doi: 10.4081/monaldi.2025.3231

SUPPLEMENTARY MATERIAL

Non-invasive ventilation in COVID-19-related acute hypoxemic respiratory failure: a narrative review

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Key words: COVID-19, respiratory function, non-invasive ventilation.

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Supplementary Table 1. A schematic and comparative table of clinical algorithms and guidelines cited.

Aspect	**Weerakkody et al. [26]**	**SIMEU [27]**	**COVID-19 Guidelines Panel**	**Prediletto & Marra [49,50]**	**Scala et al. [48]**
Study Type	Meta-analysis (2 RCTs + 83 observational studies)	Clinical position statement	Expert consensus guideline	Observational studies	Clinical algorithm recommendation for ARF management
Main NIRS Modalities Evaluated	HFNC, CPAP, BiPAP	HFNC, CPAP, NIPPV	HFNC, NIV, Mechanical Ventilation	STP/F, S/F ratio	HFNC, CPAP, NIV
Initial Oxygen Therapy Criteria	Start with standard O_2 therapy	SpO_2 < 94%; FiO_2 titrated per range	SpO_2 < 92%	SpO_2 < 92%	Start COT if SpO_2 < 92%; reevaluate within 4 hrs
Escalation Criteria for NIRS	Increased WOB, ↓ PaO_2/FiO_2, ↓ ROX index	SpO_2 < 92% after NRB 15 L/min or P/F 200–300	RR > 30, P/F < 300	P/F < 300 or SpO_2 < 93%	P/F < 300 and/or RR > 30 → HFNC; P/F < 200 → CPAP; P/F < 100 or RR > 30 w/ distress → NIV
Preferred NIRS Modalities Based on Condition	BiPAP if hypercapnic; CPAP/HFNC otherwise	HFNC preferred before NIV; NIPPV in COPD/acidosis	HFNC first-line; NIV if HFNC fails	S/F or STP/F used to stratify severity	HFNC (30–60 L/min); CPAP (PEEP ≥10); NIV (PEEP 12–16 + PS to get Vt 4–6 ml/kg/PBW)
Monitoring Parameters	Flowchart guided, clinical signs	ABG, FiO_2, Vt, SpO_2, RR	Hourly ABG, RR, SpO_2, FiO_2	S/F ratio, STP/F ratio, lab and radiologic biomarkers	Reassess: HFNC every 2, 6, 12 hrs; CPAP/NIV hourly
Failure Indicators	Hypoxemia, poor response	Vt > 9 ml/kg PBW, P/F < 150, SpO_2 < 94%, RR > 25, intolerance	P/F < 150, SAPS II > 35, APACHE II > 17	Persistent low S/F, poor clinical trend	Worsening SpO_2 or ↑ $PaCO_2$, arrest, hemodynamic instability, NIRS intolerance → switch to invasive ventilation
HFNC vs. NIV Recommendations	HFNC + mask NIV ↓ intubation/mortality	HFNC before NIV; NIV in COPD or respiratory acidosis	HFNC preferred for initial therapy	HFNC for early ARF, S/F ≥ 200; STP/F used for mortality prediction	Use HFNC first if P/F > 200; CPAP if P/F 100–200; NIV if P/F < 100
Use of P/F and S/F Ratios	Not emphasized	S/F used for monitoring	Used in stratification	S/F correlates with severity; STP/F more physiologically accurate	P/F used for stepwise support; no S/F or STP/F specifically discussed
Role of STP/F Ratio	Not addressed	Not discussed	Not discussed	STP/F superior to P/F in mortality prediction	Not discussed

RCT, randomized controlled trial; ARF, acute respiratory failure; HFNC, high flow nasal cannula; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; NIPPV, noninvasive positive pressure ventilation; NIV, noninvasive venitlation; COT, continuous oxygen therapy; WOB, work of breathing; NRB, non-rebreather mask; RR, respiratory rate.

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Supplementary Table 2. Clinical trials of non-invasive ventilation in COVID-19-related acute respiratory failure.

PUBBLICATION	PATIENT POPULATION	TREATMENT	INTUBATION RATE	MORTALITY RATE
Bellani et al. [58], 2021	COVID-19 AHRF Median PaO2/FiO2 172 mmHg	NIV + CPAP n=798 215 [27%] patients with limitations of treatment Helmet was used for 617 patients, face mask for 248 Noninvasive respiratory support initiated 1 day after hospital admission PEEP was 10.8 cmH20, ranging from 2 to 20	Noninvasive respiratory support failure 38% [95% CI 34 to 41] in the overall cohort Noninvasive respiratory support failure 27% [23 to 30] in patients with no limitations of treatment cohort Noninvasive respiratory support failure 67% [61 to 73] in patients with limitations of treatment cohort	Overall mortality was 25% [95% CI 22 to 28]
Bertaina et al. [52], 2021	COVID-19 AHRF 51% of patients had SpO2<92% on room air	NIV n= 390	NIV failure 44% [95% CI 40 to 49] Received ETI 16% [95% CI 13 to 20]	Overall cohort 38% [95% CI 33 to 43] Among intubated patients 58% [95% CI 46 to 70%]
Burns et al. [62], 2020	COVID-19 AHRF SpO2<94% in Venturi Mask 40%	CPAP n=23 BIPAP n=5 BIPAP settings: max PEEP=10.2 cmH2O max Pinsp=22.4 cmH2O CPAP settings: Max PEEP=12.7 cmH2O	Not reported	BIPAP 40% [95% CI 12 to 77] CPAP 52% [33 to 71]
Duca et al. [53], 2020	COVID-19 AHRF CPAP Median PaO2/FiO2 131 mmHg NIV Median PaO2/FiO2 87 mmHg IMV at arrival Median PaO2/FiO2 76 mmHg	CPAP n=71 Helmet CPAP, PEEP=15cmH2O NIV n=7 NIV, PEEP=16 cmH2O IMV on arrival=7 IMV at arrival, PEEP=18 cmH2O	CPAP intubation rate 37% [95% CI 26 to 48] NIV intubation rate 0% [95% CI 0 to 35] CPAP failure 92% [95% CI 83 to 96] NIV failure 57% [95% CI 25 to 84	CPAP 76% [95% CI 65 to 84] NIV 57% [95% CI 25 to 84] IMV at arrival 100% [95% CI 65 to 100]
Faraone et al. [54], 2020	COVID-19 AHRF Median PaO2/FiO2 130 mmHg 25 [50%] patients had patients with	NIV n=25 CPAP n=25 Interface: full face or oronasal mask PEEP started at 5 cmH2O,	Patients with no limitations of treatment: 36% [95% CI 20 to 55] CPAP failure 44% [95% CI 27 to 63] NIV failure 68% [95% CI 48 to 83]	Patients with limitations of treatment 88% [95% CI 70 to 96] Patients with no limitations of treatment 12% [95%

	limitations of treatment	up to 12 cmH2O IPAP set at 15cmH2O, up to 20–25 cmH2O		CI 4 to 30]
Franco et al. [68], 2020	COVID-19 AHRF Median PaO/FiO2 138 mmHg	HFNO n=163 CPAP n=330 PEEP 10.2 cmH2O Helmet 149 [99%] Face mask 2 [1%] NIV n=177 PEEP 9.5 cmH2O Pressure Support 17.3 cmH2O Helmet 15 Face mask 57	Recieved IMV: HFNO 29% [95% CI 24 to 36] CPAP 25% [95% CI 20 to 30] NIV 28% [95% CI 22 to 35] HFNO Failure 38% [CI 31 to 47] CPAP Failure 47% [95% CI 42 to 53] NIV Failure 53% [95% CI 46 to 60]	30-day mortality: HFNO 16% [95% CI 11 to 22] CPAP 30% [95% CI 26 to 35] NIV 31% [95% CI 24 to 38]
Fu et al. [46], 2021	COVID-19 AHRF NIV as initial therapy Median PaO2/FiO2 174.4 mmHg NIV as rescue therapy Median PaO2/ FiO2 179.27 mmHg	NIV as initial therapy N=22 NIV as rescue therapy N=17 PEEP in NIV success: 6 PEEP in NIV failure: 6 Pressure Support in NIV success: 7 Pressure Support in NIV failure: 6	NIV as initial therapy 23% [95% CI 10 to 43] NIV as rescue therapy 65% [95% CI 41 to 83]	NIV initial therapy 5% [95% CI 8 to 22] NIV as rescue therapy 12% [95% CI 3 to 34]
Grieco et al. [78], 2021	COVID-19 AHRF NIV PaO2/FiO2 105 mmHg HFNO PaO2/FiO2 102 mmhg	Helmet NIV n=54 Continuous treatment PEEP 12 cmH2O Pressure Support 10 cmH2O HFNO n=55	Helmet NIV 30% [95% CI 19 to 43] HFNO 51% [95% CI 38 to 64]	HFNO 25% [16 to 38] Helmet NIV 24% [95% CI 15 to 37]
Hua et al. [55], 2020	COVID-19 AHRF	SOT n=204 IMV n=113 NIV n=152	Not reported	SOT 6% [95% CI 4 to 11] IMV 92% [95% CI 86 to 96] NIV 41% [95% CI 33 to 49]
Liu et al. [76], 2021	COVID-19 AHRF	HFNO n=366 NIV n=286	HFNO 56% [95% CI 51 to 61] NIV 74% 95% CI [68 to 78]	HFNO 49% [95% CI 44 to 54] NIV 62% [95% CI 56 to 67]

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Menzella et al. [56], 2021	COVID-19 AHRF Median PaO2/FiO2 120.1 mmHg	NIV n=79 PEEP: 9.46 cmH2O IPAP: 17.7 cmH2O	ETI rate after the exclusion of patients with limitations of treatment and 2 sudden deaths 36% [95% CI 25 to 48] NIV failure in the overall cohort 52% [95% CI 41 to 63]	Mortality in the 20 intubated patients were 43% [95% CI 25 to 63] 18 [23%] patients had patients with limitations of treatment 2 [3%] patients died of sudden death
Mukhtar et al. [77], 2020	COVID-19 AHRF	NIV n=39	Need for ETI 23% [13 to 38] NIV failure 31% [95% CI 19 to 46]	26% [15 to 41]
Rose´n et al. [89], 2021	COVID-19 AHRF Standard care n=39 PaO2/FiO2 standard care 115 mmHg] Prone n=36 PaO2/FiO2 prone 115 mmHg	HFNO standard care n=29 HFNO prone n=31 NIV standard care n=27 PEEP 8 cmH20 NIV prone n=21 PEEP 7 cmH20	Standard care group 33% [95% CI 20 to 49] Prone group 33% [95% CI 20 to 50]	Control group 8% [95% CI 3 to 20] Prone group 17% [95% CI 8 to 22]
Sivaloganathan et al. [79], 2020	COVID-19 AHRF Worst PaO2/FiO2 ratio: NIV only: 127.5 mmHg NIV + MV: 104.26 mmHg IMV only: 115 mmHg NIV – limitations of treatment: 75 mmHg	NIV only n=31 NIV + MV n=27 IMV only n=21 NIV–limitations of treatment n=24	Patients with no limitations of treatment: 47% [95% CI 34 to 59]	Patients with no limitations of treatment: 5% [95% CI 2 to 14] Patients with limitations of treatment: 83% [95% CI 64 to 93]
Vianello et al. [74], 2020	COVID-19 AHRF Median PaO2/FiO2 108 mmHg	HFNO n=28 Rescue NIV n=9	HFNO failure 32% [95% CI 18 to 51] Rescue NIV failure 56% [95% CI 27 to 81] ETI 18% [95% CI 8 to 36]	11% [95% CI 4 to 27]
Wang et al. [59], 2020	COVID-19 AHRF Median PaO2/FiO2 209 mmHg in success patients Median PaO2/FiO2 142 mmHg in failure patients	HFNO n=17 only IMV n=1 first line NIV n=9 rescue NIV n=7	HFNO failure and rescue NIV 41% [95% CI 22 to 64] HFNO 12% [95% CI 3 to 34] First line NIV failure 11% [2 to 42] Rescue NIV failure 29% [8 to 64]	Not reported
Wendel Garcia et al.	COVID-19 AHRF	SOT n=87	SOT 64% [95% CI 53 to 63]	SOT 18% [95% CI 11 to

[75], 2021	Median PaO2/FiO2 123 mmHg	HFNO n=87 NIV n=87 MV n=92	HFNO 52% [95% CI 41 to 62] NIV 49% [95% CI 39 to 60]	27] HFNO 20% [95% CI 13 to 29] NIV 37% [27 to 47

AHRF, acute hypoxemic respiratory failure; NIV, non-invasive ventilation; CPAP, continuous positive airway pressure.

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