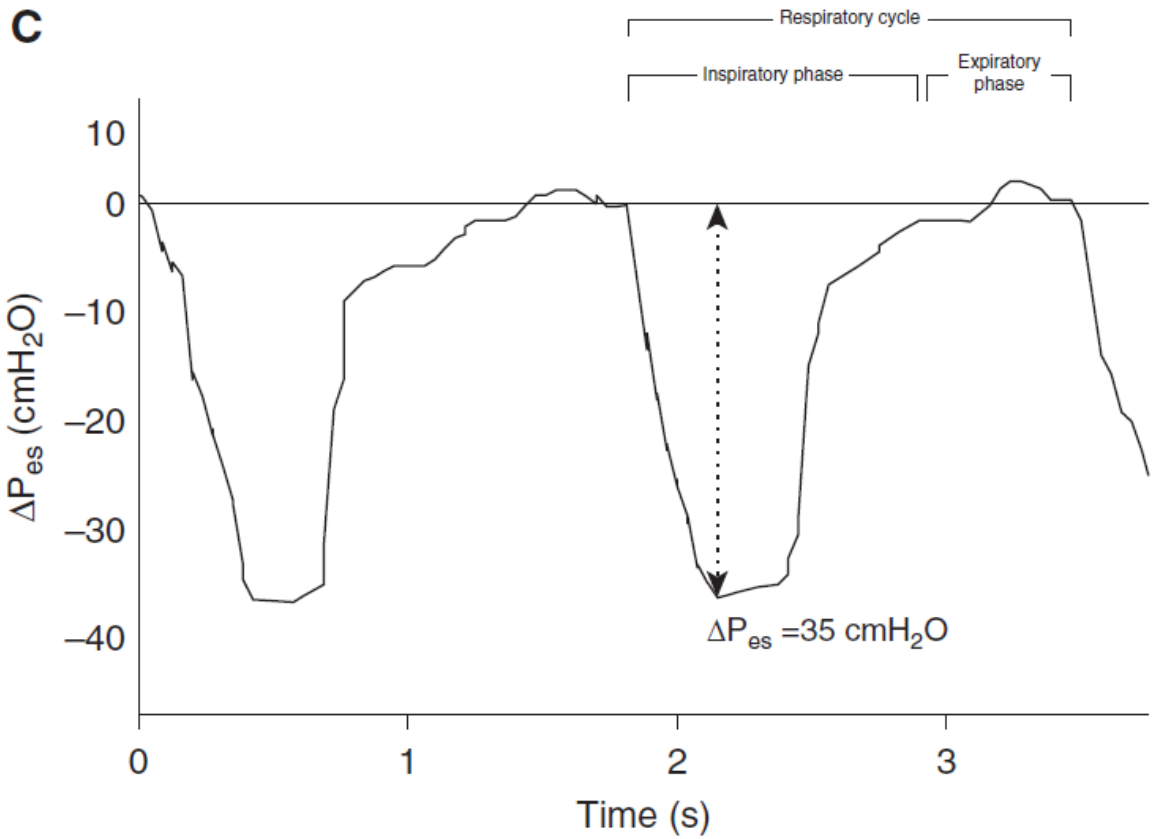


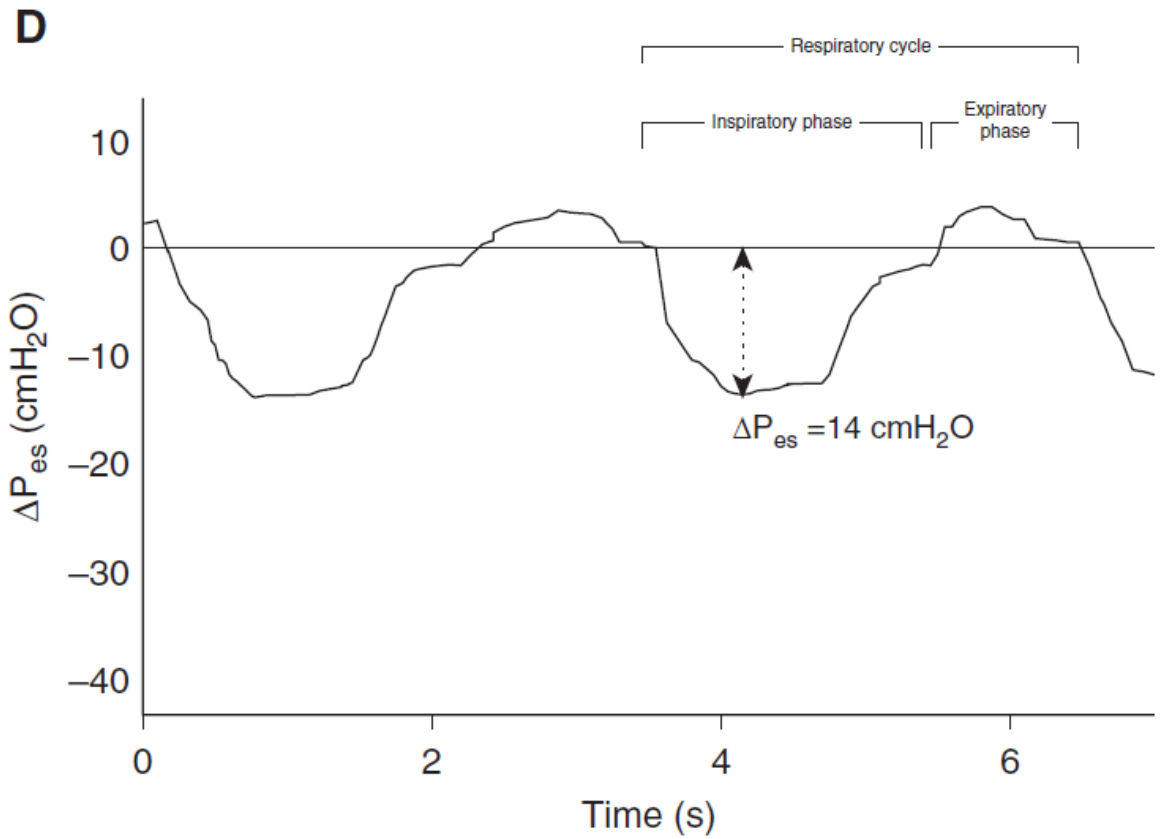
Fig. 1 Principles of lung and diaphragm-protective ventilation. ΔP: change in airway pressure during inspiration; PEEP: positive end-expiratory pressure; P-SILI: patient self-inflicted lung injury; VILI: ventilator-induced lung injury; V_T: tidal volume

Early Inspiratory Effort Assessment by Esophageal Manometry Predicts Noninvasive Ventilation Outcome in *De Novo* Respiratory Failure

A Pilot Study

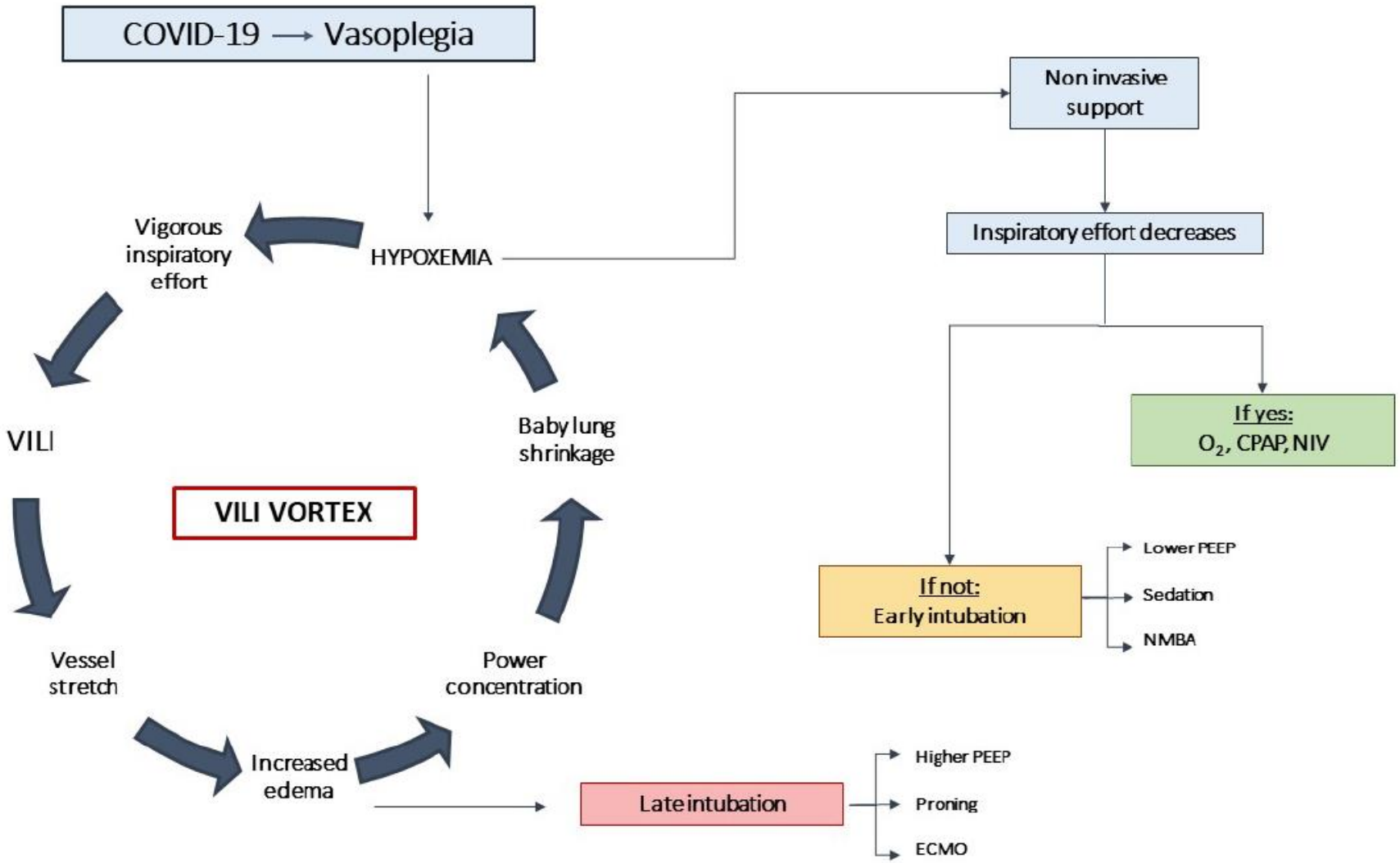
Roberto Tonelli[1,2], Riccardo Fantini[1], Luca Tabbì[1], Ivana Castaniere[1,2], Lara Pisani[3], Maria Rosaria Pellegrino[1], Giovanni Della Casa[4], Roberto D'Amico[5], Massimo Girardis[6], Stefano Nava[3], Enrico M. Clini[1], and Alessandro Marchioni[1]





Management of COVID-19 Respiratory Distress

John J. Marini, MD; Luciano Gattinoni, MD



Early Inspiratory Effort Assessment by Esophageal Manometry Predicts Noninvasive Ventilation Outcome in *De Novo* Respiratory Failure

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Table 3. Association between Physiological and Clinical Variables and NIV Failure at 24 Hours

Feature	OR	95% CI	*P* Value
$\Delta Pes < 10$ cm H_2O post 2 h NIV	15	2.8–110	0.001
$V_TE > 9.5$ ml/kg of PBW	7.9	1.5–72	0.02
HACOR score >5 post 2 h NIV	6.3	0.9–49	0.046
RR > 30 bpm	5.5	0.8–112	0.14
$Pa_{O_2}/F_{I_{O_2}}$ ratio < 150 mm Hg	2	0.5–9.8	0.4
$V_TE/\Delta P_L$ ratio < 0.33 ml/kg/cm H_2O	2	0.4–9.8	0.36

Nonmechanically Ventilated Adults With Hypoxemic Respiratory Failure

Recommendations

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV) **(BIIa)**.
- In the absence of an indication for endotracheal intubation, the Panel recommends a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure and for whom HFNC is not available **(BIIa)**.
- For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, the Panel recommends considering a trial of awake prone positioning to improve oxygenation **(CIIa)**.
- The Panel **recommends against** using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation **(AIII)**.
- If intubation becomes necessary, the procedure should be performed by an experienced practitioner in a controlled setting due to the enhanced risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure to health care practitioners during intubation **(AIII)**.

PICO question 2: Should HFNC or NIV be used in patients with acute hypoxaemic respiratory failure?

We suggest the use of **HFNC over NIV** in patients with acute hypoxaemic respiratory failure (conditional recommendation, very low certainty of evidence).

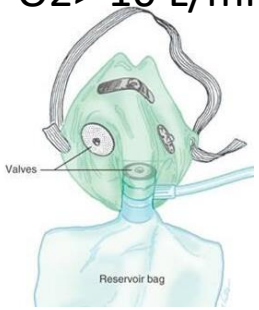
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., Sébastien Perbet, M.D., Gwénael Prat, M.D., Thierry Boulain, M.D.,

PEEP= 2-10 cmH2O (5±1)
PS to reach VT 7-10 mL/kg (8±3)

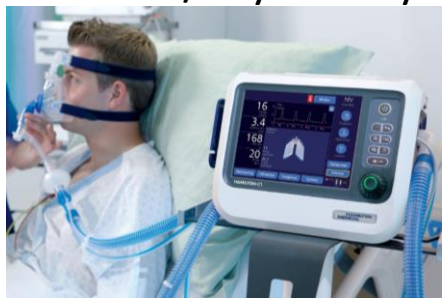
310 pz
RR >25 a/min; PaO2/FiO2 ≤300, PaCO2 ≤45 mmHg
No chronic respiratory diseases

O2> 10 L/min



For 2 days

>8hrs/day x 2 days

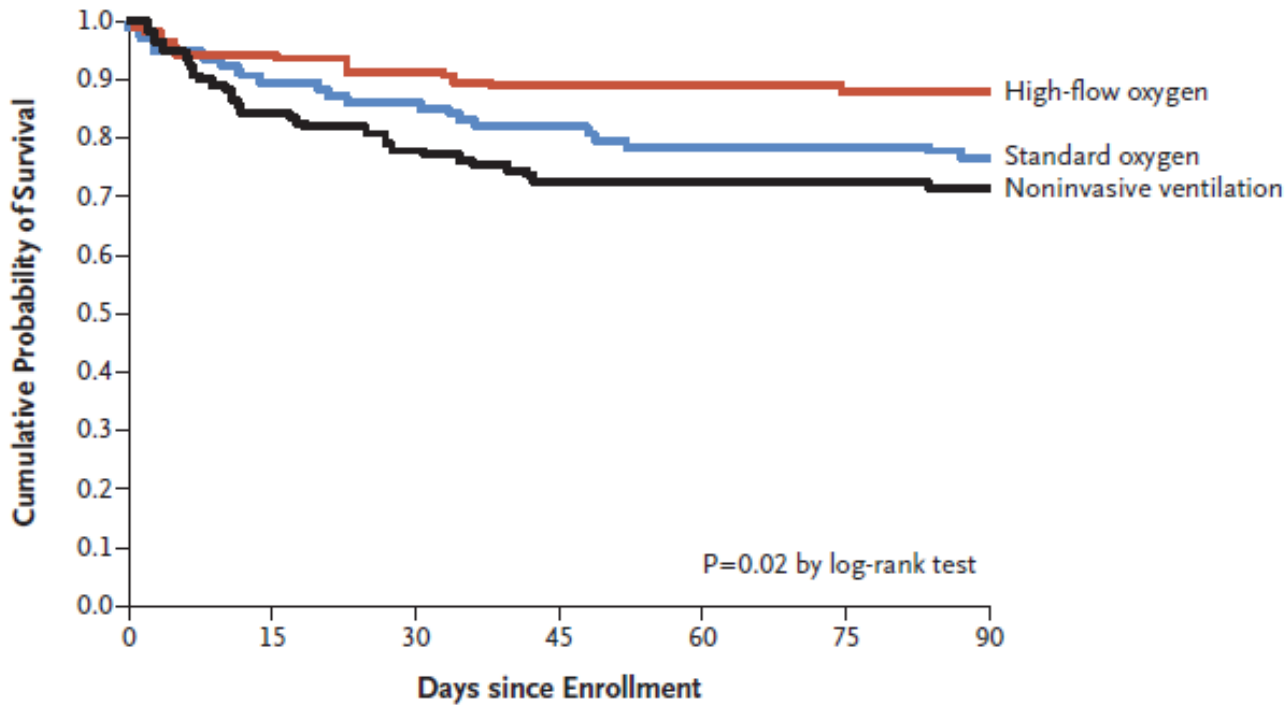


SpO2 ≥92%

94 Oxygen group	**106** HFNC group	**110** NIV/HFNC group

N Engl J Med 2015;372:2185-96.

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure



No. at Risk							
High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

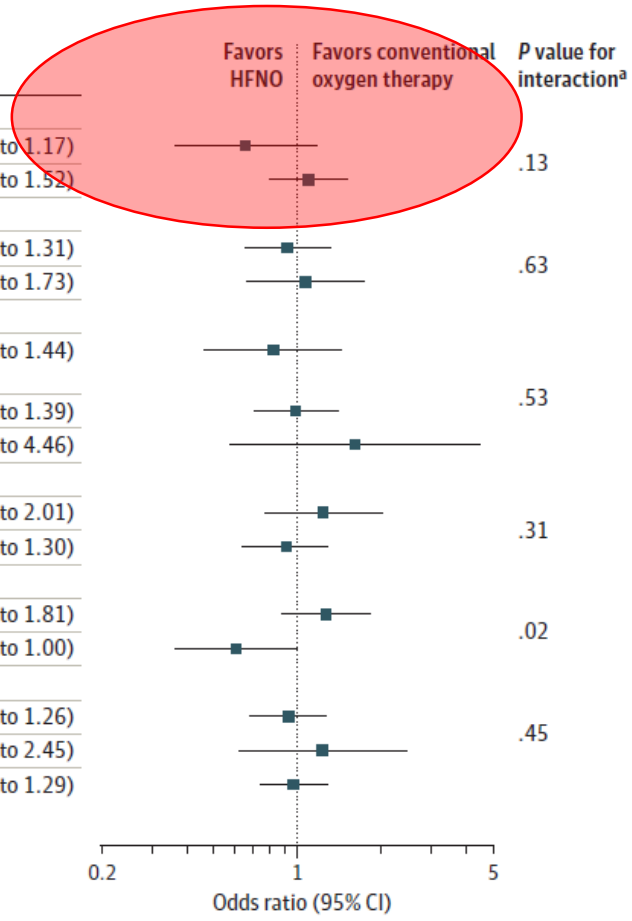
N Engl J Med 2015;372:2185-96.

Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19

The RECOVERY-RS Randomized Clinical Trial

Figure 3. Unadjusted Subgroup Analyses for Tracheal Intubation or Mortality Within 30 Days in the High-Flow Nasal Oxygen (HFNO) Group vs the Conventional Oxygen Therapy Group

Subgroup	No./total (%) of patients		Absolute difference (95% CI), %	Odds ratio (95% CI)	P value for interaction[a]
	HFNO	Conventional oxygen therapy			
Age group, y					
<50	31/108 (29)	37/97 (38)	-9 (-22 to 3)	0.65 (0.36 to 1.17)	.13
≥50	153/307 (50)	129/271 (48)	2 (-6 to 10)	1.09 (0.79 to 1.52)	
Sex					
Male	126/271 (46)	116/239 (49)	-2 (-11 to 7)	0.92 (0.65 to 1.31)	.63
Female	58/144 (40)	50/129 (39)	2 (-10 to 13)	1.07 (0.66 to 1.73)	
Race and ethnicity					
Black, Asian, or racial and ethnic minority group	46/106 (43)	44/91 (48)	-5 (-19 to 9)	0.82 (0.47 to 1.44)	.53
White	122/275 (44)	110/246 (45)	-0.4 (-9 to 8)	0.99 (0.70 to 1.39)	
Not given	16/34 (47)	10/28 (36)[b]	11 (-13 to 36)	1.60 (0.57 to 4.46)	
Time from onset to randomization, d					
≤7	75/132 (57)	68/132 (52)	5 (-7 to 17)	1.24 (0.76 to 2.01)	.31
>7	107/280 (38)	94/232 (41)	-2 (-11 to 6)	0.91 (0.64 to 1.30)	
Fio_2					
≤0.60	106/263 (40)	83/238 (35)	5 (-3 to 14)	1.26 (0.88 to 1.81)	.02
>0.60	72/139 (52)	75/117 (64)	-12 (-24 to -0.3)	0.60 (0.36 to 1.00)	
Body mass index[c]					
≤35	141/333 (42)	137/309 (44)	-2 (-10 to 6)	0.92 (0.67 to 1.26)	.45
>35	42/80 (53)	26/55 (47)	5 (-12 to 22)	1.23 (0.62 to 2.45)	
Overall	184/415 (44)	166/368 (45)	-1 (-8 to 6)	0.97 (0.73 to 1.29)	



HFNC

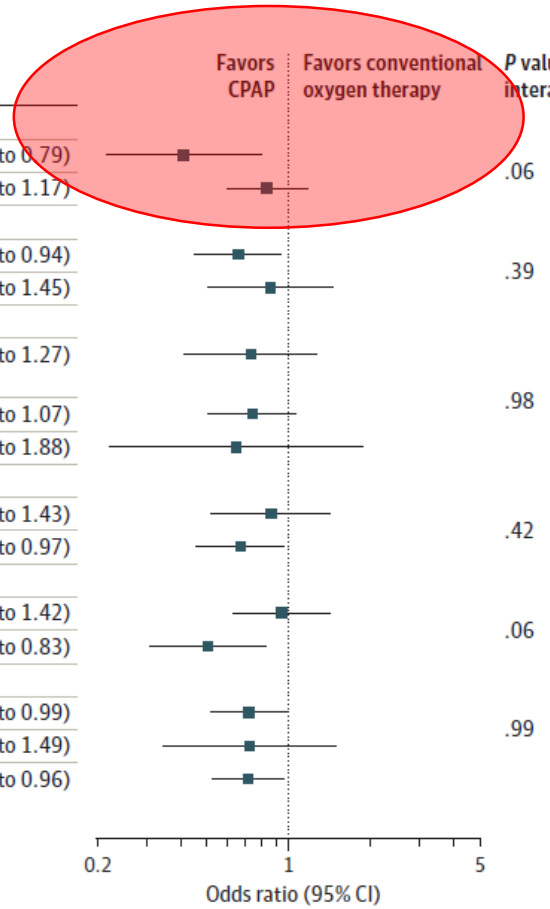
JAMA. 2022;327(6):546-558. doi:10.1001/jama.2022.0028

Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19

The RECOVERY-RS Randomized Clinical Trial

Figure 2. Unadjusted Subgroup Analyses for Tracheal Intubation or Mortality Within 30 Days in the Continuous Positive Airway Pressure (CPAP) Group vs the Conventional Oxygen Therapy Group

Subgroup	No./total (%) of patients		Absolute difference (95% CI), %	Odds ratio (95% CI)	*P* value for interaction[a]
	CPAP	Conventional oxygen therapy			
Age group, y					
<50	20/102 (20)	34/92 (37)	-17 (-30 to -5)	0.42 (0.22 to 0.79)	.06
≥50	117/275 (43)	124/264 (47)	-4 (-13 to 4)	0.84 (0.60 to 1.17)	
Sex					
Male	92/257 (36)	110/239 (46)	-10 (-19 to -2)	0.65 (0.46 to 0.94)	.39
Female	45/120 (38)	48/117 (41)	-4 (-16 to 9)	0.86 (0.51 to 1.45)	
Race and ethnicity					
Black, Asian, or racial and ethnic minority group	40/103 (39)	47/101 (47)	-8 (-21 to 6)	0.73 (0.42 to 1.27)	.98
White	88/241 (37)	97/221 (44)	-7 (-16 to 2)	0.74 (0.51 to 1.07)	
Not given	9/33 (27)	11/30 (37)[b]	-9 (-32 to 14)	0.65 (0.22 to 1.88)	
Time from onset to randomization, d					
≤7	56/122 (46)	59/119 (50)	-4 (-16 to 9)	0.86 (0.52 to 1.43)	.42
>7	81/254 (32)	96/233 (41)	-9 (-18 to -1)	0.67 (0.46 to 0.97)	
Fio_2					
≤0.60	67/215 (31)	70/216 (32)	-1 (-10 to 8)	0.94 (0.63 to 1.42)	.06
>0.60	68/146 (47)	79/125 (63)	-17 (-28 to -5)	0.51 (0.31 to 0.83)	
Body mass index[c]					
≤35	110/314 (35)	127/296 (43)	-8 (-16 to -0.2)	0.72 (0.52 to 0.99)	.99
>35	26/62 (42)	28/56 (50)	-8 (-26 to 10)	0.72 (0.35 to 1.49)	
Overall	137/377 (36)	158/356 (44)	-8 (-15 to -1)	0.72 (0.53 to 0.96)	



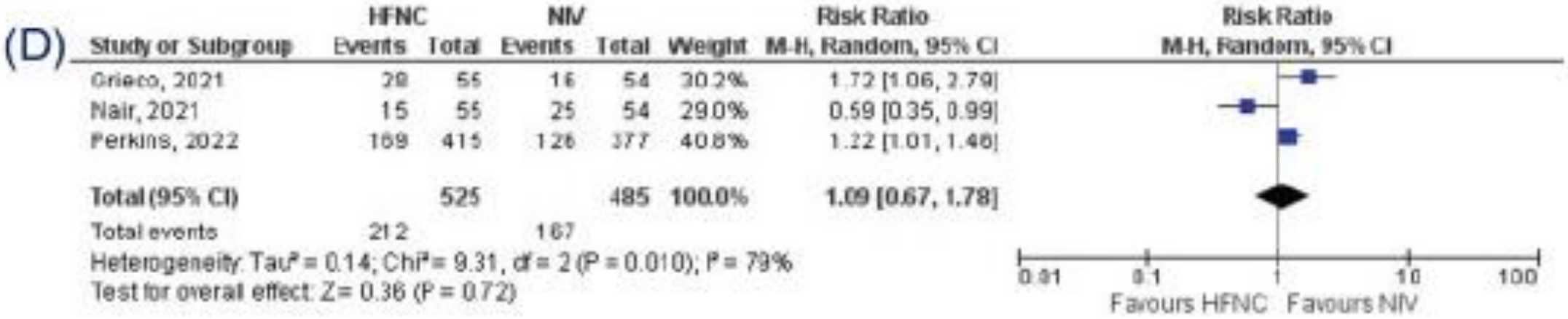
CPAP

JAMA. 2022;327(6):546-558. doi:10.1001/jama.2022.0028

High-Flow Nasal Cannula Oxygen versus Non-Invasive Ventilation in Subjects with COVID-19: A Systematic Review and Meta-analysis of Comparative Studies

RESPCARE 2022; 10.4187/respcare.09987

Conclusions: Our study showed that despite the greater improvement in PaO2/FiO2 ratio with NIV, the intubation and length of hospital stay were similar between HFNC and NIV. Although mortality was lower with HFNC than NIV, the prediction interval included the null value, and there was no difference in mortality between HFNC and NIV on a subgroup of RCTs. Future large-scale RCTs are necessary to prove our findings.



Subgroup analysis of randomized controlled trials for the intubation rate.

Should HFNC or COT be used during breaks from NIV in patients with acute hypoxaemic respiratory failure?

We suggest the use of **HFNC over COT** during **breaks from NIV** in patients with acute hypoxaemic respiratory failure (conditional recommendation, low certainty of evidence).

Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study

Anna Coppo, Giacomo Bellani, Dario Winterton, Michela Di Pierro, Alessandro Soria, Paola Faverio, Matteo Cairo, Silvia Mori, Grazia Messinesi, Ernesto Contro, Paolo Bonfanti, Annalisa Benini, Maria Grazia Valsecchi, Laura Antolini, Giuseppe Foti

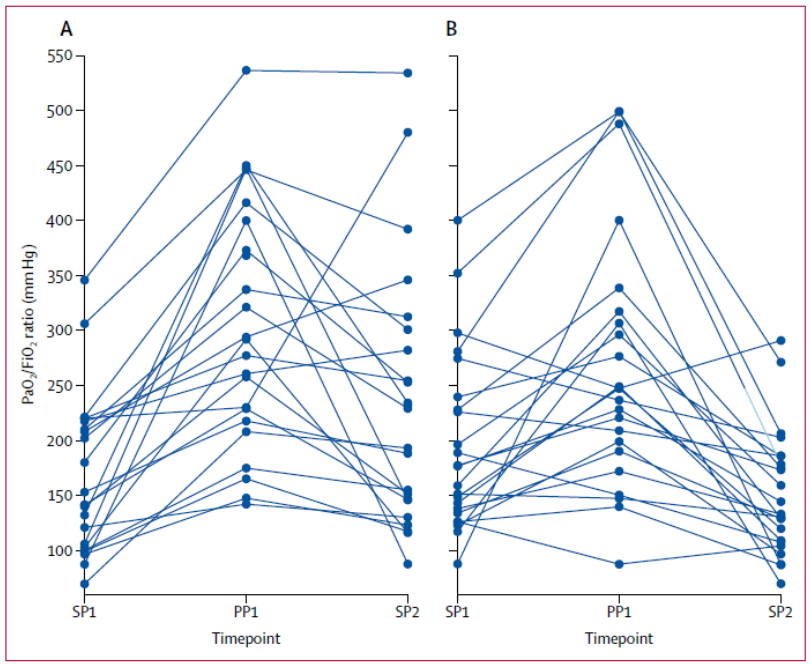


Figure 3: Per-patient trajectory of PaO_2/FiO_2 at the three study timepoints, SP1, PP1, and SP2, for responders (A) and non-responders (B)

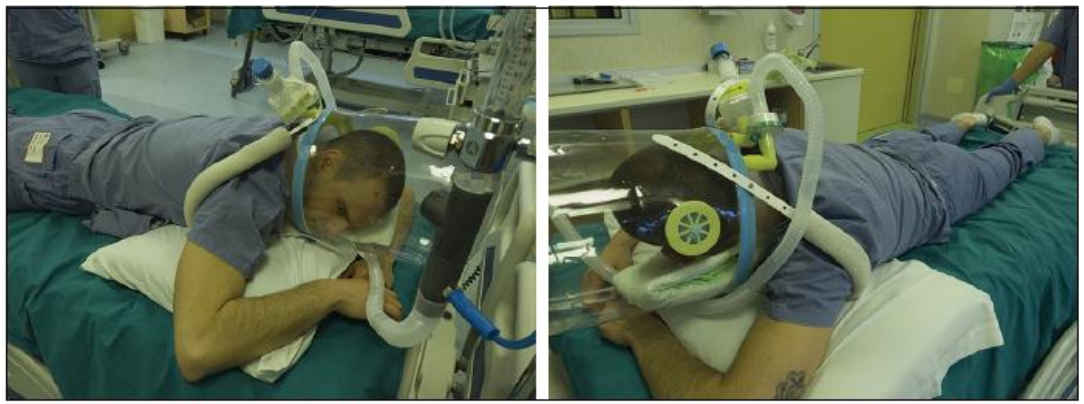
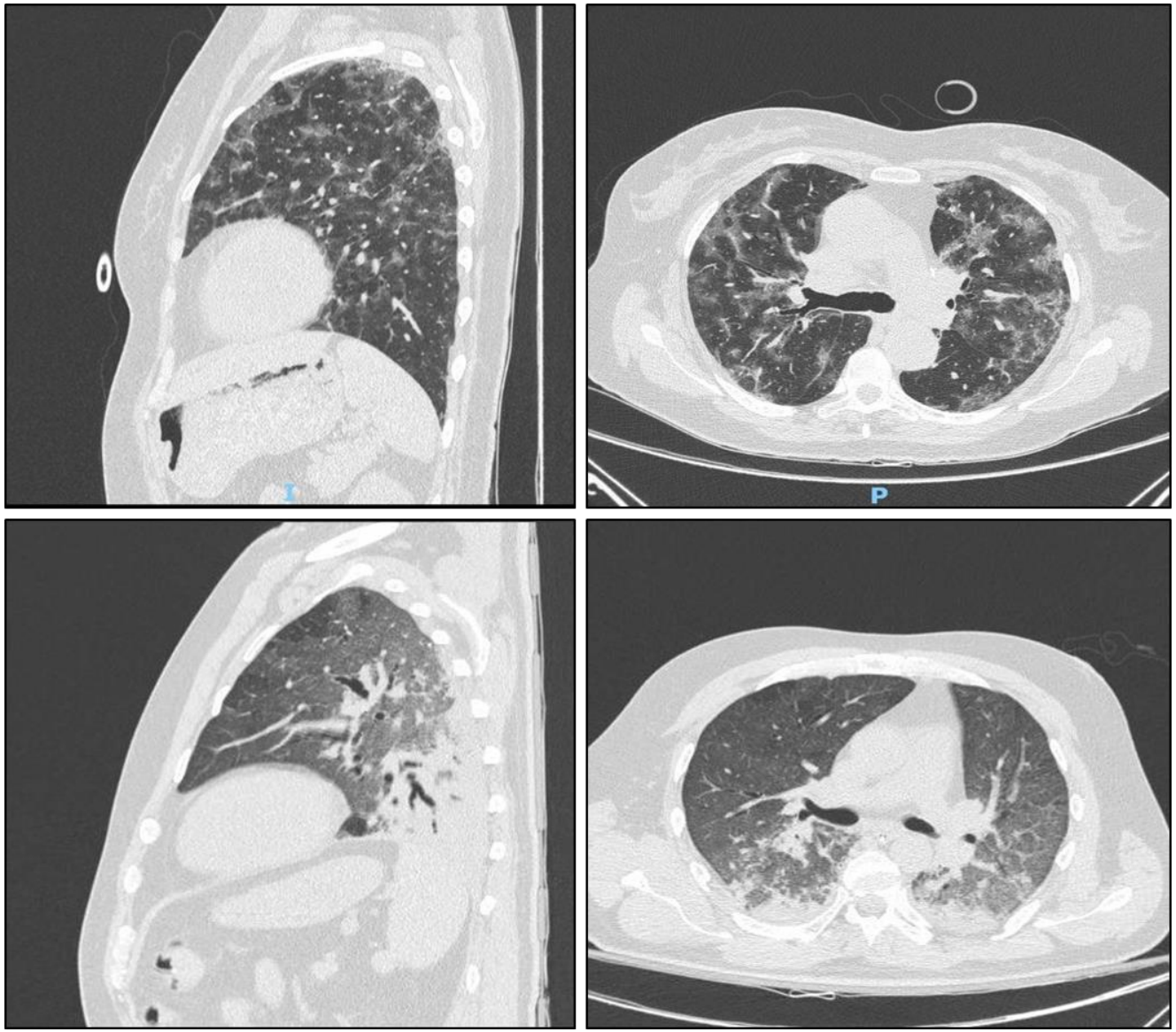


Figure 1: Prone positioning with a helmet interface to enable continuous positive airway pressure
Example demonstrated by volunteer.

Interpretation Prone positioning was feasible and effective in rapidly ameliorating blood oxygenation in awake patients with COVID-19-related pneumonia requiring oxygen supplementation. The effect was maintained after resupination in half of the patients. Further studies are warranted to ascertain the potential benefit of this technique in improving final respiratory and global outcomes.

Amount and distribution of parenchymal abnormalities at CT-scan do not predict awake prone position outcome in Covid-19



Novelli et al. Submitted

Amount and distribution of parenchymal abnormalities at CT-scan do not predict awake prone position outcome in Covid-19

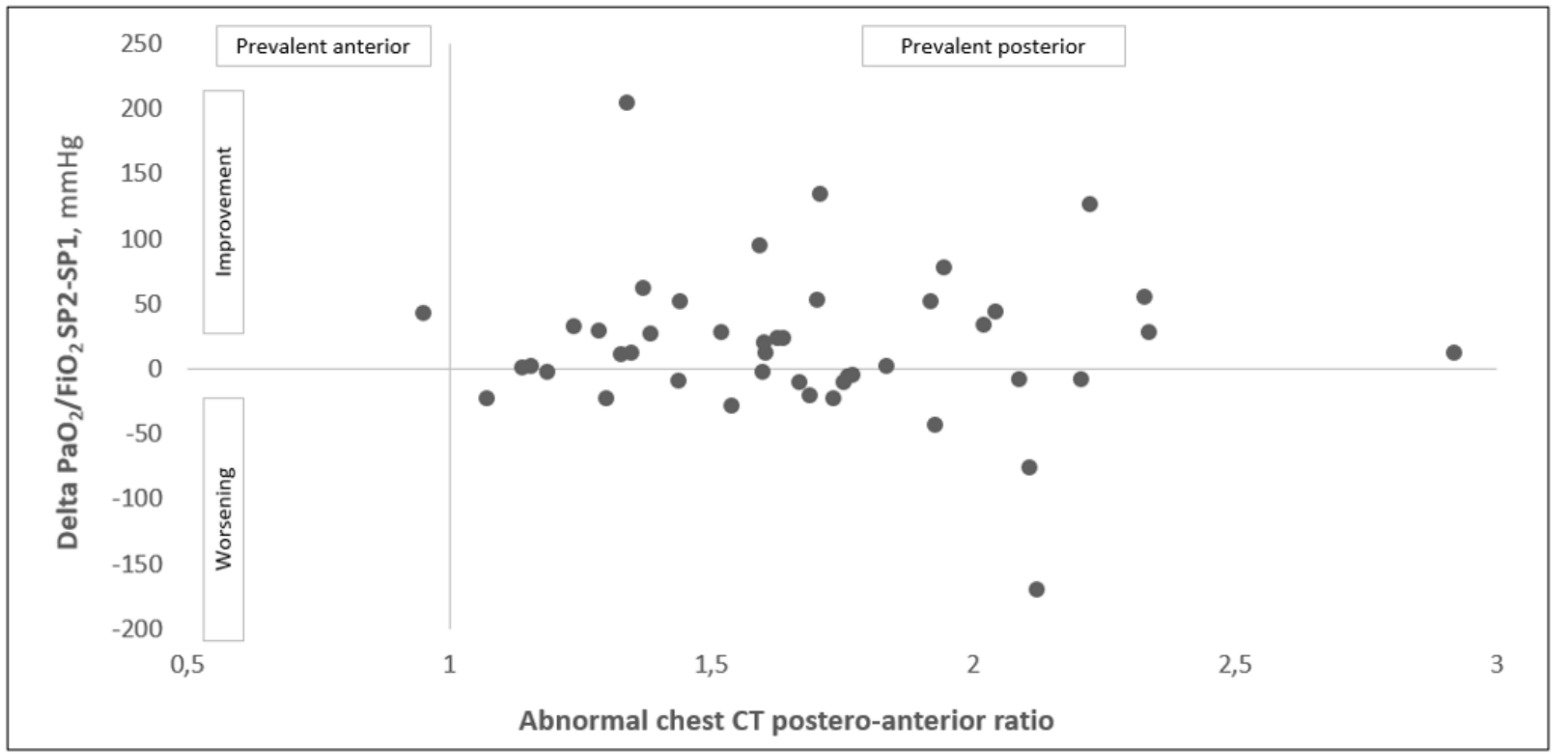


Figure 2. Correlation between the distribution of parenchymal abnormalities (i.e. ratio between the percentage of parenchymal involvement of posterior and anterior regions, with 1 = homogeneous distribution, <1 = predominant anterior; and >1 = predominant dorsal involvement), and changes of PaO_2/FiO_2 ratio before and after prone positioning (supine position after, SP2, *minus* supine position before, SP1, prone position). Results of Pearson correlation test: $R^2 = 0.009$, p= 0.526.

Novelli et al. Submitted

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

Stephan Ehrmann, Jie Li*, Miguel Ibarra-Estrada*, Yonatan Perez*, Ivan Pavlov*, Bairbre McNicholas*, Oriol Roca*, Sara Mirza, David Vines, Roxana Garcia-Salcido, Guadalupe Aguirre-Avalos, Matthew W Trump, Mai-Anh Nay, Jean Dellamonica, Saad Nseir, Idrees Mogri, David Cosgrave, Dev Jayaraman, Joan R Masclans, John G Laffey, Elsa Tavernier, for the Awake Prone Positioning Meta-Trial Group†*

Lancet Respir Med 2021;
9: 1387–95

Methods In this prospective, a priori set up and defined, collaborative meta-trial of six randomised controlled open-label superiority trials, adults who required respiratory support with high-flow nasal cannula for acute hypoxaemic respiratory failure due to COVID-19 were randomly assigned to awake prone positioning or standard care. Hospitals from six countries were involved: Canada, France, Ireland, Mexico, USA, Spain. Patients or their care providers were not masked to allocated treatment. The primary composite outcome was treatment failure, defined as the proportion of patients intubated or dying within 28 days of enrolment. The six trials are registered with ClinicalTrials.gov, NCT04325906, NCT04347941, NCT04358939, NCT04395144, NCT04391140, and NCT04477655.

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

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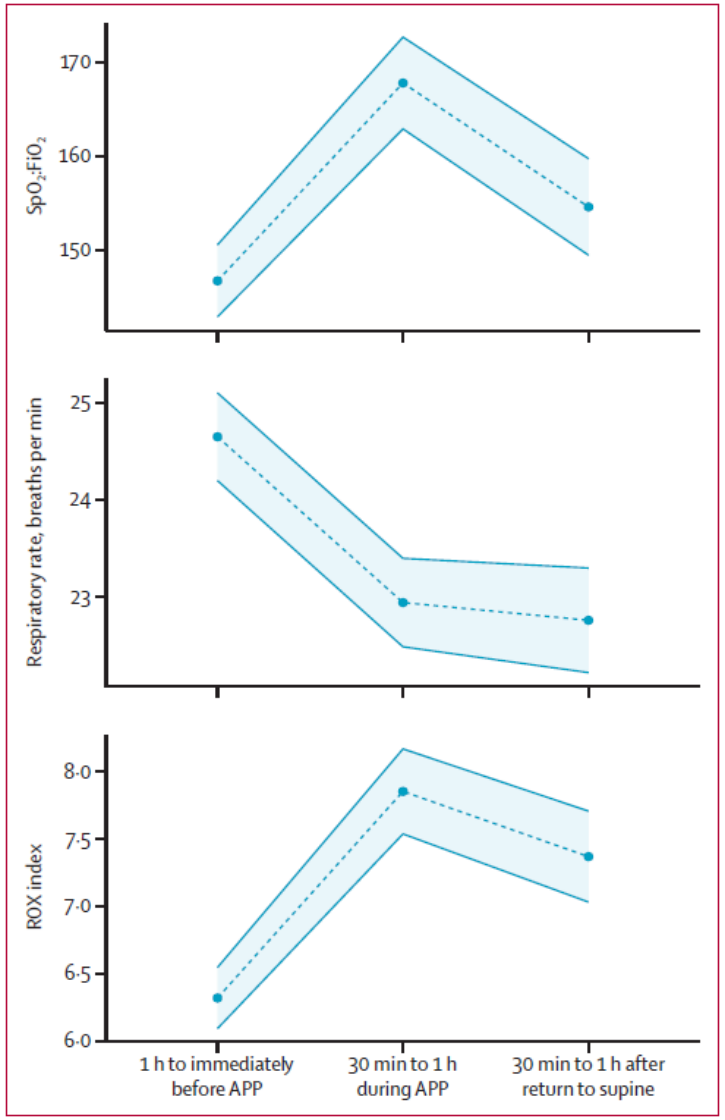
Lancet Respir Med 2021; 9: 1387–95

	Awake prone positioning group (n=564)	Standard care group (n=557)
Age, years	61·5 (13·3)	60·7 (14·0)
Female sex	184 (33%)	191 (34%)
Male sex	380 (67%)	366 (66%)
Body-mass index, kg/m²	29·7 (4·6)	29·7 (4·6)
Clinical parameters at enrolment		
Respiratory rate, breaths/min	24·7 (5·1)	24·9 (5·6)
Mean arterial pressure, mmHg	88·2 (12·1)	87·4 (11·4)
SpO_2:FiO_2	147·9 (43·9)	148·6 (43·1)
Recruitment of individual trials		
Mexico	216 (38%)	214 (38%)
France	200 (35%)	202 (36%)
USA	112 (20%)	110 (20%)
Spain	17 (3%)	13 (2%)
Ireland	12 (2%)	12 (2%)
Canada	7 (1%)	6 (1%)



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Stephan Ehrmann, Jie Li*, Miguel Ibarra-Estrada*, Yonatan Perez*, Ivan Pavlov*, Bairbre McNicholas*, Oriol Roca*, Sara Mirza, David Vines, Roxana Garcia-Salcido, Guadalupe Aguirre-Avalos, Matthew W Trump, Mai-Anh Nay, Jean Dellamonica, Saad Nseir, Idrees Mogri, David Cosgrave, Dev Jayaraman, Joan R Masclans, John G Laffey, Elsa Tavernier, for the Awake Prone Positioning Meta-Trial Group†*

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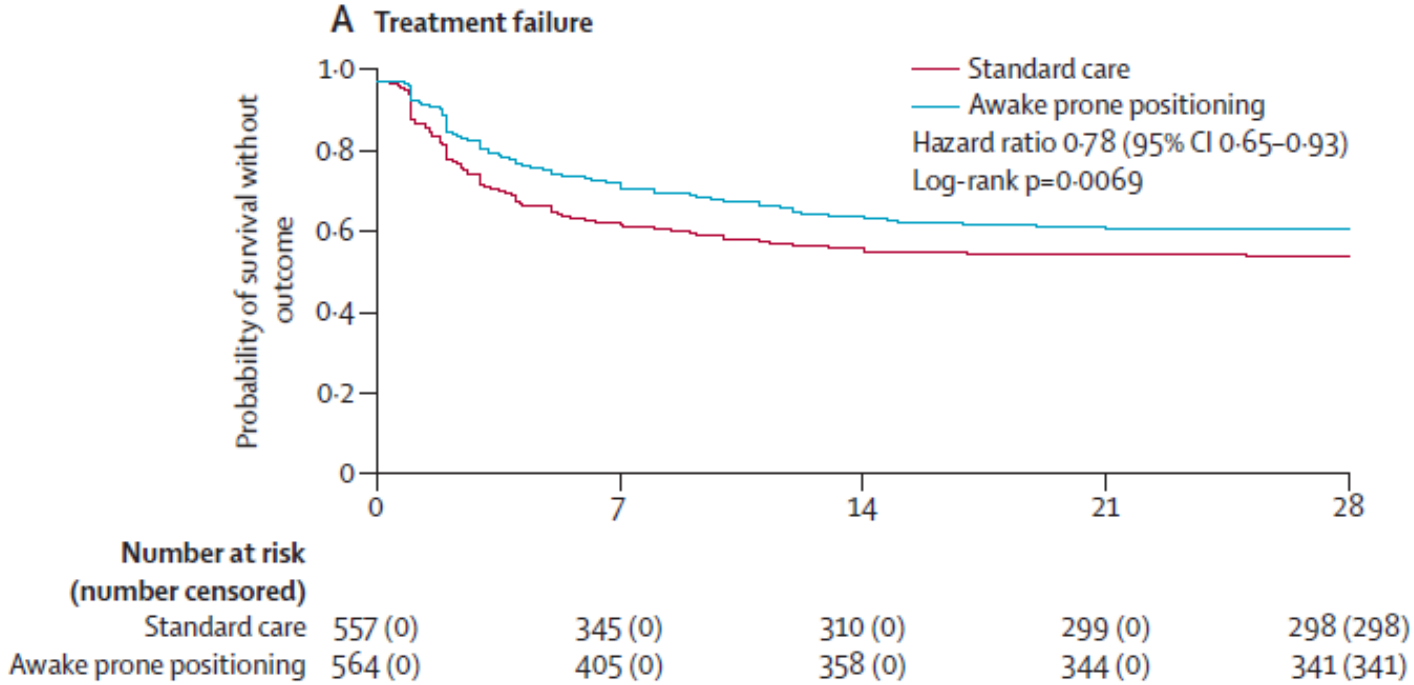


Number at risk (number censored)					
Standard care	557 (0)	345 (0)	310 (0)	299 (0)	298 (298)
Awake prone positioning	564 (0)	405 (0)	358 (0)	344 (0)	341 (341)

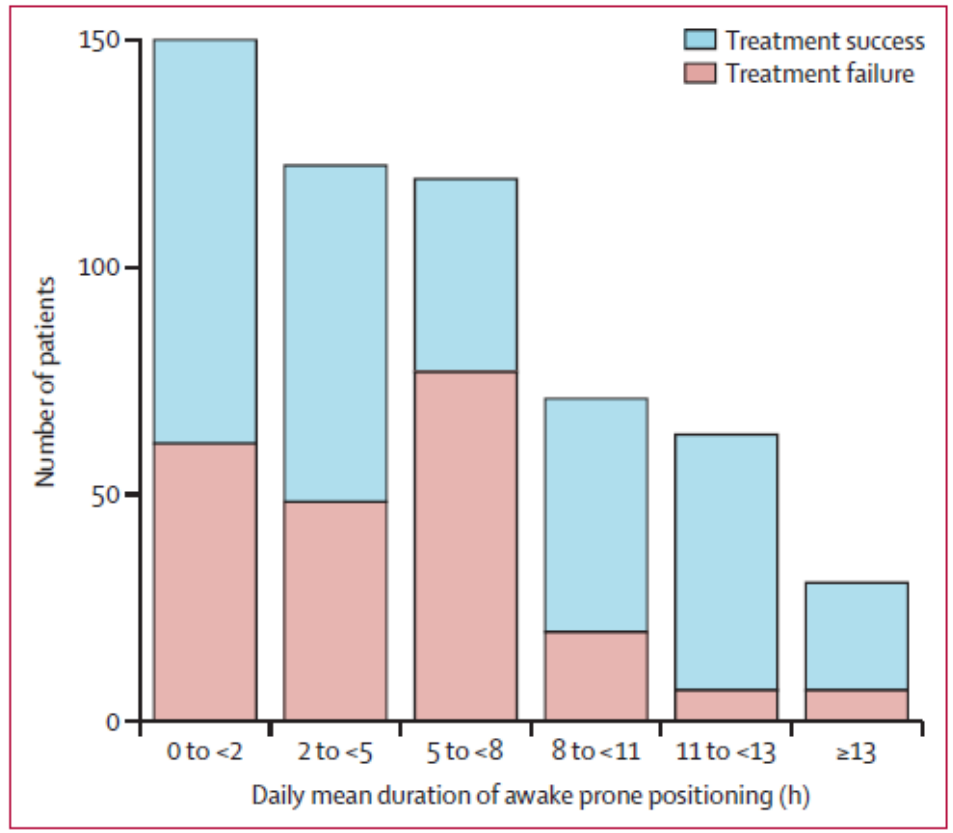


Figure 4: **Daily mean duration of prone positioning and outcomes in patients allocated to awake prone positioning**

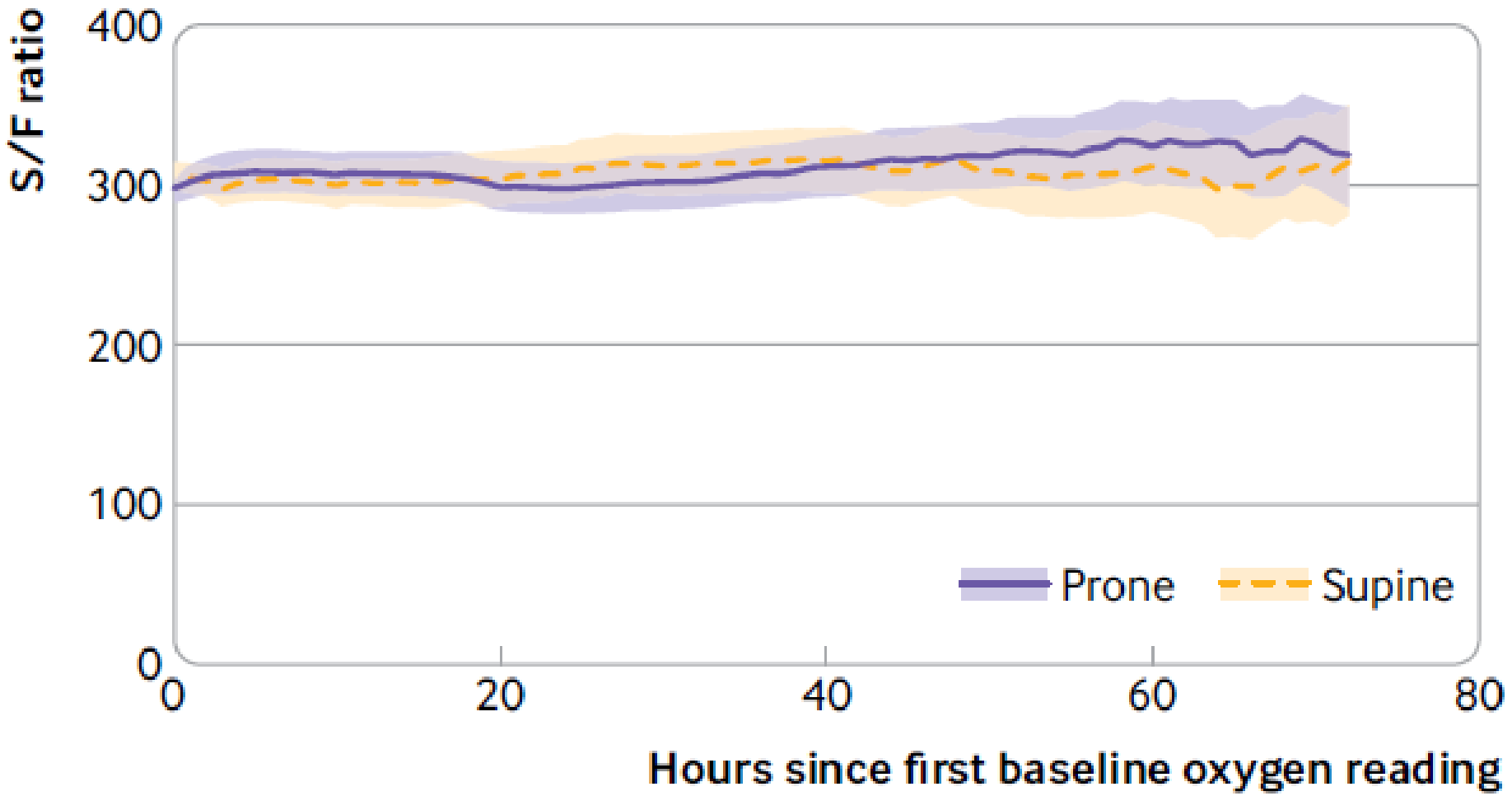
Each bar represents the total number of patients having received a mean daily duration of awake prone positioning indicated on the horizontal axis in the population of patients with treatment success (patient was alive and did not require intubation after 28 days) and treatment failure (intubation or death by day 28).

Prone positioning of patients with moderate hypoxaemia due to covid-19: multicentre pragmatic randomised trial (COVID-PRONE)

Table 1 | Baseline characteristics of included patients. Values are numbers (percentages) unless stated otherwise

Characteristics	Prone (n=126)	Control (n=122)
Median (IQR) age, years	59.5 (45-68)	54 (44-62)
Age group:		
<50 years	37 (29)	44 (36)
50-70 years	67 (53)	66 (54)
>70 years	22 (17)	12 (10)
Female sex	44 (35)	45 (37)
Comorbid conditions:		
Diabetes	36 (29)	31 (25)
Hypertension	56 (44)	42 (34)
Current smoker	0 (0)	7 (6)
COPD or asthma	12 (10)	15 (12)
Heart failure	4 (3)	2 (2)
Illness severity:		
Median (IQR) lymphocyte count, 10^9/L	0.8 (0.6-1.1)	0.9 (0.6-1.2)
Median (IQR) creatinine, µmol/L	79 (66-97)	78 (65-94)
Median (IQR) systolic BP, mm Hg	124 (116-135)	121 (112-130)
Median (IQR) oxygen saturation, %	94 (93-95)	94 (93-96)
Median (IQR) FiO_2, %	32 (28-36)	32 (28-36)
Median (IQR) S/F ratio	303 (261-336)	305 (267-339)
FiO_2 delivery method:		
Nasal prong	110 (87)	112 (92)
High flow nasal cannula	5 (4)	2 (2)
Face mask	8 (6)	7 (6)

Prone positioning of patients with moderate hypoxaemia due to covid-19: multicentre pragmatic randomised trial (COVID-PRONE)



thebmj | *BMJ* 2022;376:e068585 | doi: 10.1136/bmj-2021-068585

Prone positioning of patients with moderate hypoxaemia due to covid-19: multicentre pragmatic randomised trial (COVID-PRONE)

Table 2 | Primary and secondary study outcomes. Values are numbers (percentages) unless stated otherwise

	Prone (n=126)	Control (n=122)	Effect estimate (95% CI)
Primary outcome			
Composite of death, mechanical ventilation, and FiO_2>60	18 (14)	17 (14)	OR*: 0.92 (0.44 to 1.92)
Components of composite:			
Death	1 (1)	1 (1)	-
Mechanical ventilation	6 (5)	5 (4)	-
FiO_2>60%	18 (14)	17 (14)	-
Secondary outcomes			
Median (IQR) S/F ratio after 72 hours	336 (216-438)	336 (232-443)	MD†: 8 (−18 to 35)
Median (IQR) change in S/F ratio in first 72 hours	14 (−52-94)	49 (−32-102)	MD†: 20 (−17 to 36)
Median (IQR) days to discharge	5 (3-9)	4 (3-8)	-
Discharged	115 (91)	118 (97)	HR: 0.83 (0.64 to 1.08)
Serious adverse events			
Serious adverse event composite	5 (4)	3 (2)	OR: 1.37 (0.32 to 6.96)
Components of composite:			
Aspiration pneumonia	2 (2)	1 (1)	OR: 1.38 (0.12 to 31.53)
Venous thromboembolism	3 (2)	2 (2)	OR: 1.35 (0.22 to 10.57)
Other	0 (0)	0 (0)	-
Hours spent prone			
Median (IQR) in first 72 hours	6 (1.5-12.8)	0 (0-2)	MD: 6.0 (4.0 to 7.9)
Missing first 72 hours	8 (6)	5 (4)	
Median (IQR) from 72 hours to 7 days	0 (0-12)	0 (0-0)	MD: 4.3 (1.7 to 6.9)
Missing 72 hours to 7 days	13 (10)	12 (10)	

For primary outcome, risk difference was −0.01 (95% CI −0.07 to 0.10) and risk ratio was 0.93 (0.48 to 1.70).
CI=confidence interval; FiO_2=fraction of inspired oxygen; HR=hazard ratio; IQR=interquartile range; MD=mean difference; OR=odds ratio; S/F ratio=ratio of saturation of oxygen to fraction of inspired oxygen.
*Adjusted for age and sex.
†Adjusted for baseline S/F ratio as well as age and sex.

Prone positioning of patients with moderate hypoxaemia due to covid-19: multicentre pragmatic randomised trial (COVID-PRONE)

CONCLUSION

Among non-critically ill patients with hypoxaemia who were admitted to hospital with covid-19, a multifaceted intervention to increase prone positioning did not improve outcomes. However, wide confidence intervals preclude definitively ruling out benefit or harm. Adherence to prone positioning was poor, despite multiple efforts to increase it. Subsequent trials of prone positioning should aim to develop strategies to improve adherence to awake prone positioning.

the**bmj** | *BMJ* 2022;376:e068585 | doi: 10.1136/bmj-2021-068585

Assessment of Awake Prone Positioning in Hospitalized Adults With COVID-19

A Nonrandomized Controlled Trial

JAMA Intern Med. doi:10.1001/jamainternmed.2022.1070
Published online April 18, 2022.

Table 1. Participant Demographic and Disease Characteristics at Baseline

Characteristic	No. (%)	
	Usual care group	Prone positioning group
No.	243	258
Baseline severity[a]		
Low flow	162 (66.7)	170 (65.9)
High flow	62 (25.5)	71 (27.5)
NIV	19 (7.8)	16 (6.2)
Unknown or missing	0	1 (0.4)
Age, mean (SD), y	60.3 (15.2)	61.6 (15.4)
Sex		
Female	105 (43.2)	112 (43.4)
Male	138 (56.8)	146 (56.6)

Assessment of Awake Prone Positioning in Hospitalized Adults With COVID-19

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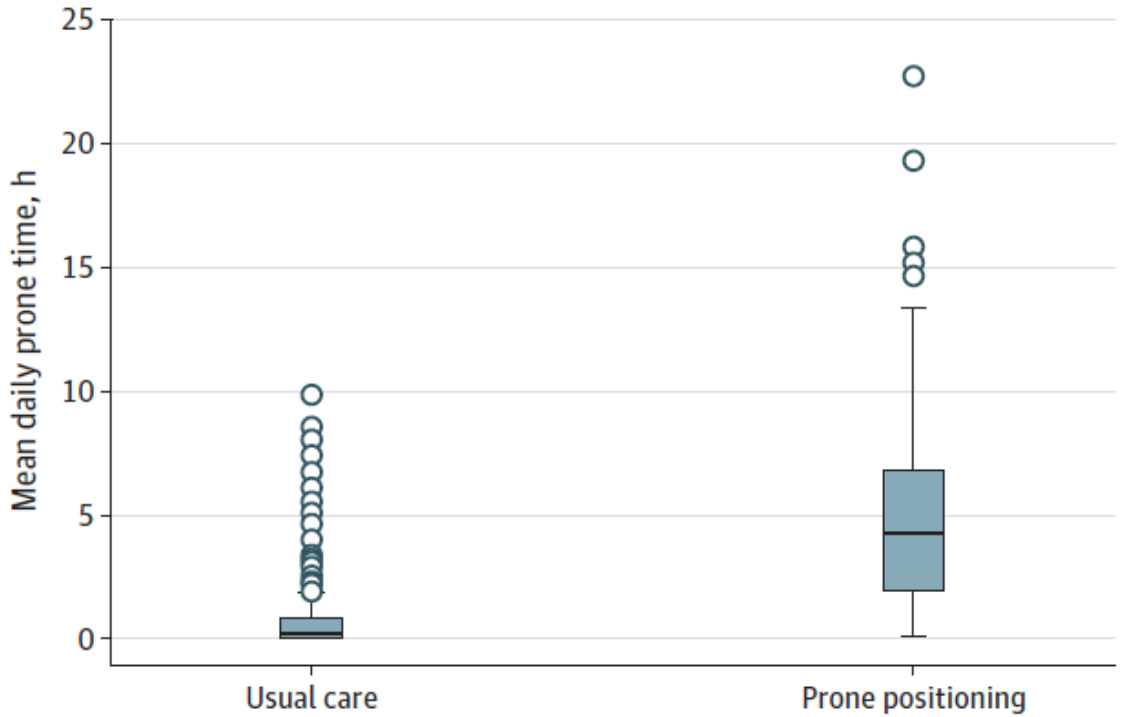
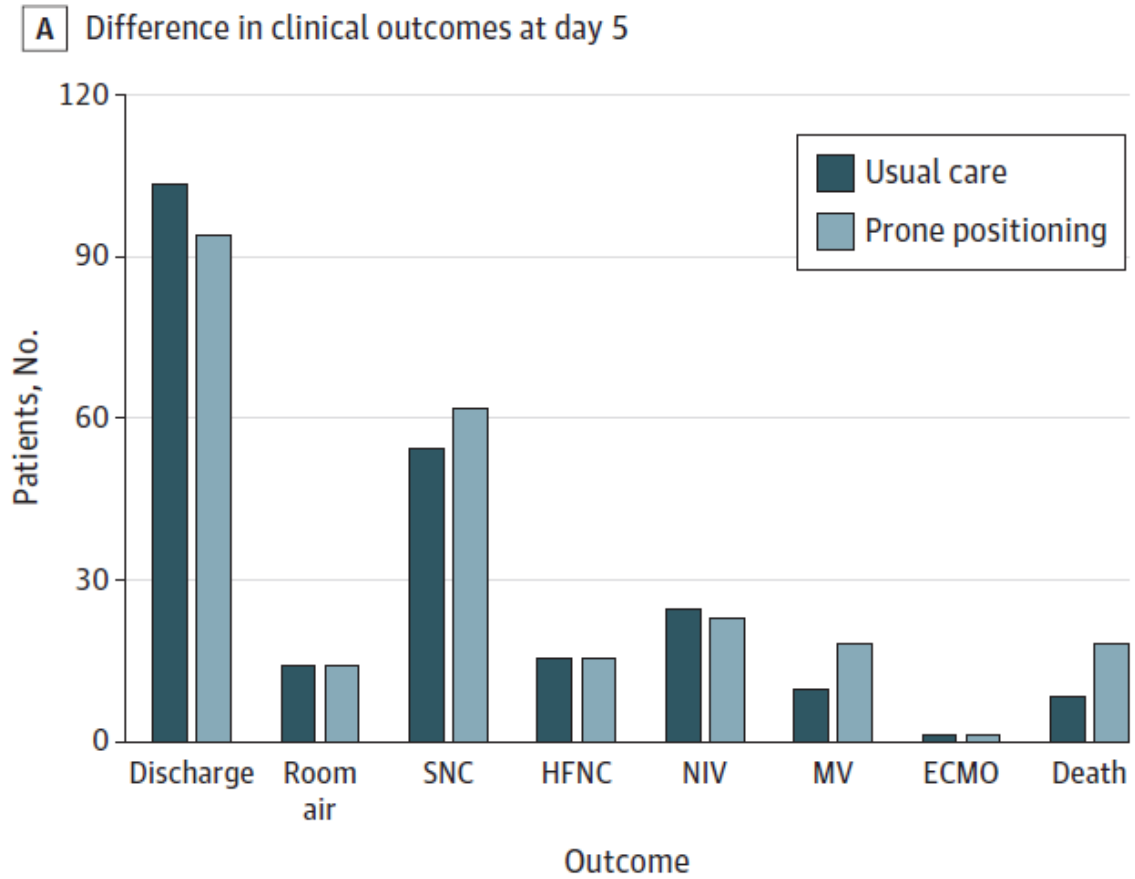
Figure 2. Nursing Estimations of Duration of Prone Positioning



The horizontal line inside the boxes represents the median. The whiskers represent distances of 1.5 IQR higher and lower than the third and first quantiles, respectively. The dots represent outliers that are outside of this range.



Assessment of Awake Prone Positioning in Hospitalized Adults With COVID-19

A Nonrandomized Controlled Trial

JAMA Intern Med. doi:10.1001/jamainternmed.2022.1070
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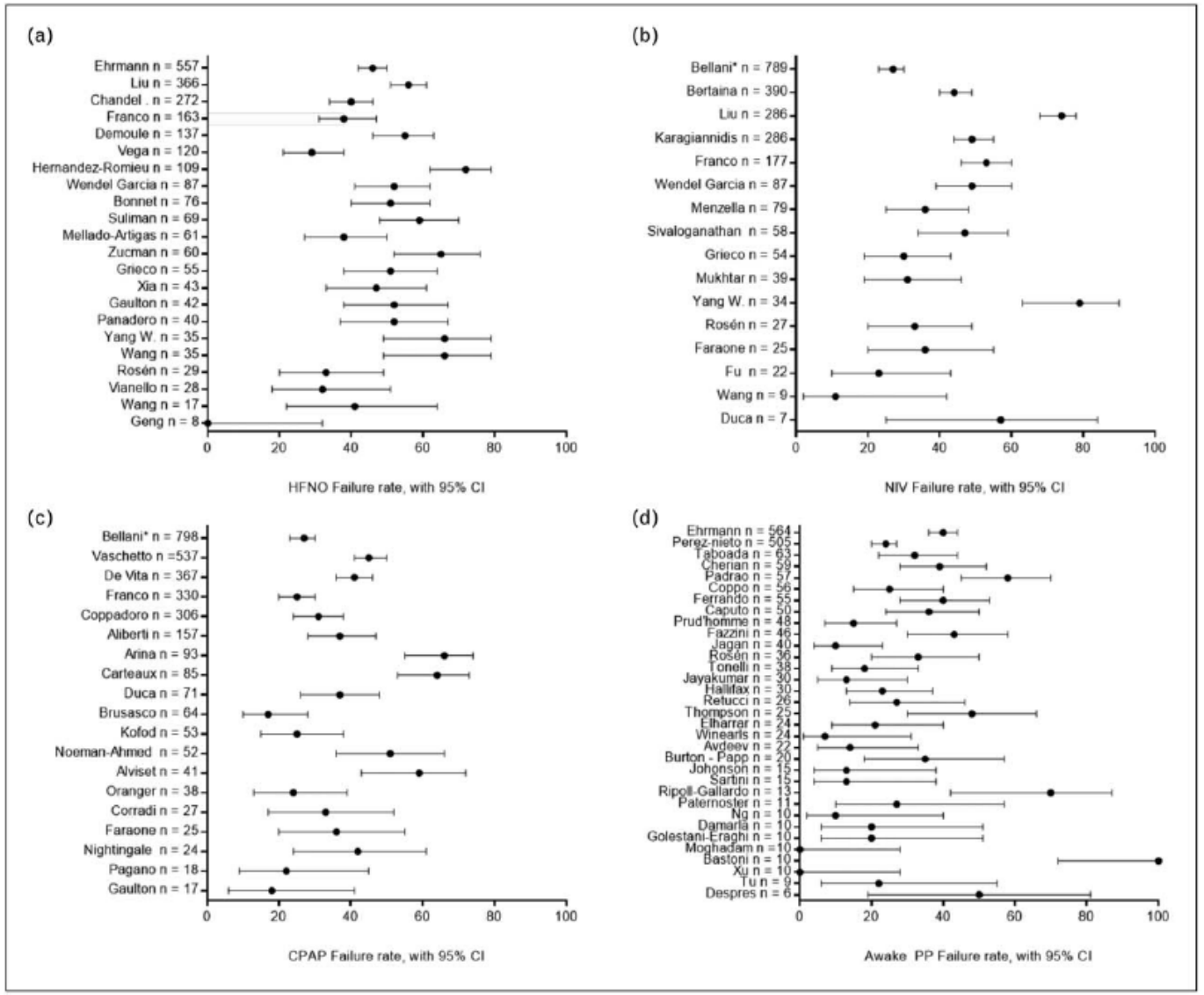
CONCLUSIONS AND RELEVANCE In this nonrandomized controlled trial, prone positioning offered no observed clinical benefit among patients with COVID-19–associated hypoxemia who had not received mechanical ventilation. Moreover, there was substantial evidence of worsened clinical outcomes at study day 5 among patients recommended to receive the awake prone positioning intervention, suggesting potential harm.

Noninvasive respiratory support for acute respiratory failure due to COVID-19

Luca S. Menga[a,b], *Cecilia Berardi*[a,b], *Ersilia Ruggiero*[a,b], *Domenico Luca Grieco*[a,b], *and Massimo Antonelli*[a,b]

Curr Opin Crit Care 2022, 28:25–50

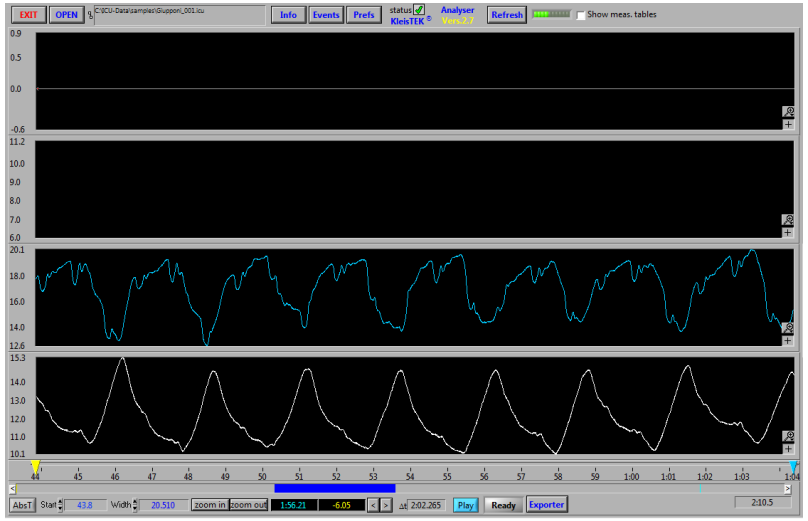


Summary

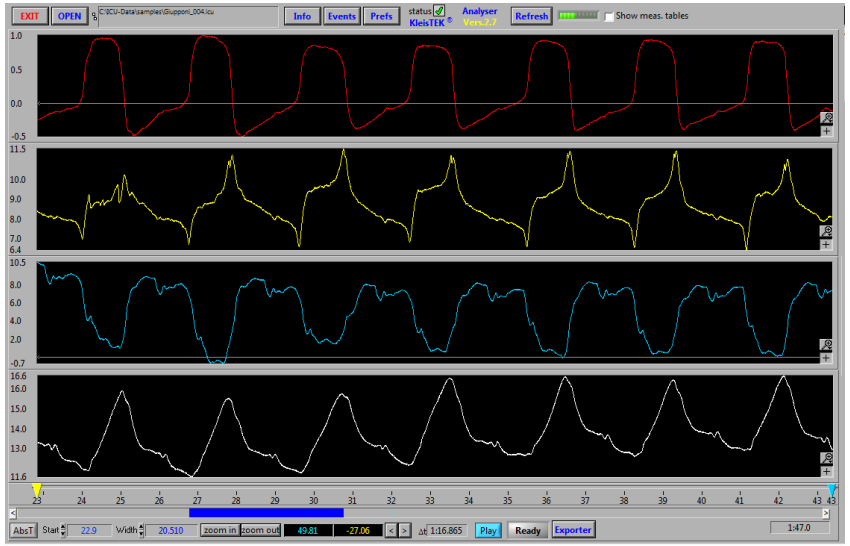
Noninvasive respiratory support and awake prone position are tools possibly capable of averting endotracheal intubation in COVID-19 patients; carefully **monitoring** during any treatment is warranted to avoid delays in endotracheal intubation, especially in patients with PaO_2/FiO_2<200 mmHg.

Monitoring of Covid19 patients under noninvasive respiratory support

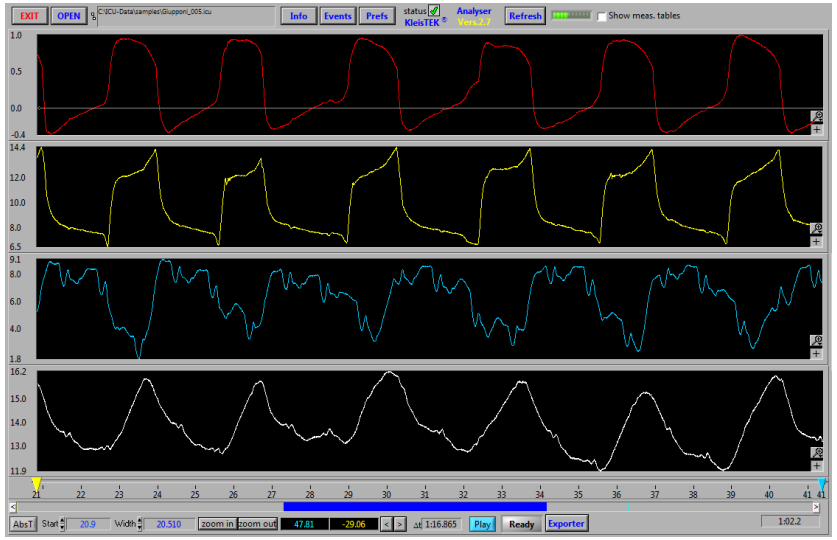
Venturi mask



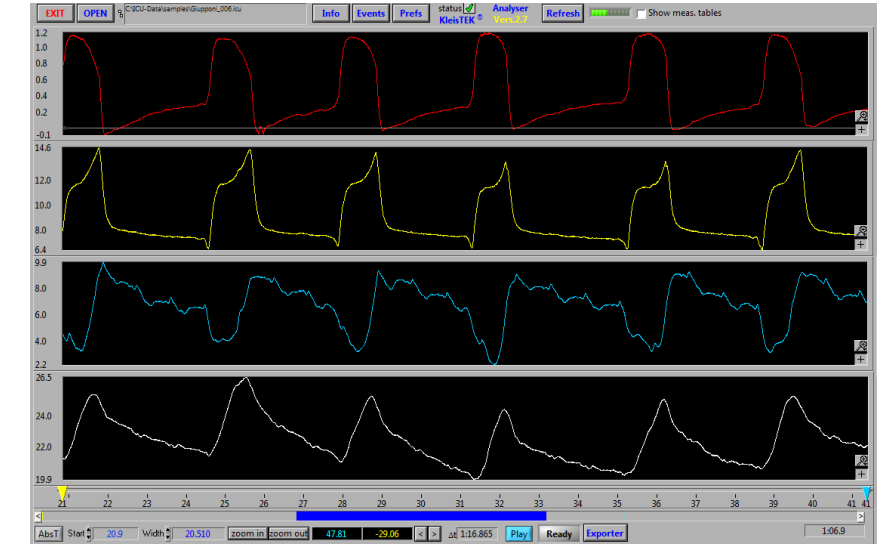
NIV
Supine
No sedation



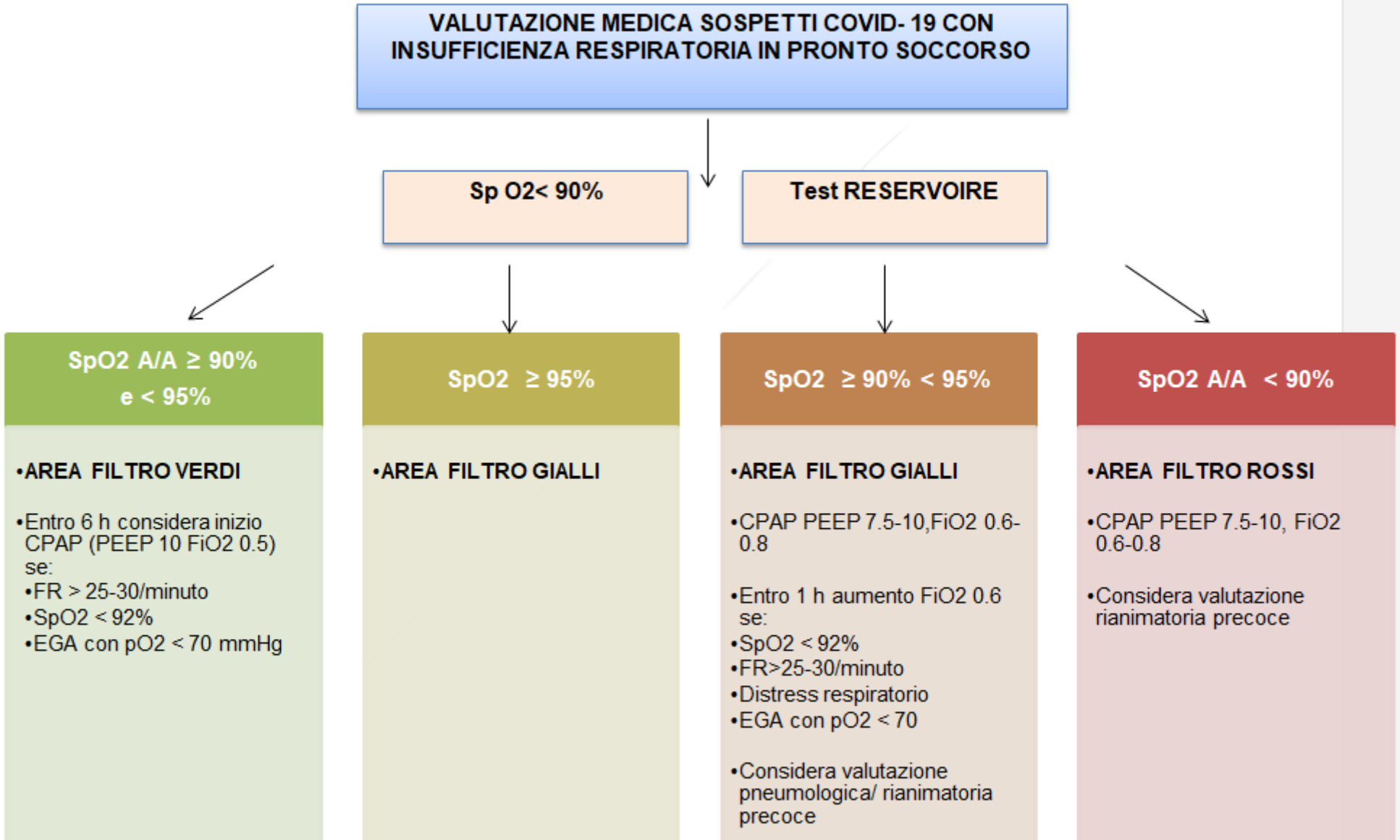
NIV
Supine
Sedation



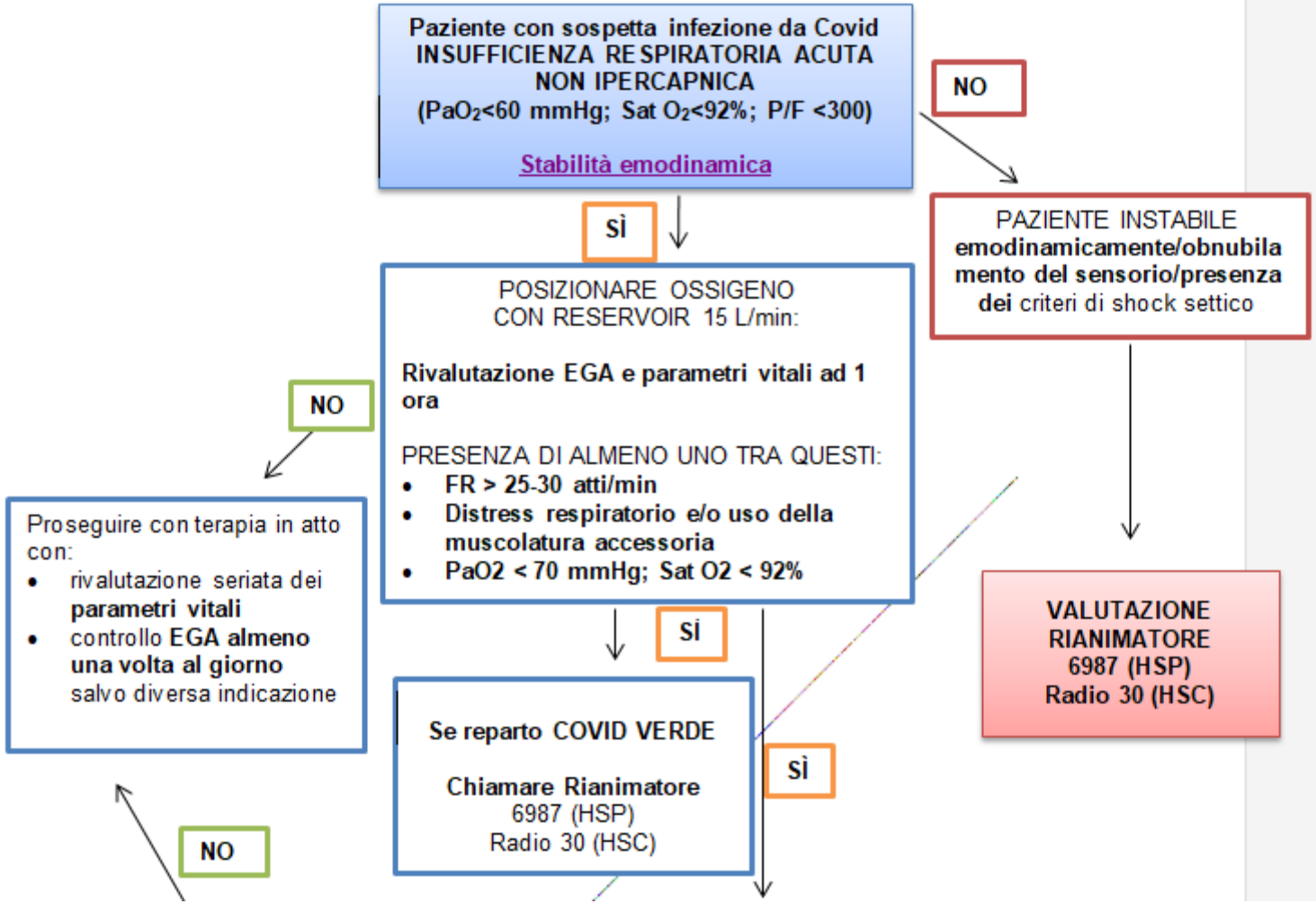
NIV
Prone
Sedation

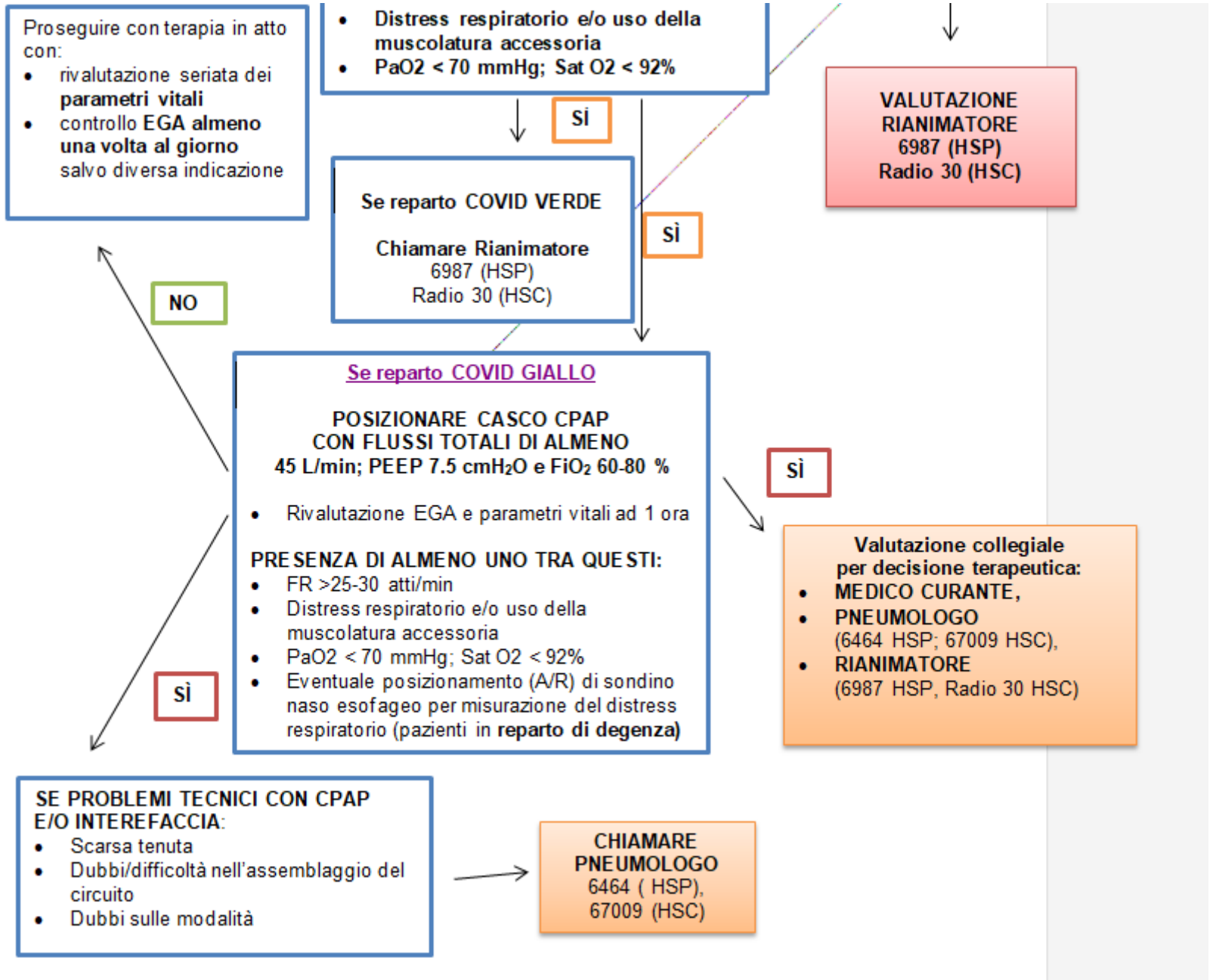


5.5. FLOW CHART VALUTAZIONE MEDICA SOSPETTI COVID- 19 CON INSUFFICIENZA RESPIRATORIA IN PRONTO SOCCORSO



5.6 FLOW CHART GESTIONE INSUFFICIENZA RESPIRATORIA




Proseguire con terapia in atto con:
• rivalutazione seriata dei parametri vitali
• controllo EGA almeno una volta al giorno salvo diversa indicazione
• Distress respiratorio e/o uso della muscolatura accessoria
• PaO2 < 70 mmHg; Sat O2 < 92%
SÌ
VALUTAZIONE RIANIMATORE
6987 (HSP)
Radio 30 (HSC)
Se reparto COVID VERDE
Chiamare Rianimatore
6987 (HSP)
Radio 30 (HSC)
SÌ
NO
Se reparto COVID GIALLO
POSIZIONARE CASCO CPAP
CON FLUSSI TOTALI DI ALMENO
45 L/min; PEEP 7.5 cmH2O e FiO2 60-80 %
• Rivalutazione EGA e parametri vitali ad 1 ora
PRESENZA DI ALMENO UNO TRA QUESTI:
• FR >25-30 atti/min
• Distress respiratorio e/o uso della muscolatura accessoria
• PaO2 < 70 mmHg; Sat O2 < 92%
• Eventuale posizionamento (A/R) di sondino naso esofageo per misurazione del distress respiratorio (pazienti in reparto di degenza)
SÌ
Valutazione collegiale per decisione terapeutica:
• MEDICO CURANTE,
• PNEUMOLOGO (6464 HSP; 67009 HSC),
• RIANIMATORE (6987 HSP, Radio 30 HSC)
SÌ
SE PROBLEMI TECNICI CON CPAP E/O INTEREFACCIA:
• Scarsa tenuta
• Dubbi/difficoltà nell'assemblaggio del circuito
• Dubbi sulle modalità
CHIAMARE PNEUMOLOGO
6464 (HSP),
67009 (HSC)