SALA VIOLANTE/GINEVRA

URGENZE RESPIRATORIE

Moderatori: **Salvatore Maggiore – Giorgio Carbone**

Francesca Nori

Alti flussi, NIV, CPAP nelle polmoniti

XII congresso nazionale
simeu
RICCIONE 13-15 MAGGIO 2022

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Alti flussi, NIV e CPAP nelle polmoniti

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Papa Innocenzo X, D Velasquez

Studio del ritratto di Papa Innocenzo X di Velazquez, F Bacon

Eur Respir J 2017; 50: 1602426

Certainty of evidence[¶]
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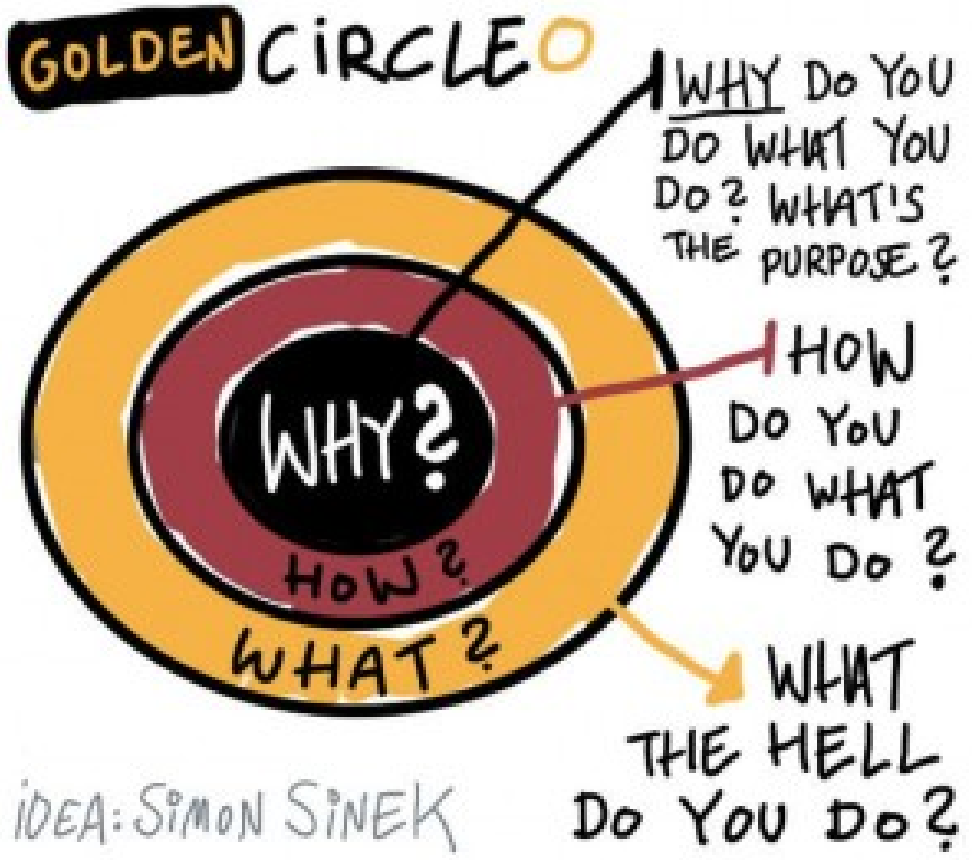
GOLDEN CIRCLE
WHY?
HOW?
WHAT?
WHY DO YOU DO WHAT YOU DO? WHAT'S THE PURPOSE?
HOW DO YOU DO WHAT YOU DO?
WHAT THE HELL DO YOU DO?
IDEA: SIMON SINEK

WHY?

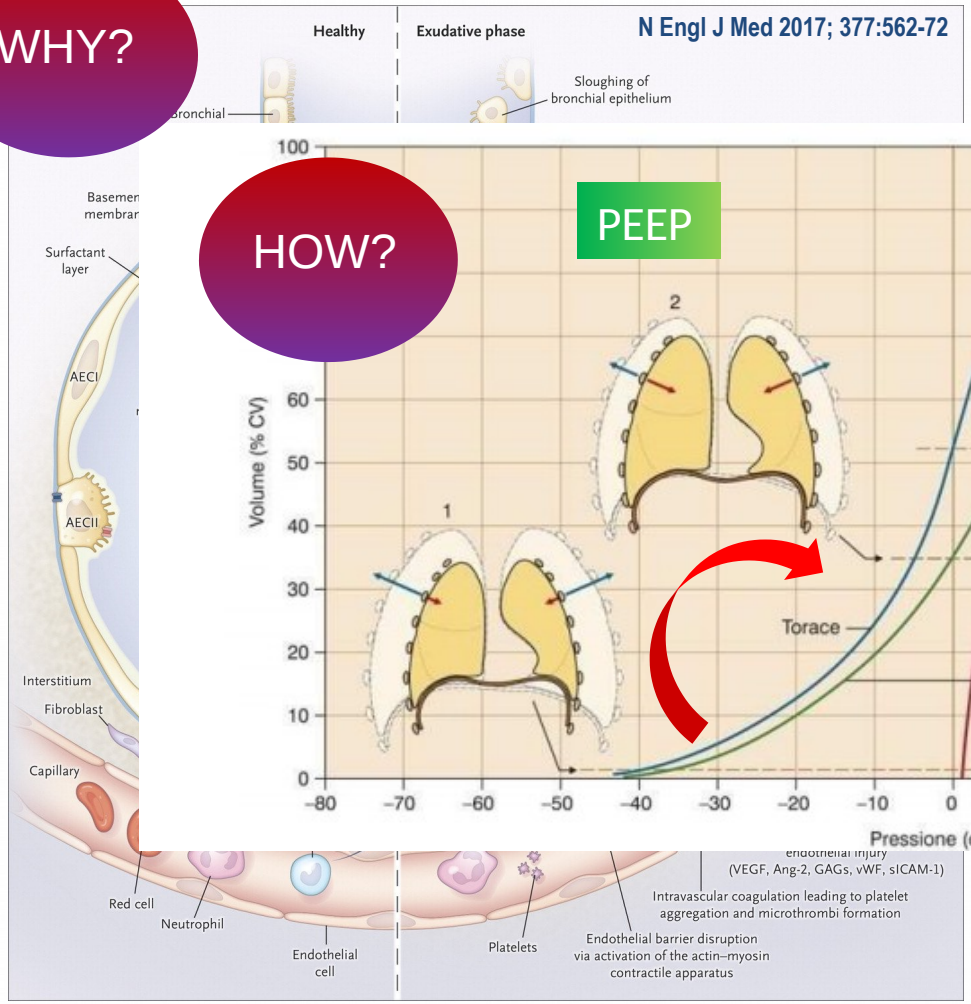

Table 2. Risk Factors for ARDS.

Direct lung-injury risk factors

HOW?

PEEP

Riduzione del V/Q

zone di polmone ipoventilate (V) rispetto alla perfusione (Q)

WHAT ?
(the hell)

American Journal of Emergency Medicine 36 (2018) 347–351

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American Journal of Emergency Medicine

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Original Contribution

Outcomes and predictors of failure of non-invasive ventilation in patients with community acquired pneumonia in the ED☆,☆☆

Amjad Al-Rajhi, MD [a], Anwar Murad, MD [a], P.Z. Li, MSc [b], Jason Shahin, MSc [a,b,c,*]

1. Introduction

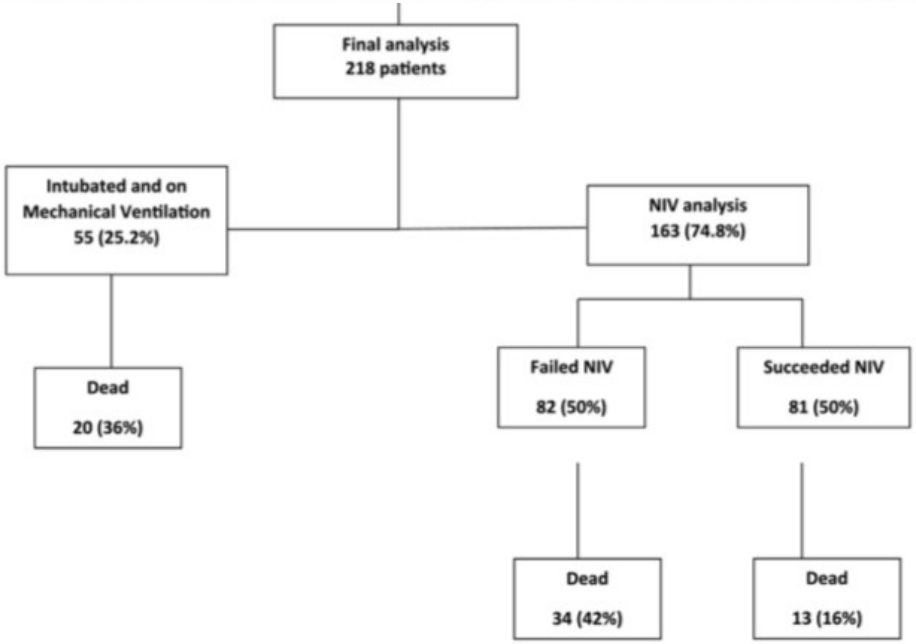
The use of non-invasive ventilation (NIV) in the emergency department (ED) as first line ventilatory therapy for acute hypoxemic respiratory failure has increased. The current literature provides strong evidence for the use of NIV in patients with hypercapneic respiratory failure and cardiogenic pulmonary edema yet, few data exist for the use of NIV in community-acquired pneumonia (CAP) [1].

While the clinical practice guidelines on evidence-based application of NIV for community-acquired pneumonia [1] did not provide a recommendation for its use, the Infectious Disease Society of America/American Thoracic Society guidelines on management of CAP did suggest a cautious trial of NIV [2]. Most studies on NIV and treatment of acute hypoxemic respiratory failure, including CAP, have been carried out in the critical care setting and have reported controversial results with varying failure rates for NIV use [3-15]. Nevertheless, NIV continues to be commonly used for the treatment of severe CAP, especially in the ED [16]. Given the lack of data, it is unclear if NIV is an efficacious therapeutic option for patients with CAP presenting to the ED [17].

Given the lack of data for NIV use in CAP in the ED, we set out to provide both an epidemiological description and an analysis of the predictors of NIV failure in patients with CAP who receive NIV in the ED as a first line ventilatory therapy.

2.4. Outcome

The primary outcome was NIV failure defined as the need for rescue intubation and mechanical ventilation after at least 1 h of NIV. Secondary outcomes were acute hospital mortality and hospital length of stay. The outcome was assessed during the whole course of the patient's acute hospital stay.



2.2. Selection of participants

Patients who required ventilation were identified by cross referencing respiratory therapy and ICU databases. Multiple databases were used to assure full capture of ventilated patients and avoid any missed patients in our study sample. We included both intubated and non-intubated patients who required ventilator support. No patients received high flow nasal cannula therapy. All patients who presented to the ED with a diagnosis of respiratory failure or pneumonia were screened for inclusion. CAP was defined as being present if a new chest X-ray infiltrate was seen along with three of the following: a white blood cell count < 4000 cells/mm^3 or $> 12{,}000$ cells/mm^3, temperature < 36 °C or > 38 °C, or a clinical history suggestive of pneumonia [18]. The data collectors had no a priori knowledge of the patient's outcomes when determining if CAP was present. Patients were excluded if: 1) they were transferred to or from another hospital prior to ED presentation; 2) if they received any form of home ventilator therapy or 3) if CAP was not the most likely etiology of the patient's respiratory failure on ED presentation.

DNR esclusi
Intubazione a discrezione del medico

Table 1
Baseline characteristics for whole cohort and separated by non-invasive ventilation status.

Characteristics	Whole NIV cohort (163)	Successful NIV (81)	Failed NIV (82)	p-Value[a]
Demographics				
Mean age, n (SD)	73(13)	75(13)	71(13)	0.02
Male sex, n (%)	101(62)	49(60.5)	52(63.4)	0.70
Acute severity of illness				
Mean APACHE II score (SD)	13.4(6.7)	12.7(6)	14.2(7.2)	0.21
Severe comorbidities n (%)				
Any prior illness	154(94.5)	79(97.5)	75(91.5)	0.09
Severe cardiovascular disease	43(26.4)	25(30.9)	18(22)	0.20
Severe respiratory disease	29(17.8)	17(21)	12(14.6)	0.30
History of COPD	51(31.3)	35(43.2)	16(19.5)	0.001
Renal disease	27(16.6)	15(18.5)	12(14.6)	0.51
Chronic liver disease	6(3.7)	3(3.7)	3(3.7)	0.99
Hematologic malignancy	5(3.1)	3(3.7)	2(2.4)	0.64
Metastatic disease	16(9.8)	7(8.6)	9(11)	0.62
Immunological dysfunction	17(10.4)	5(6.2)	12(14.6)	0.10
Interstitial lung disease	7(4.3)	2(2.5)	5(6.1)	0.30
Neuromuscular disease	5(3.1)	2(2.5)	3(3.7)	0.70
Dementia	17(10.4)	11(13.6)	6(7.3)	0.20
No. of CXR quadrants affected n (%)				
1	73(44.8)	50(61.7)	23(28.1)	<0.001
2	55(33.7)	22(27.2)	33(40.2)	
3	21(12.9)	7(8.6)	14(17.1)	
4	14(8.6)	2(2.5)	12(14.6)	
Physiological parameters prior to ventilation				
Need for haemodynamic support n (%)	12(7.4)	1(1.2)	11(13.4)	0.003
Mean arterial pressure (SD)	92.3(24.6)	93.3(24.4)	91.3(25)	0.59
Respiratory rate, mean (SD)	30.3(7.8)	30.1(7.2)	30.5(8.4)	0.81
PaO_2/FiO_2 ratio, mean (SD)	145(91.1)	161.3(95.8)	133.1(86.3)	0.10
pH, mean (SD)	7.30(0.10)	7.30(0.10)	7.30(0.20)	0.80
$PaCO_2$, mean(SD)	54.8(26)	58.1(25.4)	51(26.8)	0.02
Mean tidal volume achieved in cc (SD)	575(170.5)	578(175)	572(167)	0.84
Final destination from ED n (%)				
Critical care unit	111(68.1)	32(39.5)	79(96.3)	<0.001
Ward	48(29.4)	45(55.6)	3(3.7)	
Home	4(2.5)	4(4.9)	0(0)	
Acute hospital mortality n (%)	47(28.8)	13(16.1)	34(41.5)	<0.001
Median length of hospital stay (IQR)	14(8–26)	10(5–17)	22.5(12–38)	<0.001

Table 2
Adjusted odds ratio (OR) for association between non-invasive ventilation failure and baseline demographic, clinical and physiological risk factors.

Variables	OR	95% C.I.	p-Value
Risk factors at baseline[a]			
COPD	0.42	0.18–0.97	0.05
Hemodynamic support	11.48	1.24–106.71	0.03
APACHEII score (per 1 point increase)	1.06	1.01–1.13	0.05
CXR quadrants			
1	REF		0.01
2	2.47	1.05–5.78	
3	3.28	1.04–10.30	
4	11.25	1.83–57.53	
Physiological risk factors after at least 2 h of NIV[b]			
Respiratory rate (RR)			
≤20	REF		0.06
>20 ≤ 35	0.52	0.19–1.35	
>35	1.64	0.48–5.66	
pH			
>7.35	REF		0.04
>7.2 ≤ 7.35	0.99	0.46–2.12	
≤7.2	4.96	1.41–17.49	
Hemodynamic support	7.84	2.52–23.10	<0.001

In conlusione...

Al baseline...

No COPD

APACHE II

...

Instabilità emodinamica

Our study has several limitations worth noting. First, the retrospective study design limited the number of risk factors that could be studied and limits any conclusions about the causal nature of the studied risk factors and NIV failure. Moreover, even though the definition of CAP used is a standard definition there may have been some misclassification in our cohort. Finally, there was no established protocol to initiate, adjust or abandon NIV and therefore we could not ascertain if the NIV was managed in the most optimal fashion.

To our knowledge, it is one of the largest studies to evaluate the failure of NIV as first line ventilatory support in the management of CAP with respiratory failure in the ED. The majority of observational data on NIV use has examined critically ill patients admitted to an intensive care unit and has ignored the NIV use in the ED. By studying all patients with CAP and respiratory failure, we have achieved the true denominator of NIV use and avoided any selection bias that studies looking at patients admitted to an ICU may have encountered. Furthermore, the

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Non-invasive positive pressure ventilation in pneumonia outside Intensive Care Unit: An Italian multicenter observational study

Anna Maria Brambilla[a,*], Elena Prina[b], Giovanni Ferrari[c], Viviana Bozzano[d], Rodolfo Ferrari[e], Paolo Groff[f], Giuseppina Petrelli[f], Raffaele Scala[g], Fabio Causin[h], Paola Noto[i], Emanuela Bresciani[j], Antonio Voza[k], Stefano Aliberti[l], Roberto Cosentini[m], 3P study group

Recent audits reported a use of NIV in patients with ARF due to pneumonia in different settings. According to a recent European survey, up to 17% patients with non-hypercapnic ARF, including those with community-acquired pneumonia (CAP), were treated with NIV [8]. An Italian survey investigated NIV use outside the Intensive Care Unit (ICU) and reported 41% of the participating hospitals using NIV to treat pneumonia in non-immunocompromised patients and 63% pneumonia in immunocompromised patients[9]. Two recent randomized controlled trials (RCTs) also showed the efficacy of Continuous Positive Airway Pressure (CPAP) versus standard oxygen therapy in mild-to-severe pneumonia in a selected population [2,10]. Although supported by limited evidence, the application of NIV in ARF patients with pneumonia seems to be widely applied in clinical practice.

The aims of this study were to evaluate NIV use in "real life" to treat ARF due to pneumonia outside the ICU in Italy, comparing CPAP versus noninvasive positive pressure ventilation (NPPV), and to identify risk factors for in-hospital mortality in these patients.

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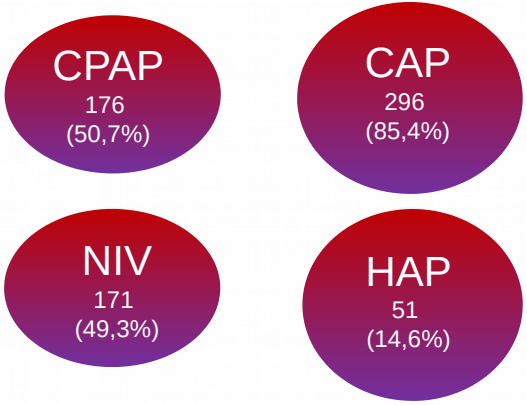

ARF

- ✓ P/F <250
- ✓ pH<7.35 con paCO2 >45
- ✓ Distress respiratorio

DNI inclusi

CPAP PEEP media 8 cmH20

NIV PEEP media 6 cmH20
PSV media 16 cmH20

Table 1
General characteristics of the population.

	Total population (n = 347)	CPAP (n = 176, 50.7%)	NPPV (n = 171, 49.3%)	p	Missing
Age, mean (± SD) median [IQR]	73.78 (± 14) 77 [66–85]	72.42 (± 15) 76 [64–84]	75.18 (± 12) 79 [68–85]	0.072	0
Men	201 (57.9)	108 (61.4)	93 (54.4)	0.188	0
Type of pneumonia					
CAP	296 (85.4)	148 (84.1)	148 (86.5)	0.518	0
HAP	51 (14.6)	28 (15.3)	23 (12.9)	0.664	0
Bilateral pneumonia	103 (31)	62 (35)	41 (26)	0.057	0
Interstitial pneumonia	58 (17)	28 (16)	30 (19)	0.490	0
Severity					
CURB65 ≥ 3[b]	139/275 (50)	73/142 (64)	66/137 (48)	0.199	21
PSI ≥ 4[b]	242/282 (85)	111/140 (79)	131/142 (92)	0.006	14
APACHEII	18.45 (± 5.7)	16.9 (± 5.9)	19.98 (± 5.3)	0.000	10
Shock index ≥0.8	116 (39.7)	65 (43.9)	51 (35.4)	0.152	5
Severe sepsis	255 (74)	130 (75)	125 (74)	0.802	5
Comorbidities					
COPD	159 (45.8)	55 (31.3)	104 (60.8)	< 0.001	0
Congestive heart failure	79 (22.8)	26 (14.8)	53 (31)	< 0.001	0
Chronic kidney disease	89 (25.6)	46 (26.1)	43 (25.1)	0.833	0
Obesity	60 (17.3)	24 (13.6)	36 (21.1)	0.068	0
Neoplastic disease	74 (21.3)	40 (22.7)	34 (19.8)	0.510	0
Charlson Comorbidity Index	204 (58.8)	111 (63.1)	93 (54.4)	0.150	0
< 3	104 (30)	50 (28.4)	54 (31.6)		
3–4	39 (11.2)	15 (8.5)	24 (14)		
≥ 5					
Do not intubation order (DNI)	103 (29.7)	49 (27.8)	54 (31.6)	0.446	0
de novo ARF[a]	117 (33.7)	86 (48.9)	31 (18.1)	< 0.001	0

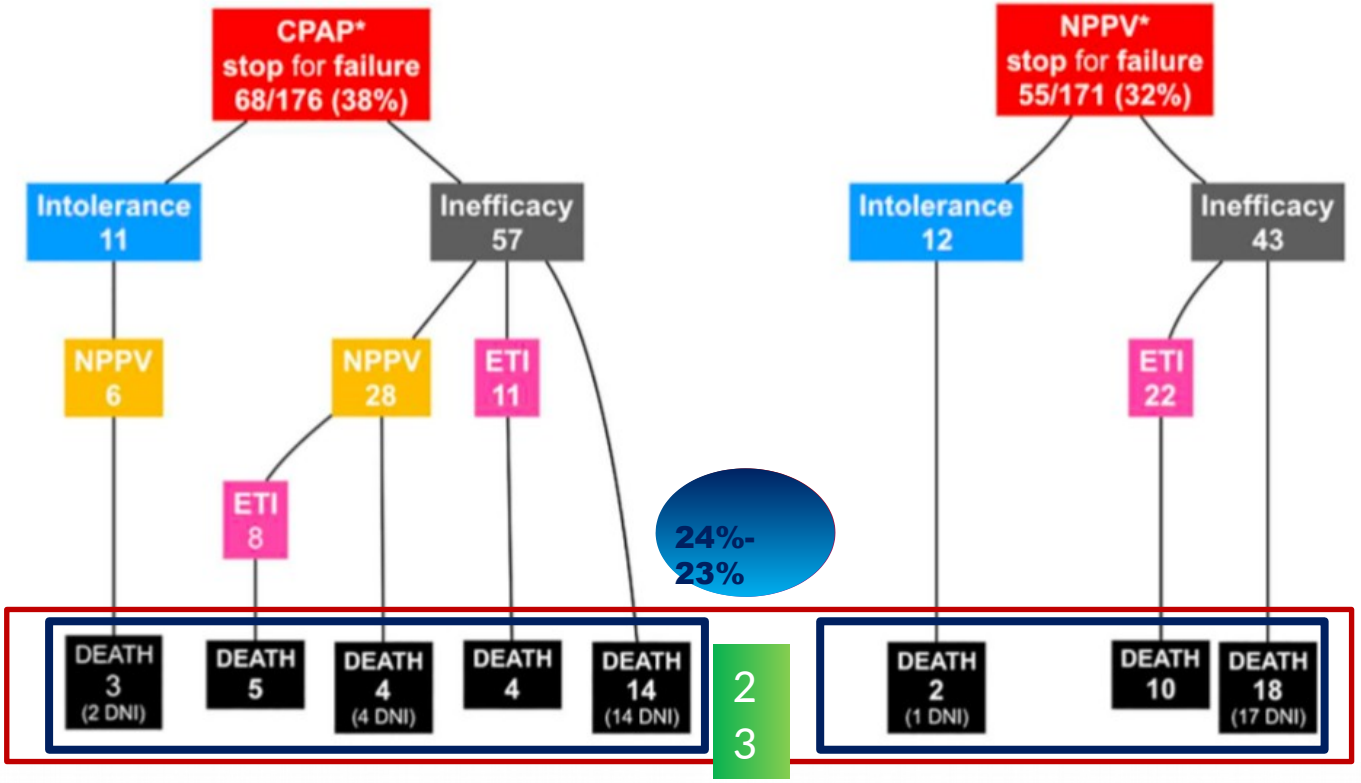
CPAP*
stop for failure
68/176 (38%)
Intolerance
11
Inefficacy
57
NPPV
6
NPPV
28
ETI
11
ETI
8
DEATH
3
(2 DNI)
DEATH
5
DEATH
4
(4 DNI)
DEATH
4
DEATH
14
(14 DNI)
24%-
23%
2
3
NPPV*
stop for failure
55/171 (32%)
Intolerance
12
Inefficacy
43
ETI
22
DEATH
2
(1 DNI)
DEATH
10
DEATH
18
(17 DNI)

Table 3
Risk factors for in-hospital mortality.

	Survivors (n = 264)	Not survivors (n = 83)	p	Missing
Age	76 [63–84]	80 [73–85]	0.002	0
Female, mean (± SD)	117 (44)	29 (35)	0.161	0
CPAP initial treatment	133 (50)	43 (52)	0.820	0
NIV initial treatment	131 (50)	40 (48)	0.820	0
COPD	124 (47)	35 (42)	0.444	0
Chronic Kidney disease	62 (23)	27 (32)	0.100	0
Obesity	54 (20)	6 (7)	0.005	0
Neoplastic disease	42 (15.9)	32 (38.5)	0.001	0
Charlson Comorbidity Index ≥3	94 (35.6)	49 (59)	0.001	0
De-novo ARF	89 (34)	28 (34)	0.997	0
Severe sepsis	187 (72)	68 (82)	0.077	5
DNI status	53 (20)	50 (60)	< 0.001	0
Systolic blood pressure mmHg, median [IQR]	130 [110–150]	130 [110–150]	0.813	5
Diastolic blood pressure mmHg, median [IQR]	70 [60–80]	70 [60–80]	0.460	5
Heart rate, mean (± SD)	100 ± 22	97 ± 23	0.489	5
pH, median [IQR]	7.35 [7.26–7.45]	7.38 [7.29–7.46]	0.228	10
$PaCO_2$ mmHg, median [IQR]	44 [35–68]	45 [34–60]	0.488	10
PaO_2/FiO_2 ratio, median [IQR]	179 [124–233]	161 [107–218]	0.087	10
Lactates > 2 mmol/L	82 (34.9)	36 (50)	0.027	10
Hb g/dL. median [IQR]	12.5 [11.0–13.9]	11.5 [10.3–13.0]	0.001	15
Platelets cell/mm^3, median [IQR]	231 [177–302]	242 [177–336]	0.397	15
Creatinine mg/dl, median [IQR]	1.11 [0.78–1.66]	1.50 [0.93–2.12]	0.002	15
C-reactive protein mg/dl, median [IQR]	13.3 [3.8–29.6]	17 [4.4–37]	0.132	15
HAP	33 (12)	18 (22)	0.041	0
CURB65 ≥ 3[a]	96/215 (45)	43/60 (72)	0.001	21
PSI ≥ 4[a]	182/222 (82)	60/60 (100)	0.000	14
APACHE II, mean (± SD)	18.02 (± 5.83)	19.87 (± 5.25)	0.01	10
Shock index ≥0.8	90 (39)	26 (40)	0.959	5
Kelly > 2	41 (18)	19 (27.1)	0.12	5

In conclusi

- ✓ Scelta fra CPAP e
- ✓ CPAP scelta più n
- ✓ NIV scelta più nel
- ✓ La mortalità si as ti clinici al baseline
- ✓ NIV dopo CPAP

NIV at a later stage in their illness and as an alternative to intubation. Conversely, in another study performed in Italy in 4 Respiratory ICUs where NIV was applied in 126 pneumonia patients, the mortality rate was 24%. Patients' characteristics in terms of respiratory and circulatory compromise were comparable to our population, confirming that patient selection seems to be crucial for NIV success [19].

In our study, in-hospital mortality was independently associated with both the DNI status and the burden of comorbidities. Several elderly or neoplastic patients are usually considered as DNI and are managed outside the ICU. In study, patients with ARF and a DNI order were offered NIV as a "ceiling treatment" [20]. Recent data reported the usefulness of NIV as palliative care in patients with "end-stage" solid tumors and ARF [21,22] and in elderly population, for whom invasive therapy is controversial [23]. It is obvious that in case of failure the mortality of these patients is higher than the rest of the population, as previous reported from Schettino et al. [24] since none of these patients undergo ETI.

We found that mortality was not associated to the severity of ARF, particularly if we consider the level of PaCO2 and PaO_2/FiO_2 ratio. These data are consistent with several studies on risk factors for NIV failure [13]. In contrast to other studies [13,25], *de-novo* ARF and severe sepsis were not associated to mortality, although patients with *de-novo* ARF were treated more frequently with CPAP than with NPPV, probably because of their "non-chronic" status.

These findings, together with the lack of association between initial respiratory compromise and failure, suggest that the global severity of patients and the early NIV application rather than the initial hypoxemia conditioned the final outcome.

ARDS-PNEUMONIA

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Critical Care

RESEARCH Open Access

A multicenter RCT of noninvasive ventilation in pneumonia-induced early mild acute respiratory distress syndrome

Hangyong He[1], Bing Sun[1], Lirong Liang[1], Yanming Li[2], He Wang[2], Luqing Wei[3], Guofeng Li[3], Shuliang Guo[4], Jun Duan[4], Yuping Li[5], Ying Zhou[5], Yusheng Chen[6], Hongru Li[6], Jingping Yang[7], Xiyuan Xu[7], Liqiang Song[8], Jie Chen[8], Yong Bao[9], Feng Chen[9], Ping Wang[10], Lixi Ji[10], Yongxiang Zhang[11], Yanyan Ding[11], Liangan Chen[12], Ying Wang[12], Lan Yang[13], Tian Yang[13], Heng Weng[14], Hongyan Li[14], Daoxin Wang[15], Jin Tong[15], Yongchang Sun[16], Ran Li[16], Faguang Jin[17], Chunmei Li[17], Bei He[18], Lina Sun[18], Changzheng Wang[19], Mingdong Hu[19], Xiaohong Yang[20], Qin Luo[20], Jin Zhang[21], Hai Tan[21], Chen Wang[22,23,24,25*] and for the ENIVA Study Group

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg $< Pao_2/Fio_2 \leq$ 300 mm Hg with PEEP or CPAP $\geq$5 cm H_2O[c]
Moderate	100 mm Hg $< Pao_2/Fio_2 \leq$ 200 mm Hg with PEEP $\geq$5 cm H_2O
Severe	$Pao_2/Fio_2 \leq$ 100 mm Hg with PEEP $\geq$5 cm H_2O

Background

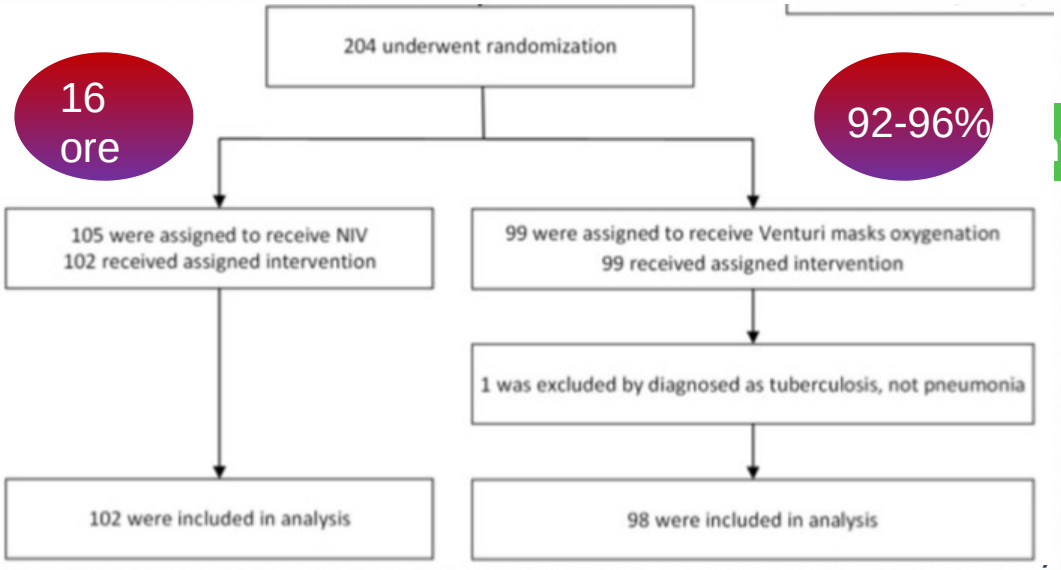
- ✓ NIV ha mortal
- ✓ Molti dei pazi

Aim

- ✓ Primario: n di
- ✓ Secondario: m

Criteri di in

- ✓ Diagnosi di pc
- ✓ Infiltrati bilaterali all'rx
- ✓ PF fra I 200 e I 300 (in maschera Venturi al 50%)



- ✓ Utilizzo muscoli accessori

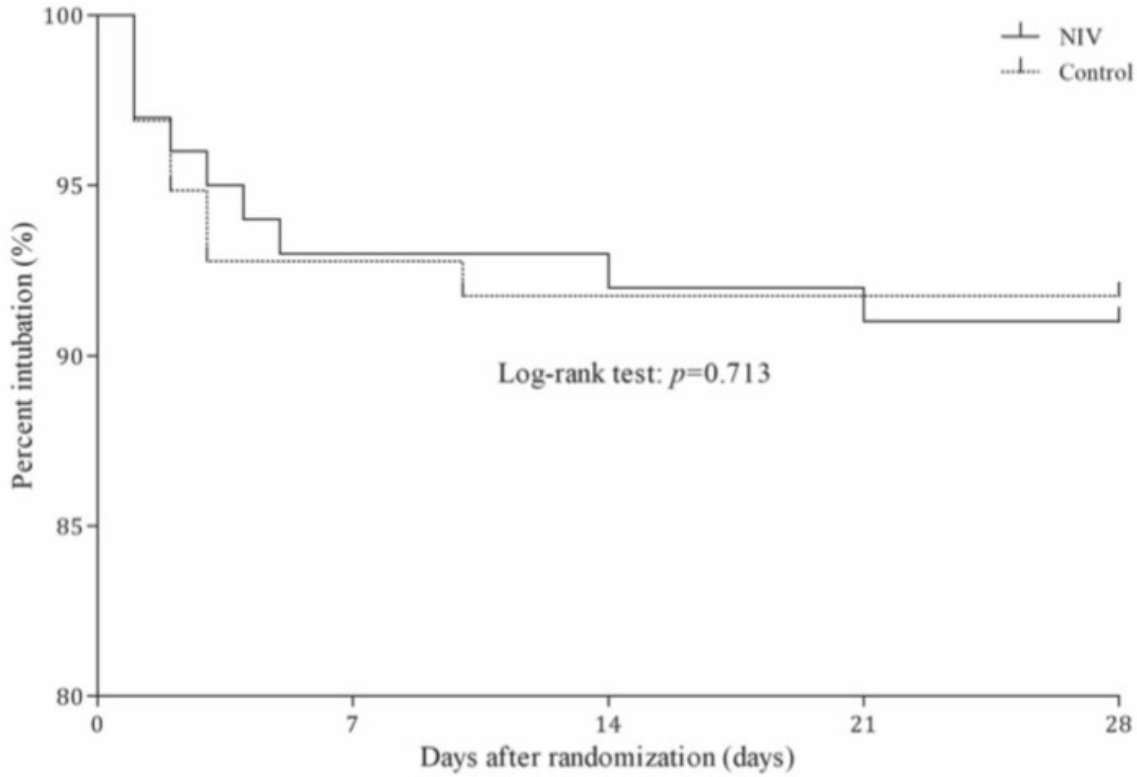


Fig. 2 Kaplan-Meier estimates of the probability of the need for endotracheal intubation based on the criteria for endotracheal intubation. No difference was found for the cumulative probability for endotracheal intubation of the two groups (log-rank test: $p = 0.71$)

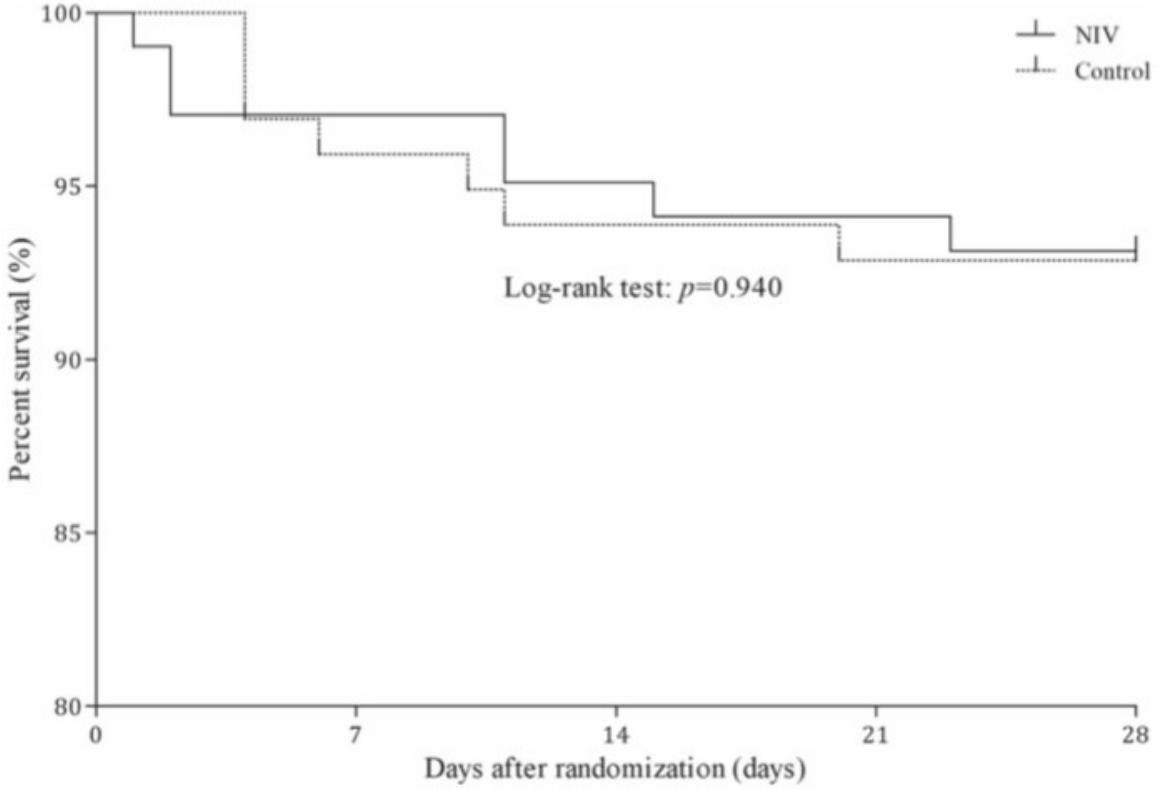


Fig. 3 Kaplan-Meier estimates of the probability of mortality. No difference was found for the cumulative probability for endotracheal intubation of the two groups (log-rank test: $p = 0.94$)

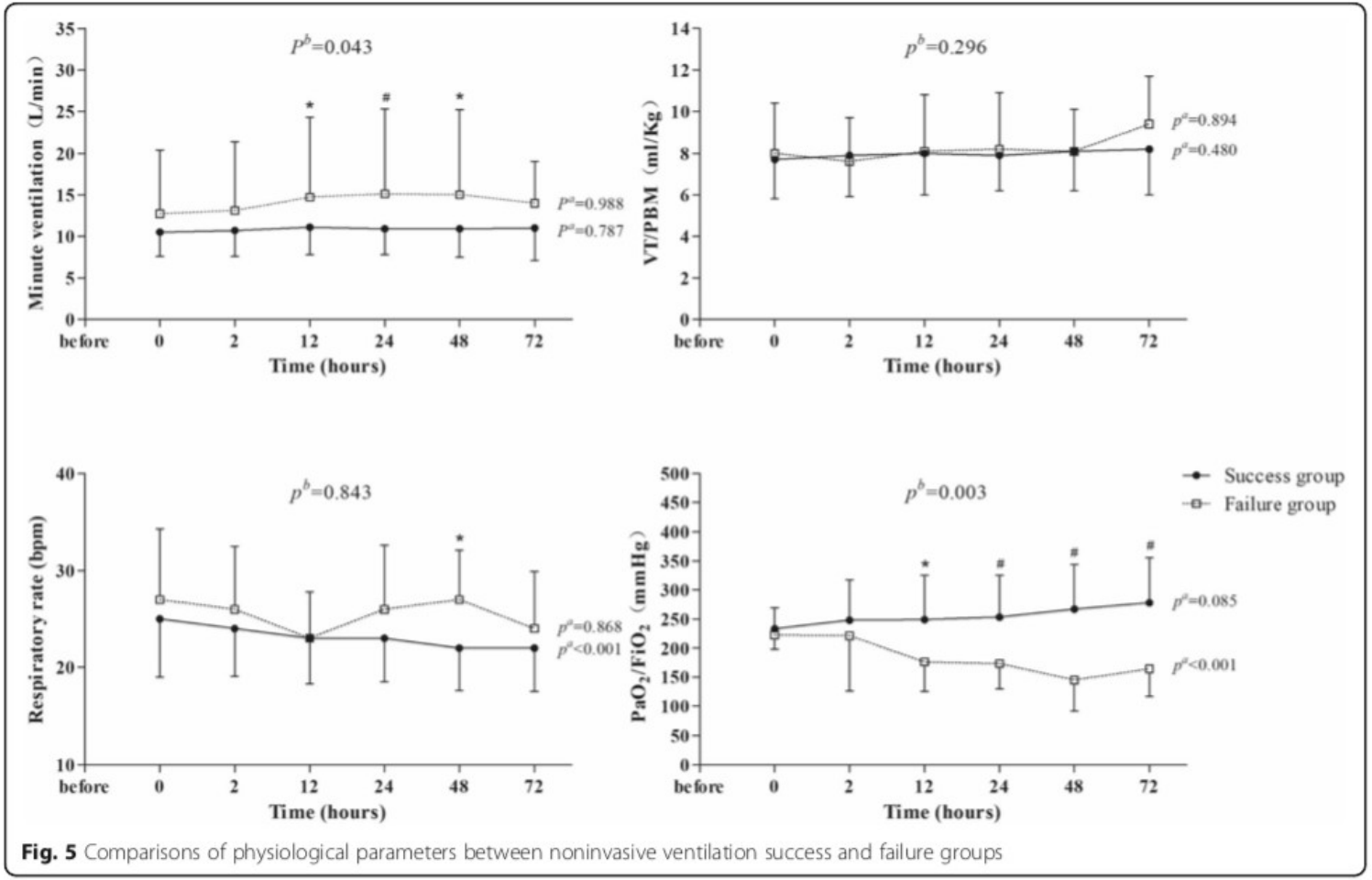


Fig. 5 Comparisons of physiological parameters between noninvasive ventilation success and failure groups

1°

2°

3°

early pneumonia-induced mild ARDS. The
ngth of our study is its high homogeneity with
only pneu uced
The maj r
the Vent dic
ation or mor pneur

L/min; 1 point each for a respiratory rate ≥ 30 and immune suppression [EALI score]). A score greater than or equal to 2 points identified patients who progressed to equiring NIV [16].The average respiratory rate

ati
in the EALI
for including
our finding
with NIV fai
inclusion cri
for a low intu

The rate of the need for intubation is lower than expected in our study. This may reflect patients being included in a very early stage of mild ARDS. In a previous ation was based on a simple e lung injury score (1 point -6 L/min or 2 points for > 6

The primary outcome analysis of our study showed no difference in the need for intubation between the NIV and control groups. This may reflect the lack of recruitment responsiveness to NIV positive airway pressure in early mild ARDS patients. A meta-analysis revealed that higher airway pressure levels were associated with improved survival among the subgroup of ARDS patients with PaO_2/FIO_2 less than 200 mmHg [18], who demonstrate better recruitment with positive airway pressure. In our study, we included patients with a PaO_2/FIO_2 higher than 200 mmHg, who may be less responsive to NIV, leading to a negative result for NIV compared to

4°

receiving NIV for acute hypoxemic respiratory failure. The high tidal volume resulting from the high respiratory drive in these patients may lead to lung injury and NIV failure [26]. High tidal volume and minute ventilation were also found in NIV patients in LUNG SAFE [10]. A

5°

car

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plained by lung injury cause

during NIV. Based on our c

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min in early mild ARDS.

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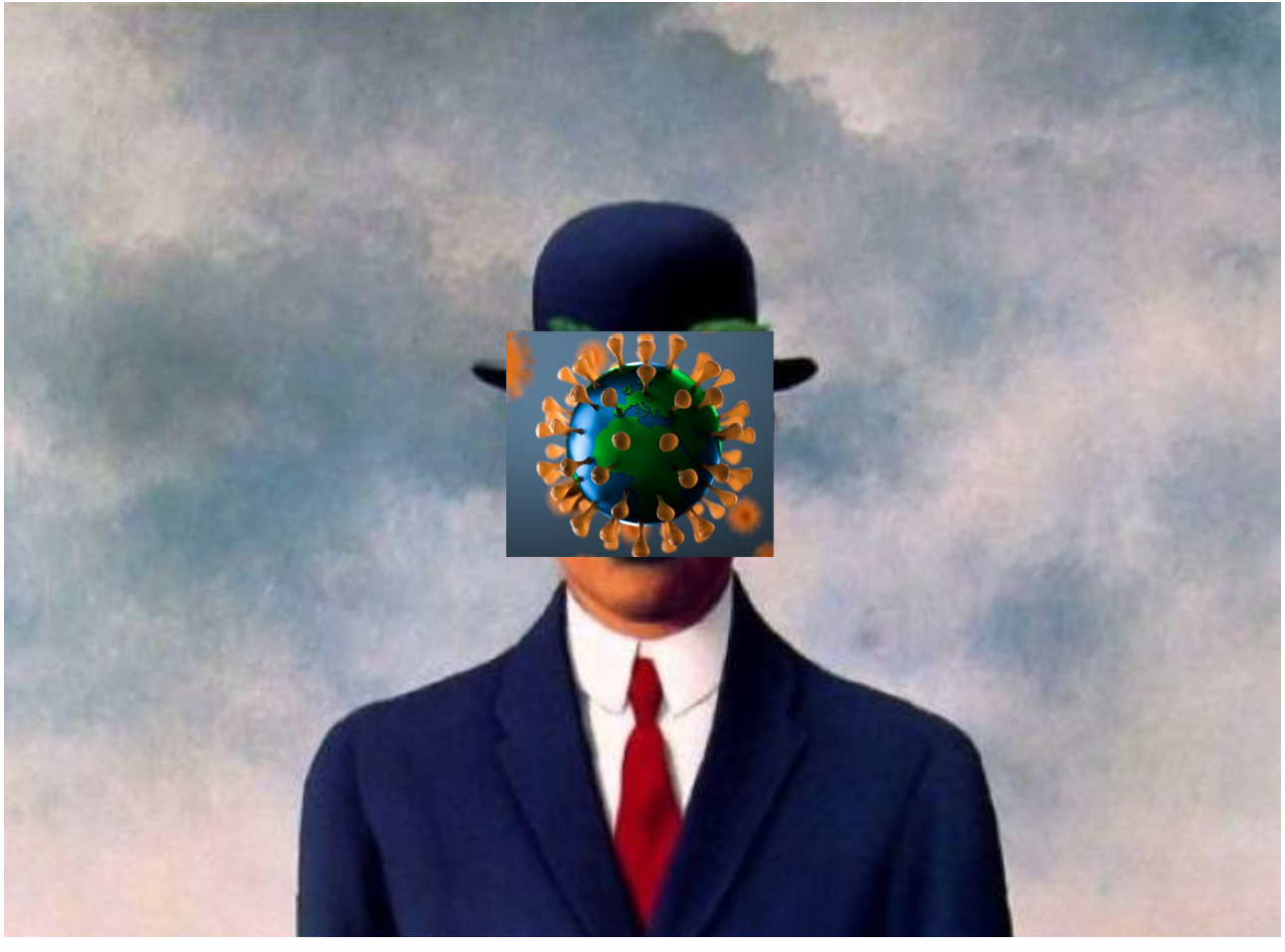
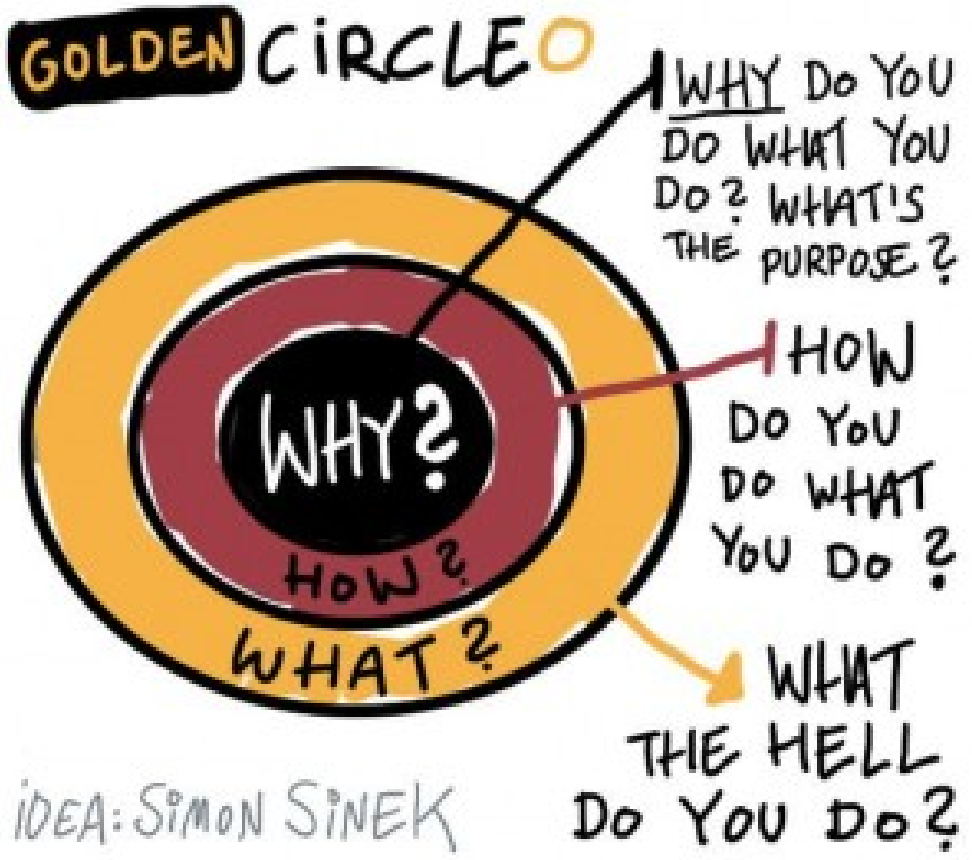
And recently, a HACOR score was proposed for patients with NIV failure in hypoxic patients [28]. HACOR score improves in patients with NIV success and remains un-

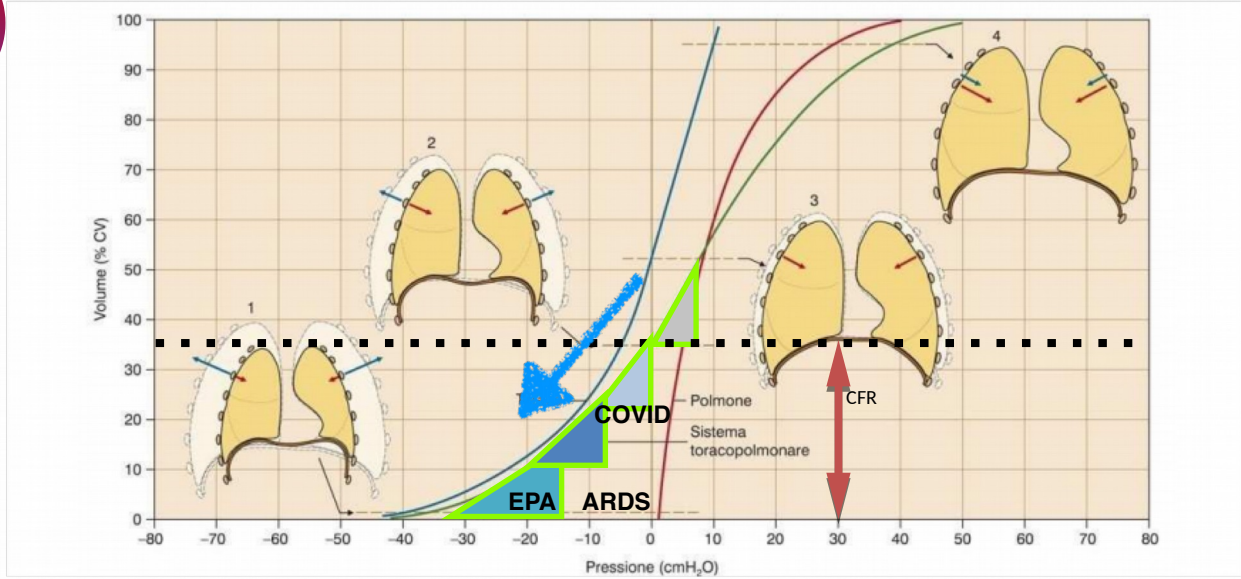
atients with NIV failure, which also empha-

The main limitation of our study was that the definition of early mild ARDS was based on the American-European consensus conference criteria for ALI. Patients did not receive positive pressure at inclusion assessment. This results in our patients having lower severity of mild ARDS than those meeting the Berlin definition. Inclusion of pneumonia patients with very early stage of mild ARDS may have resulted in lower progression to ARDS and the need for intubation than expected. Although




GOLDEN CIRCLE
WHY?
HOW?
WHAT?
WHY DO YOU DO WHAT YOU DO? WHAT'S THE PURPOSE?
HOW DO YOU DO WHAT YOU DO?
WHAT THE HELL DO YOU DO?
IDEA: SIMON SINEK

WHY?



Iniziale fase di danno microvascolare ed interstiziale…

…diffuso danno alveolare…

…formazione di membrane ialine, edema, fibrosi.

1. In fase iniziale compliance e resistenze del polmone pressoché normali
2. Progressivamente il danno microvascolare comporta **perdita del meccanismo di vasocostrizione ipossica** con generazione effetto shunt dx-sn

HAPPY HYPOXEMIA

REVIEW

CURRENT OPINION

Diagnosing acute respiratory distress syndrome in resource limited settings: the Kigali modification of the Berlin definition

Elisabeth D. Riviello[a,b], Egide Buregeya[c], and Theogene Twagirumugabe[c]

Table 1. ARI

	Berlin criteria	Kigali modifications
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Oxygenation	$PaO_2/FiO_2 \leq 300$	$SpO_2/FiO_2 \leq 315$
PEEP requirement	Minimum 5 cm H_2O PEEP required by invasive mechanical ventilation (noninvasive acceptable for mild ARDS)	No PEEP requirement
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or CT	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or ultrasound
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload [need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present]	Respiratory failure not fully explained by cardiac failure or fluid overload [need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present]

ARDS, acute respiratory distress syndrome; PEEP, positive end expiratory pressure.

Li and Ma *Critical Care* (2020) 24:198
https://doi.org/10.1186/s13054-020-02911-9

Critical Care

REVIEW Open Access

Acute respiratory failure in COVID-19: is it "typical" ARDS?

Xu Li and Xiaochun Ma*

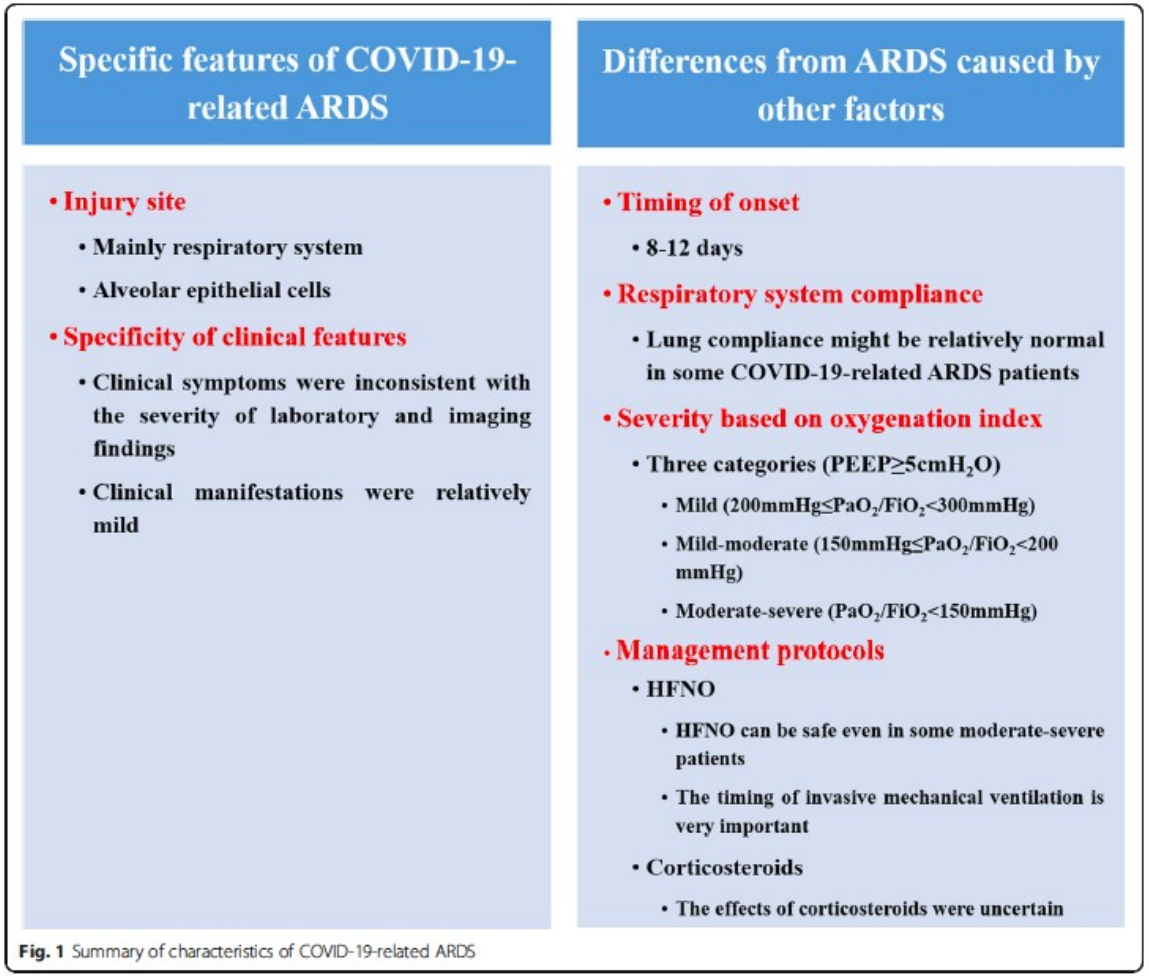


Fig. 1 Summary of characteristics of COVID-19-related ARDS

HOW?

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure

The HENIVOT Randomized Clinical Trial

Domenico Luca Grieco, MD; Luca S. Menga, MD; Melania Cesarano, MD; Tommaso Rosà, MD; Savino Spadaro, MD, PhD; Maria Maddalena Bitondo, MD; Jonathan Montomoli, MD, PhD; Giulia Falò, MD; Tommaso Tonetti, MD; Salvatore L. Cutuli, MD; Gabriele Pintaudi, MD; Eloisa S. Tanzarella, MD; Edoardo Piervincenzi, MD; Filippo Bongiovanni, MD; Antonio M. Dell'Anna, MD; Luca Delle Cese, MD; Cecilia Berardi, MD; Simone Carelli, MD; Maria Grazia Bocci, MD; Luca Montini, MD; Giuseppe Bello, MD; Daniele Natalini, MD; Gennaro De Pascale, MD; Matteo Velardo, PhD; Carlo Alberto Volta, MD; V. Marco Ranieri, MD; Giorgio Conti, MD; Salvatore Maurizio Maggiore, MD, PhD; Massimo Antonelli, MD; for the COVID-ICU Gemelli Study Group

MAIN OUTCOMES AND MEASURES The primary outcome was the number of days free of respiratory support within 28 days after enrollment. Secondary outcomes included the proportion of patients who required endotracheal intubation within 28 days from study enrollment, the number of days free of invasive mechanical ventilation at day 28, the number of days free of invasive mechanical ventilation at day 60, in-ICU mortality, in-hospital mortality, 28-day mortality, 60-day mortality, ICU length of stay, and hospital length of stay.

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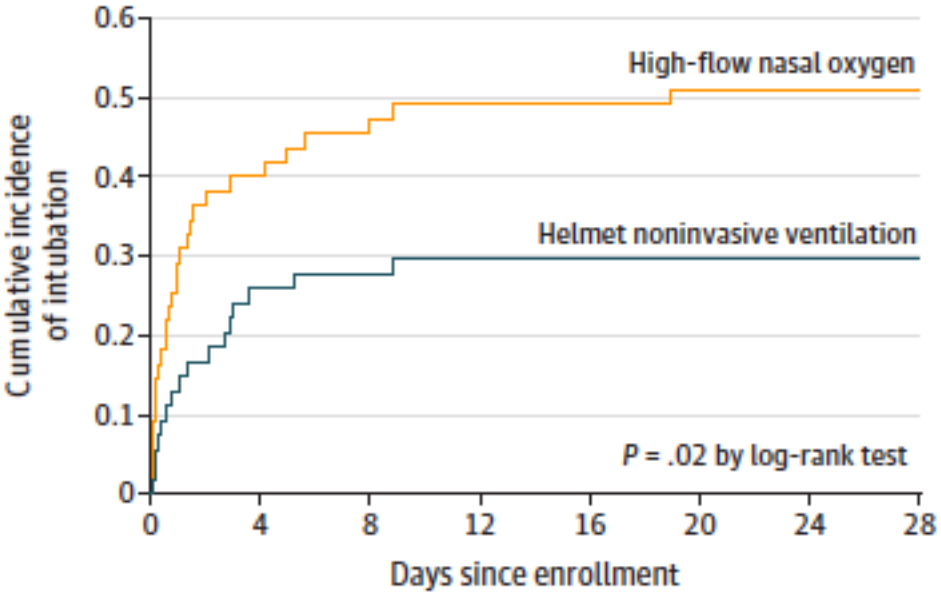
Figure 3. Cumulative Incidence of Intubation Over Time in the Helmet Noninvasive Ventilation and High-Flow Nasal Oxygen Groups to Day 28



No. at risk								
High-flow nasal oxygen	55	34	30	28	28	27	27	27
Helmet noninvasive ventilation	54	41	39	38	38	38	38	38

Table 2. Primary and Secor

Outcome	P value[c]
Primary outcome	
Respiratory support-free day median (IQR)[d]	.26

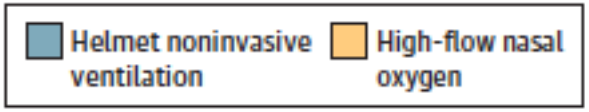
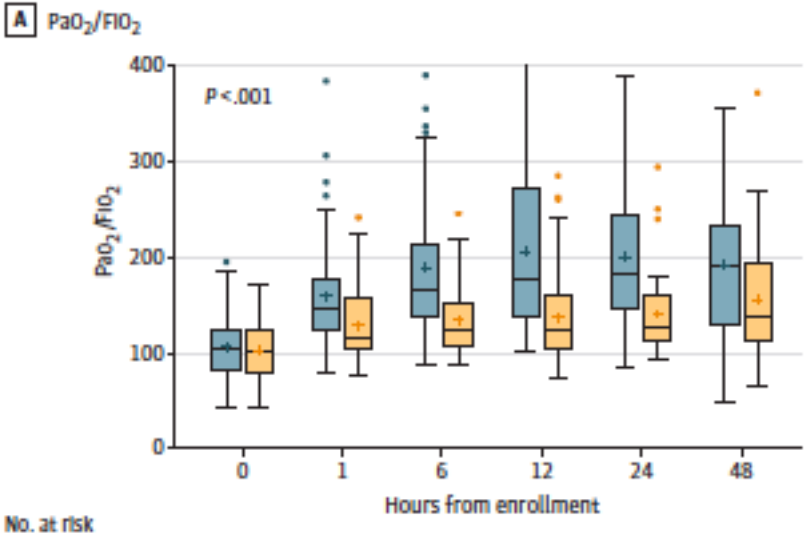
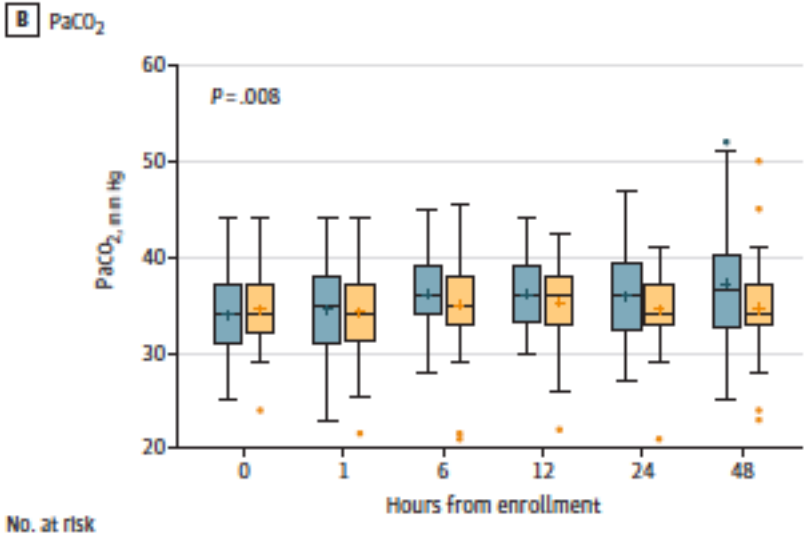
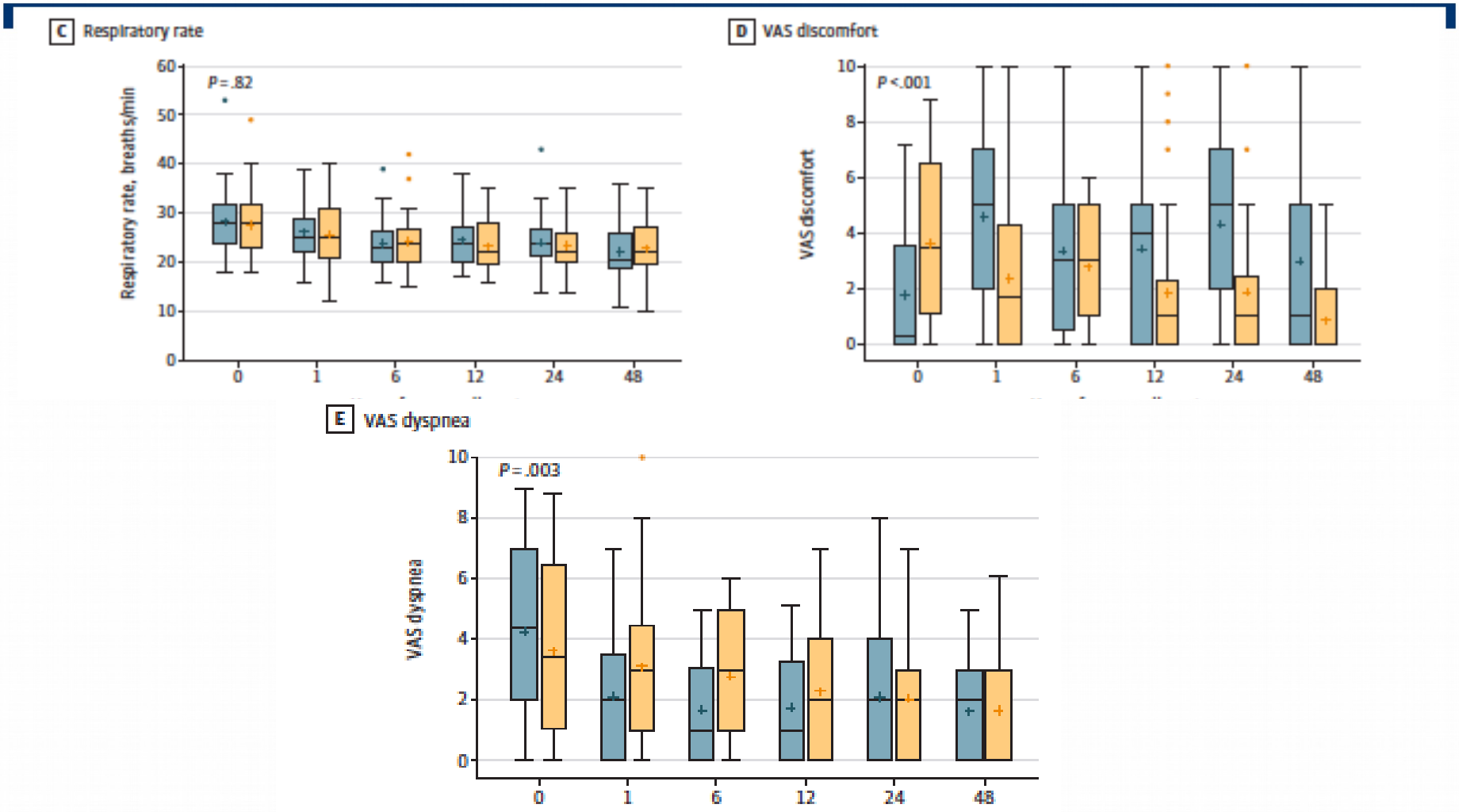


Figure 4. Physiologic Variables Over the First 48 Hours in the Helmet Noninvasive Ventilation and High-Flow Nasal Oxygen Groups






C
Respiratory rate
Respiratory rate, breaths/min
P = .82
60
50
40
30
20
10
0
0
1
6
12
24
48
D
VAS discomfort
VAS discomfort
P < .001
10
8
6
4
2
0
0
1
6
12
24
48
E
VAS dyspnea
VAS dyspnea
P = .003
10
8
6
4
2
0
0
1
6
12
24
48

scientific reports

Check for updates

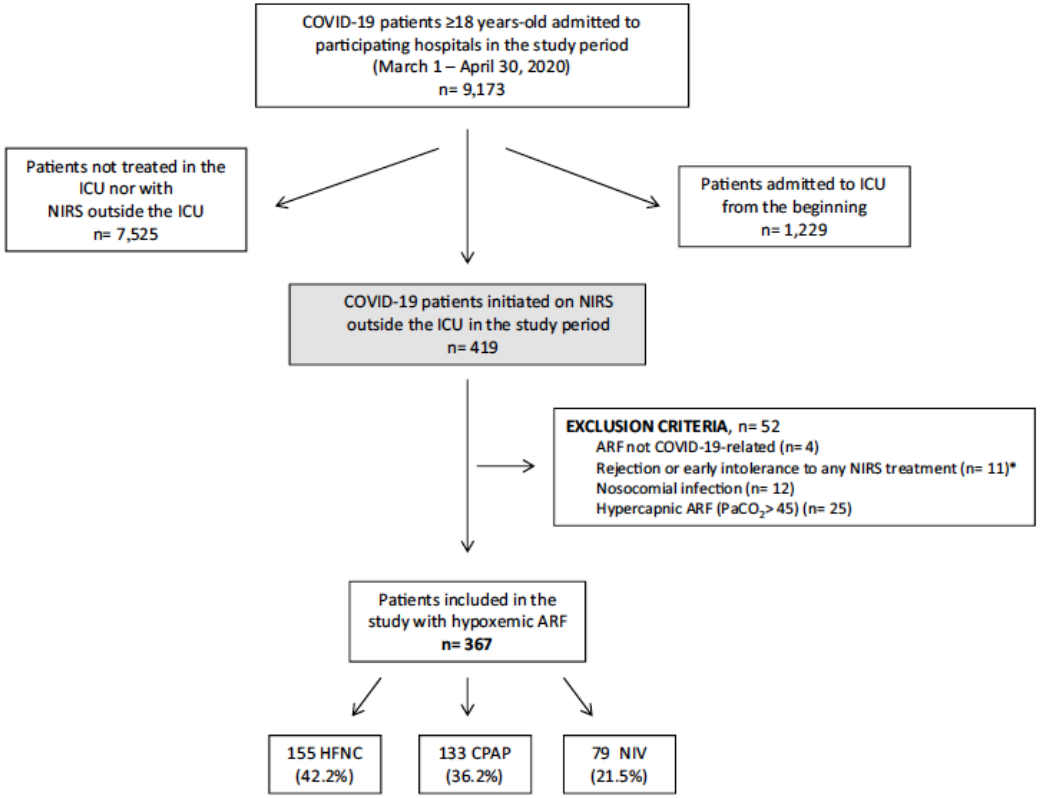
OPEN

Higher mortality and intubation rate in COVID-19 patients treated with noninvasive ventilation compared with high-flow oxygen or CPAP

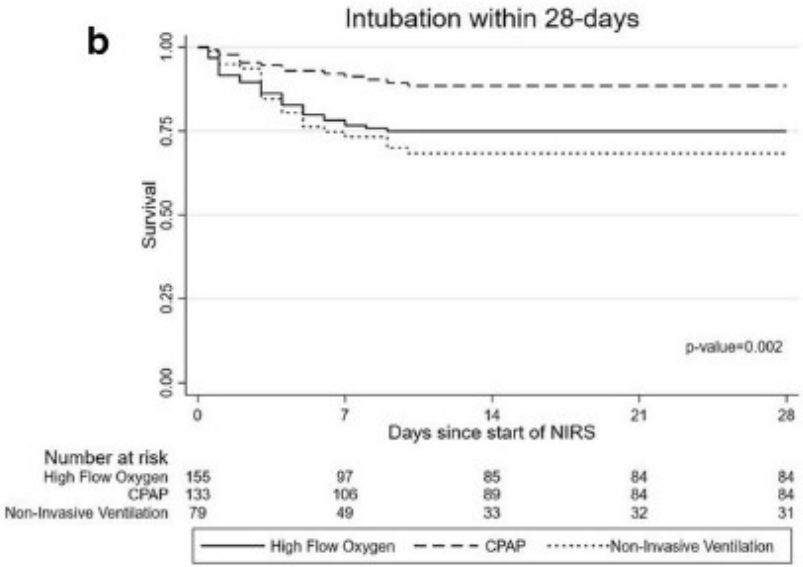
Sergi Marti[1,2,3]✉, Anne-Elie Carsin[4,5,6], Júlia Sampol[1,2,3], Mercedes Pallero[1,2,3], Irene Aldas[7], Toni Marin[7], Manel Lujan[3,8], Cristina Lalmolda[3,8], Gladis Sabater[9,10], Marc Bonnin-Vilaplana[9,10], Patricia Peñacoba[11], Juana Martinez-Llorens[3,5,12], Julia Tárrega[13,14], Óscar Bernadich[15], Ana Córdoba-Izquierdo[16], Lourdes Lozano[17], Susana Mendez[4,6], Eduardo Vélez-Segovia[1,2], Elena Prina[8], Saioa Eizaguirre[9,10], Ana Balañá-Corberó[12], Jaume Ferrer[1,2,3] & Judith Garcia-Aymerich[4,5,6]

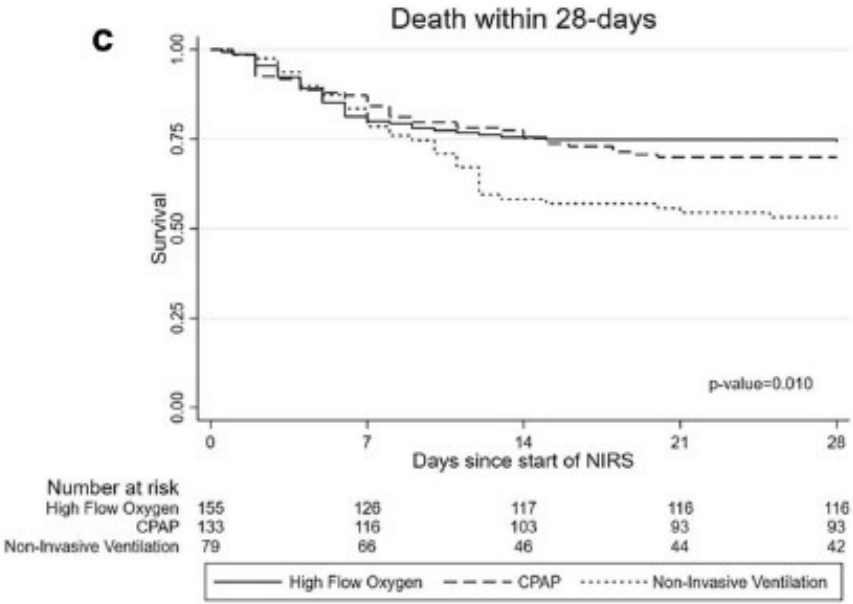
Study outcomes. The primary outcome was treatment failure, defined as endotracheal intubation or death within 28 days of NIRS initiation. Secondary outcomes were 28-day mortality, endotracheal intubation at day 28, in-hospital mortality, and duration of hospital stay.

In the HFNC group, heated and humidified oxygen was applied through nasal prongs, at an initial flow rate of 50–60 lpm if tolerated. CPAP was initially set at 8–10 cm H_2O and then adjusted according to tolerance and clinical response. In the NIV group, a pressure support ventilator mode was adjusted; a high positive end-expiratory pressure (PEEP) and a low support pressure were used to set a tidal volume < 9 ml/kg of predicted body weight[8].



Outcomes	N = 367	High-flow oxygen (N = 155)	CPAP (N = 133)	Non-invasive ventilation (N = 79)
Main outcome				
Death or intubation at day 28 after initiating NIRS	n (%), 168 (45.8%) HR (95% CI) *P* value	71 (45.8%) 1.00	49 (36.8%) 0.97 (0.63–1.50) *P* = 0.891	48 (60.8%) 2.01 (1.32–3.08) *P* = 0.001
Secondary outcomes				
Endotracheal intubation during 28 days within NIRS	n (%)†, 73 (19.9%) HR (95% CI) *P* value	36 (23.2%) 1.00	14 (10.5%) 0.64 (0.31–1.30) *P* = 0.212	23 (29.1%) 2.38 (1.29–4.39) *P* = 0.006
28-day mortality after initiating NIRS	n (%), 117 (31.9%) HR (95% CI) *P* value	40 (25.8%) 1.00	40 (30.1%) 1.11 (0.65–1.90) *P* = 0.704	37 (46.8%) 2.78 (1.61–4.78) *P* < 0.001
In-hospital mortality*	n (%), 123 (33.5%) HR (95% CI) *P* value	43 (27.7%) 1.00	43 (32.3%) 1.06 (0.63–1.78) *P* = 0.834	37 (46.8%) 2.30 (1.35–3.92) *P* = 0.002
Length of hospital stay†	median (P25-P75), 16 (10–25) exp(β) (95% CI)‡ *P* value	16 (10–26) 1.00	16 (11–22) 0.95 (0.78–1.15) *P* = 0.598	16 (9–23) 0.89 (0.73–1.10) *P* = 0.284


b
Intubation within 28-days
Survival
0.00
0.25
0.50
0.75
1.00
p-value=0.002
0
7
14
21
28
Days since start of NIRS
Number at risk
High Flow Oxygen 155 97 85 84 84
CPAP 133 106 89 84 84
Non-Invasive Ventilation 79 49 33 32 31
High Flow Oxygen
CPAP
Non-Invasive Ventilation


c
Death within 28-days
Survival
0.00
0.25
0.50
0.75
1.00
p-value=0.010
0
7
14
21
28
Days since start of NIRS
Number at risk
High Flow Oxygen 155 126 117 116 116
CPAP 133 116 103 93 93
Non-Invasive Ventilation 79 66 46 44 42
High Flow Oxygen
CPAP
Non-Invasive Ventilation

NIV so bad…

- ✓ produce overdistension → ventilation-induced lung injury
- ✓ patient-ventilator asynchronies
- ✓ minimize aerosol dispersion can modify ventilator performance
- ✓ sedation
- ✓ may impair expectoration

WHAT ?
(the hell)

AnnalsATS Volume 18 Number 6 | June 2021

ORIGINAL RESEARCH

Noninvasive Ventilatory Support of Patients with COVID-19 outside the Intensive Care Units (WARd-COVID)

Giacomo Bellani[1,2], Giacomo Grasselli[3,4], Maurizio Cecconi[5,6], Laura Antolini[1], Massimo Borelli[7], Federica De Giacomi[8], Giancarlo Bosio[8], Nicola Latronico[9,10], Matteo Filippini[10], Marco Gemma[11], Claudia Giannotti[12], Benvenuto Antonini[13], Nicola Petrucci[14], Simone Maria Zerbi[15], Paolo Maniglia[16], Gian Paolo Castelli[17], Giovanni Marino[18], Matteo Subert[19], Giuseppe Citerio[1,2,20], Danilo Radrizzani[21], Teresa S. Mediani[22], Ferdinando Luca Lorini[23], Filippo Maria Russo[23], Angela Faletti[24], Andrea Beindorf[25], Remo Daniel Covello[26], Stefano Greco[27], Marta M. Bizzarri[28], Giuseppe Ristagno[3], Francesco Mojoli[29], Andrea Pradella[5], Paolo Severgnini[30], Marta Da Macallè[30], Andrea Albertin[31], V. Marco Ranieri[32], Emanuele Rezoagli[1,2,33], Giovanni Vitale[33], Aurora Magliocca[1,33], Gianluca Cappelleri[34], Mattia Docci[1,35], Stefano Aliberti[4,36], Filippo Serra[1], Emanuela Rossi[1], Maria Grazia Valsecchi[1], Antonio Pesenti[3,4], and Giuseppe Foti[1,2]; on behalf of the COVID-19 Lombardy ICU Network

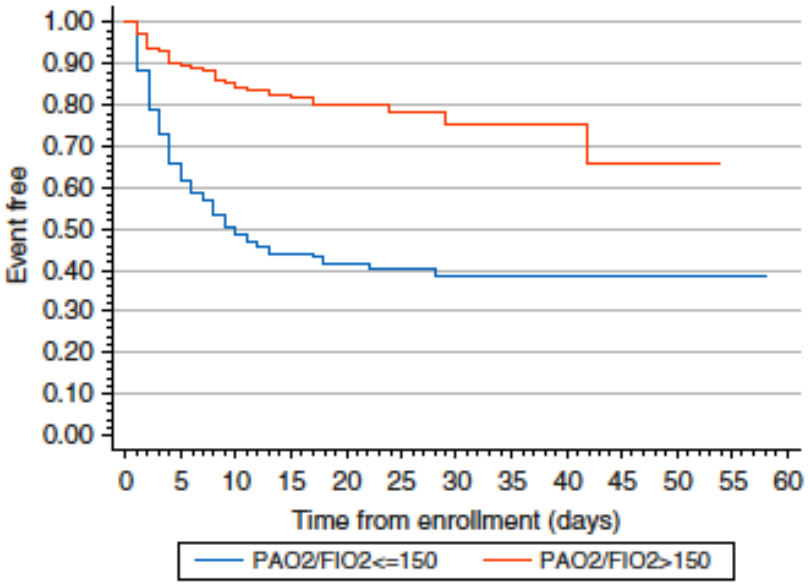
Objectives: To describe the prevalence and clinical characteristics of patients with COVID-19 treated with NIV outside the ICUs. To investigate the factors associated with NIV failure (need for intubation or death).

Table 1. Main demographic variables and comorbidities of the enrolled patients

	n	All population (*N* = 798)	Success (*n* = 498, 62.4%)	Failure (*n* = 300, 37.6%)
Respiratory parameters				
FIO_2, mean (SD), %	758	67.5 (20.5)	61.2 (18.6)	78.2 (19.1)*
PEEP, mean (SD), cm H_2O	783	10.79 (2.5)	10.6 (2.6)	11.3 (2.5)*
pH, mean (SD)	598	7.45 (0.05)	7.445 (0.04)	7.44 (0.06)*
PaO_2, mean (SD), mm Hg	599	103 (52)	113 (56)	89 (43)*
PaO_2/FIO_2, mean (SD), mm Hg	592	168 (98)	198 (104)	122 (66)*
$PaCO_2$, mean (SD), mm Hg	599	37.4 (6.9)	37.9 (6.6)	36.6 (7.2)*
$PaCO_2$ <40 mm Hg, *n* (%)	599	430 (53.9)	257 (51.6)	173 (57.7)
SaO_2 mean (SD), %	576	95.4 (4.6)	96.5 (3.4)	93.7 (5.6)*
SpO_2 mean (SD), %	164	94.6 (5.5)	96.5 (2.9)	90.8 (7.3)*
SpO_2/FIO_2, mean (SD)	141	160.3 (51.9)	175.2 (49.7)	126.5 (40)*
Respiratory rate	605	23.9 (6.6)	22.1 (5.4)	26.7 (7.4)*
Use of accessory respiratory muscles, *n* (%)	631	183 (27.64)	59 (14.4)	124 (49.2)*
Dyspnea, *n* (%)	631	179 (27.2)	60 (14.5)	119 (48.8)*

Results

- ✓ 85% treated with continuous positive airway
- ✓ delivered by helmet in 68%
- ✓ NIV failed in 38% patients
- ✓ Overall mortality was 25%
- ✓ Higher C-reactive protein and lower PaO2/FIO2 and platelet counts were independently associated with increased risk of NIV failure



RESEARCH Open Access

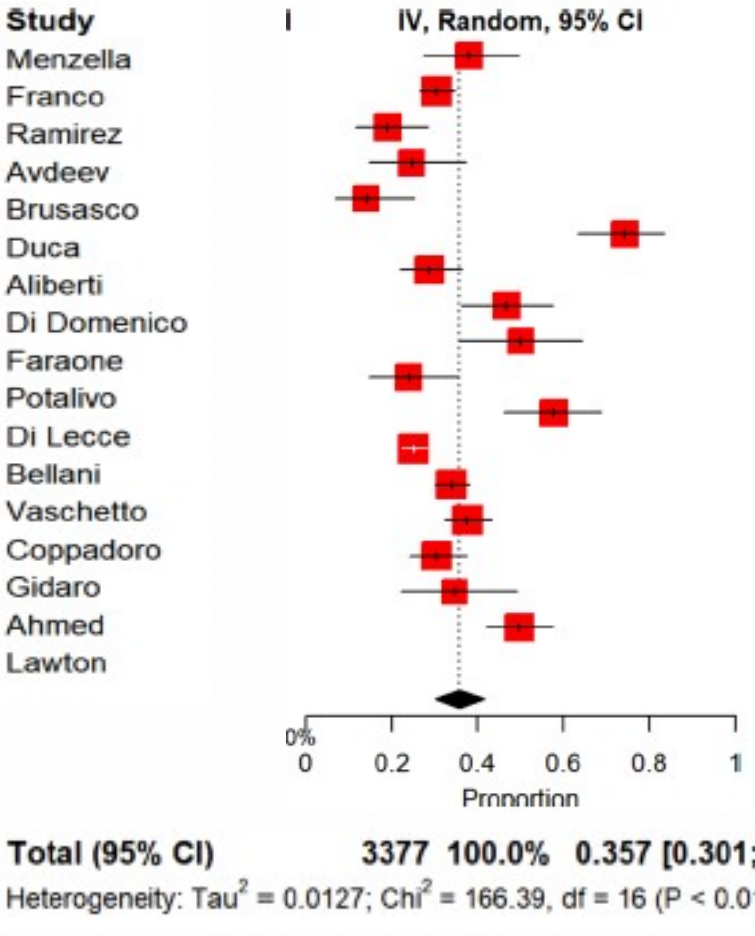
Noninvasive respiratory support outside the intensive care unit for acute respiratory failure related to coronavirus-19 disease: a systematic review and meta-analysis

Gianmaria Cammarota[1*], Teresa Esposito[2], Danila Azzolina[2], Roberto Cosentini[3], Francesco Menzella[4], Stefano Aliberti[5,6], Andrea Coppadoro[7], Giacomo Bellani[7,8], Giuseppe Foti[7,8], Giacomo Grasselli[6,9], Maurizio Cecconi[10,11], Antonio Pesenti[6,9], Michele Vitacca[12], Tom Lawton[13], V. Marco Ranieri[14], Sandro Luigi Di Domenico[15], Onofrio Resta[16], Antonio Gidaro[17], Antonella Potalivo[18], Giuseppe Nardi[18], Claudia Brusasco[19], Simonetta Tesoro[1], Paolo Navalesi[20], Rosanna Vaschetto[2†] and Edoardo De Robertis[1†]

Critical Care (2021) 25:268

The aim of this systematic review and meta-analysis was to estimate the overall intra-hospital mortality of COVID-19 patients assisted through NIRS outside the ICU

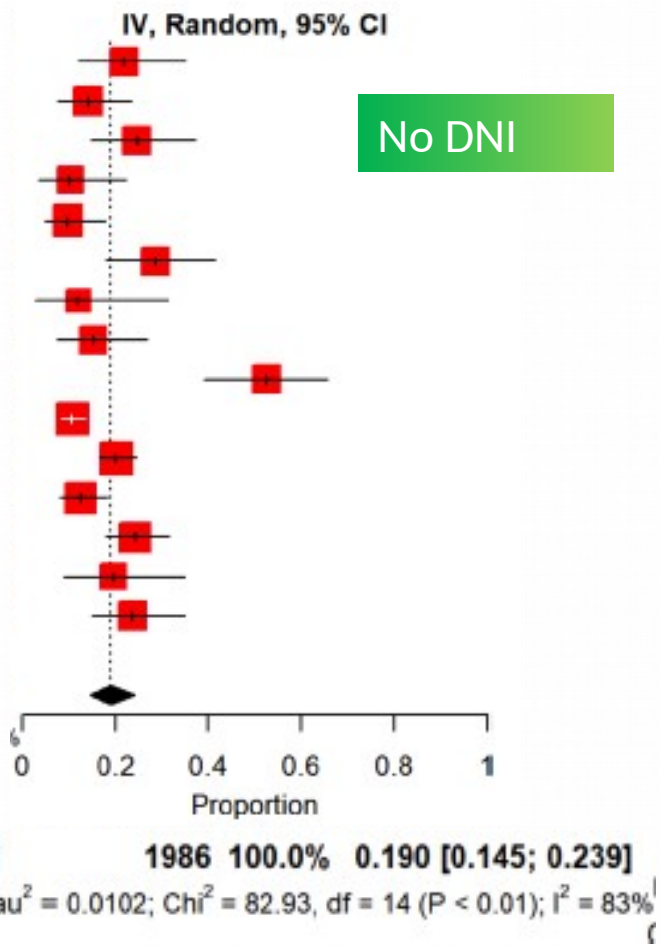
mortality



Total (95% CI) **3377 100.0% 0.357 [0.301; 0.414]**

Heterogeneity: $Tau^2 = 0.0127$; $Chi^2 = 166.39$, df = 16 ($P < 0.01$); $I^2 = 90\%$

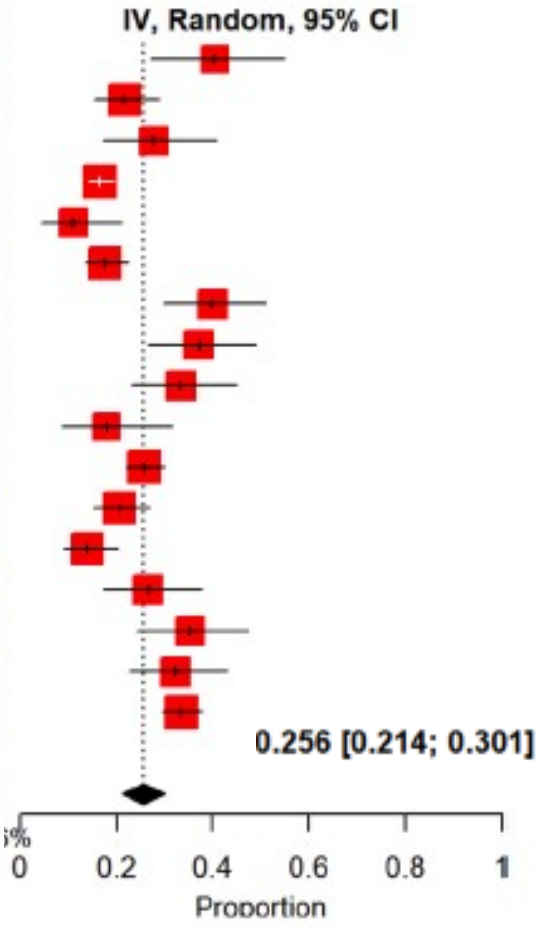
No DNI



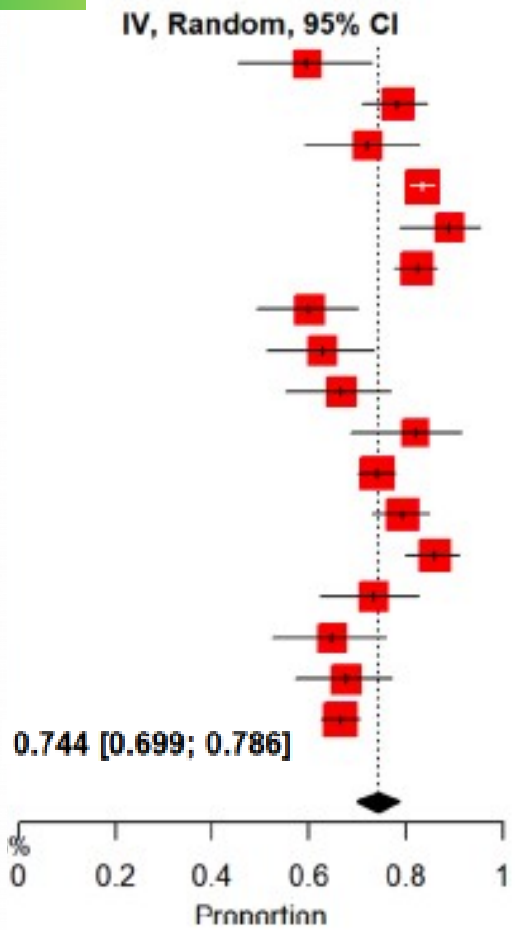
Total (95% CI) **1986 100.0% 0.190 [0.145; 0.239]**

Heterogeneity: $Tau^2 = 0.0102$; $Chi^2 = 82.93$, df = 14 ($P < 0.01$); $I^2 = 83\%$

NIV failure



NIV success



WHAT ?
(the hell)

Internal and Emergency Medicine
https://doi.org/10.1007/s11739-021-02906-6

EM - ORIGINAL

Check for updates

SIMEU position paper on non-invasive respiratory support in COVID-19 pneumonia

Roberto Cosentini[1] · Paolo Groff[2] · Anna Maria Brambilla[3] · Renzo Camajori Todeschini[4] · Gianfilippo Gangitano[5] · Stella Ingrassia[3] · Roberta Marino[6] · Francesca Nori[7] · Fiammetta Pagnozzi[8] · Francesco Panero[9] · Rodolfo Ferrari[7] on behalf of SIMEU NIV Group collaborators

Indications to oxygen therapy

Our recommendation

Start with oxygen therapy when $SpO_2 < 94\%$, obtained by an arterial blood gas analysis (BGA).

Choose high FiO_2 if $SpO_2 < 90$ (e.g., non-rebreather mask 15 L/min).

Choose low FiO_2 if SpO_2 range is 90–93% (e.g., nasal cannula 3–6 L/min).

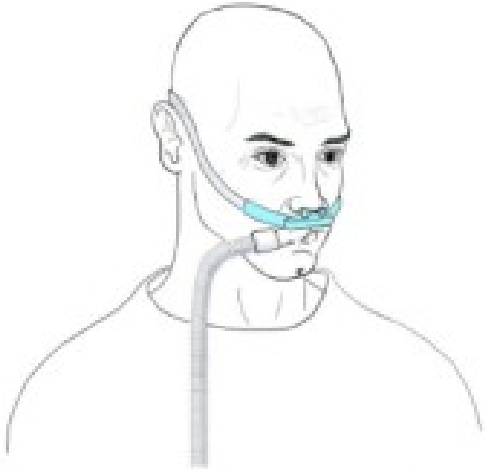
In patients with chronic pulmonary disease, start with oxygen therapy if $SpO_2 < 90$–92%

SIMEU
società italiana medicina d'emergenza-urgenza

DISPERSIONE: non nota

DISPERSIONE: 10 cm 10 l/min

DISPERSIONE: 40 cm FiO2 24%



SIMEU
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d'emergenza-urgenza

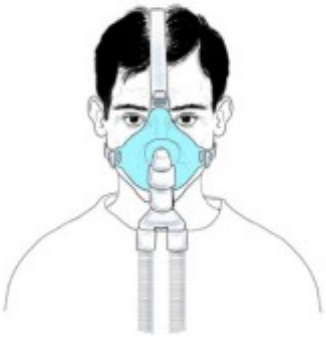
OUR RECOMMENDATION. Considering the studies analyzed, the use of HFNCO may be effective in the treatment of moderate to severe respiratory failure secondary to COVID-19-related pneumonia, preventing the use of other support techniques, such as CPAP or NIPPV.

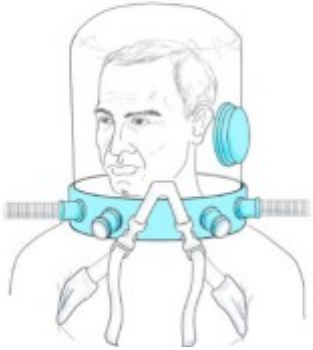
We recommend its use for 1 to 2 h in patients with $SpO_2 < 92\%$ or PaO_2/FiO_2 200–300 mmHg during treatment with a non-rebreathing mask at 15 L/min for at least 15 min, before sorting to CPAP in case of failure of the technique to correct these values.

We strongly recommend close clinical monitoring of the patient and check of gas exchange after 2 h of treatment in order not to delay the escalation of therapy in case of deterioration. The determination of a ROX index value > 4 at this timepoint correlates with a better outcome of the technique.

From a practical point of view, we recommend choosing a cannula size appropriate to the size of the patient's nostrils; adjust the flow to 60 L/min and titrate it down to patient comfort; adjust the temperature of the mixture to patient comfort starting from 31 °C; enrich the oxygen mixture by titrating it to the therapeutic target ($SpO_2 > 92\%$).

We also recommend placing a surgical mask on the patient's face during treatment.





It seems rational to recommend the early use of CPAP in hypoxaemic ARF in a moderate phase of the clinical course, for hemodynamically stable patients, with preserved neurological status (Kelly–Matthay scale = 1) [87], unscathed respiratory dynamics, RR ≥ 25 bpm, with $SpO_2 < 90\%$ or $PaO_2 < 60$ mmHg during standard oxygen with elevated FiO_2 via Venturi or non-rebreathing mask or HFNCO sustained at 50 L/min. The choice of high CPAP values, between 7.5 and 12.5 cm H_2O, and high FiO_2 is recommended to achieve the OTSR of 94–98% (69); the goal should be lower (90–92%) in patients at risk of hypercapnia.

FiO_2 has to be set to achieve OTSR, PEEP should be high enough (7.5–12 cmH_2O) to obtain adequate alveolar recruitment and oxygenation under conditions of disadvantageous compliance, inspiratory pressure to get towards a lower than normal tidal volume (4 to 6 ml/kg of ideal body weight), inspiratory trigger must be maintained with maximum sensitivity, inspiratory pressure rise time must balance rapid pressurization and leakages in both restrictive

Intensive Care Med
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NARRATIVE REVIEW

Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS

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Benefits of maintaining spontaneous breathing

- ✓ Preserves physiological pathways of airway protection (e.g. cough and clearance of secretions)
- ✓ Reduces the complications related to endotracheal intubation (e.g. laryngeal and tracheal trauma)
- ✓ Reduces ventilatory induced lung injury, ventilator-associated pneumonia
- ✓ sedation and neuromuscular paralysis
- ✓ Benefits related to lung, heart and diaphragm physiology

Harms of maintaining spontaneous breathing

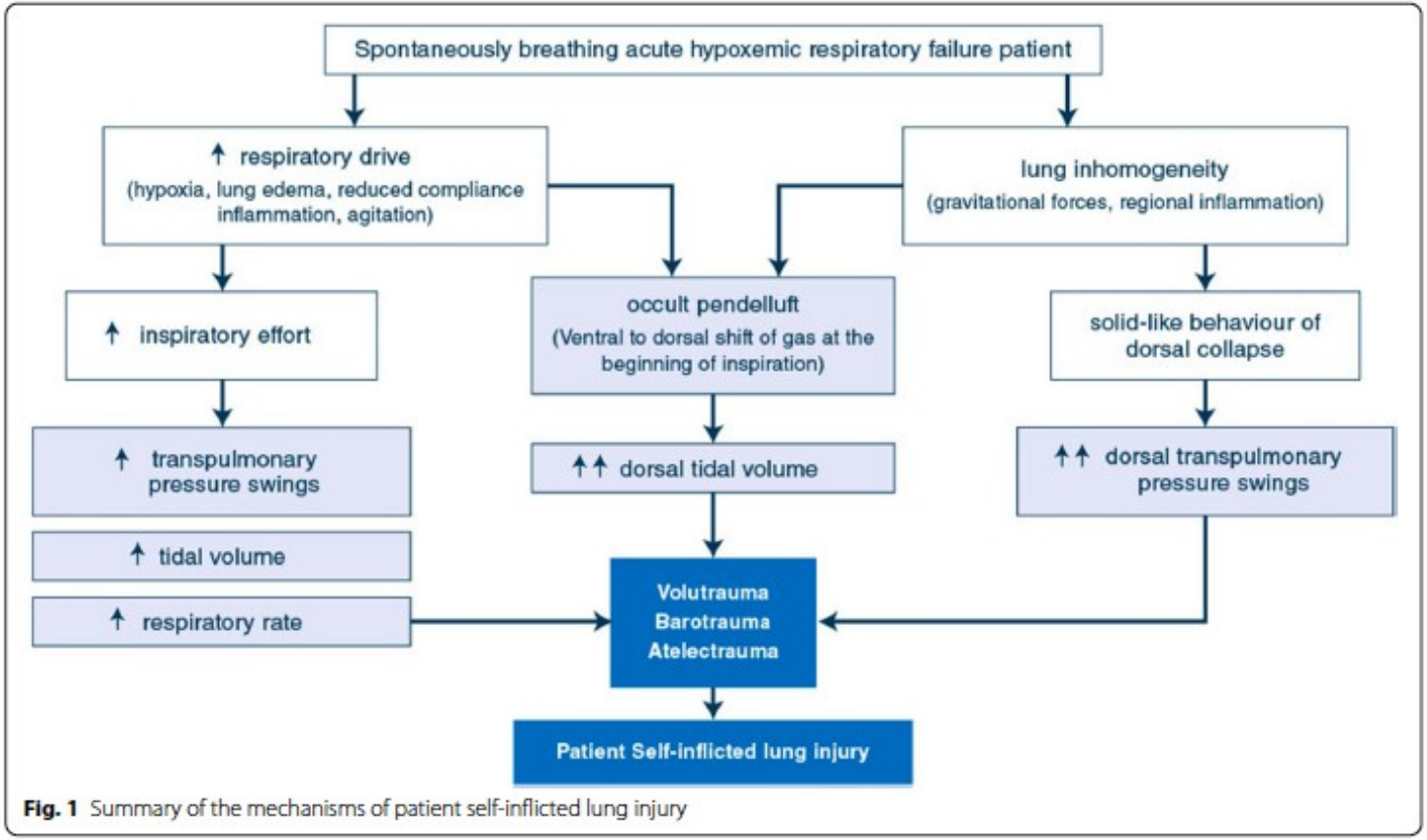

Fig. 1 Summary of the mechanisms of patient self-inflicted lung injury

Noninvasive ventilation: CPAP and Pressure Support Ventilation (PSV)

High-flow nasal oxygen

Settings
- FiO_2: 0.21-1
- Gas flow: 40-60 lpm
- Temperature: 31-37°C

Benefits
- Matches inspiratory flow
- Delivers set F_IO_2
- Delivers fully conditioned gas
- Enhances comfort
- Provides positive airway pressure (up to 4 cmH_2O)
- Washout of nasopharyngeal dead space
- Reduces inspiratory effort

Pitfalls
- Small amount of PEEP delivered

Facemask

Settings

PSV-requires a ventilator
- FiO_2: 0.21-1
- PEEP: 5-8 cmH_2O
- PS: 7-10 cmH_2O

CPAP
- Continuous flow (>30 L/min) or CPAP mode on the ventilator
- PEEP: 5-8 cmH_2O

Use of HME is advisable

Benefits
- Delivers set FiO_2
- Delivers fully conditioned gas
- Provides PEEP to allow alveolar recruitment
- Provides PS (only for PSV) to unload inspiratory muscles
- Allows to monitor tidal volume (only PSV)

Pitfalls
- Skin ulcer
- Air leaks, difficult delivery of high PEEP
- Full inspiratory synchronization may increase P_L swings and tidal volume
- Poor tolerability: need for treatment interruptions

Helmet

Settings

PSV-requires a ventilator
- FiO_2: 0.21-1
- PEEP: 10-12 cmH_2O
- PS: 10-12 cmH_2O
- No humidification needed
- Fastest pressurization time

CPAP-requires a flow generator
- Continuous flow (>60 L/min)
- PEEP valve: 10-12 cmH_2O
- Active humidification possible

Benefits
- Delivers set FiO_2
- Provides high PEEP to allow alveolar recruitment and enhance ventilator homogeneity
- Continuous treatments with good tolerability
- Provides PS (only for PSV) to reduce inspiratory effort
- Asynchronous PS may prevent positive P_L swings

Pitfalls
- Impossibility to measure tidal volume
- Upper limbs edema, with possible vasal thrombosis

Table 2 Relevant physiological measures for monitoring of hypoxemic patients on noninvasive respiratory support

Parameter	Monitoring technique/score calculation	Clinical thresholds associated with risk of failure	Limitations
SpO_2/FiO_2	Pulse oximetry	< 120 and/or worsening trend	Underestimation of severity with low $PaCO_2$
PaO_2/FiO_2	Arterial blood gas analysis	< 150–200 mmHg and/or worsening trend	Intermittent
Respiratory Rate	Clinical examination	> 25–30 and/or not decreasing with support	Poorly correlated with effort
Expired tidal volume	Ventilator	> 9–9.5 ml/kg PBW	Not feasible during HFNO, standard helmet NIV
ΔP_{ES}	Esophageal balloon catheter	> 15 cmH_2O and/or reduction < 10 cmH_2O during NIV	Needs some expertise
ROX	(SpO_2/FiO_2)/Respiratory Rate	< 2.85 at 2 h of HFNO initiation < 3.47 at 6 h of HFNO initiation < 3.85 at 12 h of HFNO initiation	Validated only for HFNO
HACOR scale[a]	Heart rate, acidosis, consciousness, oxygenation and respiratory rate[a]	> 5 at 1 h of NIV initiation	Intermittent, time consuming, validated only for NIV

PBW predicted body weight, *NIV* noninvasive ventilation, *HFNO* high-flow nasal oxygen, *DeltaPes* inspiratory effort

[a] The HACOR score is calculated as the sum of the scores for each individual variable, assigned as follows. Heart rate: ≤ 120 beats/min = 0, ≥ 121 beats/min = 1; pH: ≥ 7.35 = 0, 7.30–7.34 = 2, 7.25–7.29 = 3, < 7.25 = 4; Glasgow Coma Scale score: 15 = 0, 13–14 = 2, 11–12 = 5, ≤ 10 = 10; PaO_2/FiO_2 ratio: ≥ 201 mmHg = 0, 176–200 mmHg = 2, 151–175 mmHg = 3, 126–150 mmHg = 4, 101–125 mmHg = 5, ≤ 100 mmHg = 6; Respiratory rate: ≤ 30 breaths/min = 0, 31–35 breaths/min = 1, 36–40 breaths/min = 2, 41–45 breaths/min = 3, ≥ 46 = 4

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CONFERENCE REPORTS AND EXPERT PANEL

The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline

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Hypoxemic respiratory failure

(moderate certainty)

Strong recommendation

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Review

Noninvasive ventilation improves the outcome in patients with pneumonia-associated respiratory failure: Systematic review and meta-analysis

Istvan Ruzsics[a], Peter Matrai[b], Peter Hegyi[c,d,e], David Nemeth[c], Judit Tenk[c], Alexandra Csenkey[c], Balint Eross[c], Gabor Varga[f], Marta Balasko[c], Erika Petervari[c], Gabor Veres[g,1], Robert Sepp[h], Zoltan Rakonczay Jr[i], Aron Vincze[j], Andras Garami[c,*], Zoltan Rumbus[c,*]

Background: Noninvasive ventilation (NIV) is beneficial in exacerbations of chronic obstructive pulmonary disease (COPD), but its effectiveness in pneumonia-associated respiratory failure is still controversial. In the current meta-analysis, we aimed to investigate whether the use of NIV before intubation in pneumonia improves the mortality and intubation rates of respiratory failure as compared to no use of NIV in adults.

Conclusion

In conclusion, with meta-analysis of published RCTs, we show that the use of NIV is associated with a significant reduction of intubation rate in patients with pneumonia-associated respiratory failure, and this effect seems to be prominent in patients with pre-existing COPD. Our meta-analysis also demonstrates lower ICU mortality and seemingly, but not significantly reduced ($P = 0.085$) overall mortality with the use of NIV. Considering the relatively small number of the included studies, firm conclusions should not be drawn from this meta-analysis. Our findings clearly indicate the need for further RCTs to determine the exact patient population and clinical preconditions that can benefit the most from the use of NIV treatment.

La vita si vive nell'incertezza,
per quanto ci si sforzi del contrario.
Ogni decisione è condannata
a essere arbitraria; nessuna sarà
esente da rischi e assicurata contro
insuccesso e rimpianti tardivi.
Per ogni argomento a favore di una
scelta si trova un argomento
contrario non meno pesante.

- Zygmunt Bauman -


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