



## Editorial

## Non Invasive Respiratory Support Therapies in COVID-19 Related Acute Respiratory Failure: Looking at the Neglected Issues



### Las terapias respiratorias no invasivas en la insuficiencia respiratoria aguda asociada a COVID-19: analizando los problemas desatendidos

According with data from ISARIC, 20% of patients with COVID-19 require an admission to intensive care unit (ICU) or high dependency unit (HDU),<sup>1</sup> whereas about 29% of them received one of noninvasive respiratory support therapies (NIRT) such as continuous positive airway pressure (CPAP), bi-level noninvasive ventilation (BL-NIV) or high-flow nasal cannula (HFNC).<sup>1</sup>

Reviewing the recent publications specifically addressing the application of NIRT in COVID-19 related acute respiratory failure (ARF) we found 21 publications including 1553 patients.<sup>2–23</sup> The only important outcome always reported in all papers is the success rate in avoiding endotracheal intubation (ETI), achieved, on average, in 60%, 55% and 59% with, respectively, HFNC, CPAP and BL-NIV. Moreover, employed protocols, methodology and data collected in the published studies are extremely heterogeneous.

To be able to better interpret the prognostic impact of NIRT during current COVID-19 pandemic, more data are needed. Collecting a full set of parameters and clinical details is highly needed (Panel).

**Pulmonary and non pulmonary physiology:** Severity of lung ( $\text{PaO}_2/\text{FiO}_2$  ratio) and pump failure (pH) are strong predictors of NIRT success.

$\text{PaO}_2/\text{FiO}_2$  ratios were only described in 15 studies,<sup>2,4,6–8,10,11,13,15,16,21–23</sup> ranging from an average of 118 (minimum 103, maximum 153) in CPAP studies and 105 (minimum 69, maximum 186) in HFNC studies. Data on pH and  $\text{PaCO}_2$  are lacking in the majorities of the studies.

**Door to mask time:** timely delivery of NIRT is a critical goal. Average Door to mask time was 1.7 days and was only described in 3 papers.<sup>15,18,23</sup>

**Dedicated NIRT environment:** NIRT should be carried out in specially designated settings such as Respiratory Intermediate Care Units.

From the analyzed studies, only 2 did not describe the dedicated area<sup>14,18</sup>; in 8, the interventions were carried out in wards,<sup>3,8,10,12,15,18,19,23</sup> 4 in Respiratory Intermediate Care Units,<sup>2,4,11,24</sup> 3 in ICU's,<sup>7,9,22</sup> 3 in a mixed setting (ICU, Wards and Emergency Department)<sup>5,16,20</sup> and one at the Emergency Department.<sup>21</sup> Only one series reported using negative pressure rooms.<sup>8</sup>

**Mask-on time:** cumulative actual NIRT use should be stated. Average Mask on time was 5.9 days, described in 9 of the 13 CPAP studies,<sup>3,5,7,8,10,12,13,19,23</sup> and 4.6 days in the 5 of 8 HFNC studies.<sup>14,16–18,22</sup>

Time of NIRT to intubation was stated in <sup>7,5,8,10,13,16,18,23</sup> studies, ranging from 4 h<sup>8</sup> to 4 days.<sup>23</sup>

**NIRT Equipment:** type of ventilators and interfaces should clearly reported. Helmet CPAP mainly using a flow generator was applied in 8 studies,<sup>4,7,9,13,19–21,23</sup> while Oro-nasal mask CPAP was used in 6 studies.<sup>3,5,8,10–12</sup> In 4 studies portable home ventilators were used<sup>3,8,11,12</sup> in 3 advanced NIV-ventilators,<sup>4,10,21</sup> while in 2 ICU ventilators.<sup>5,17</sup>

**Escalation plan:** In three HFNC studies,<sup>5,15,16</sup> escalation plan did not include NIV or CPAP. Studies included a mean of 22.3% of patients with do-not-intubate orders (ranging from 0,<sup>3,8,9</sup> to 100%<sup>12</sup>).

**NIRT rotation:** sequential application of HFNC and Bi-NIV sessions may improve tolerance and efficacy on oxygenation. Therapies rotation was only described in 4 studies,<sup>4,9,12,20</sup> basically HFNC during CPAP/NIV intervals,<sup>4,9,20</sup> for feeding<sup>20</sup> and sleep,<sup>9</sup> and night-time CPAP after NIV weaning.<sup>12</sup>

**NIRT complementary therapies:** NIRT outcome may be improved with pronation and analgo-sedation.

Four studies included awake proning sessions.<sup>4,5,16,23</sup> There was no mention of sedation in any reports.

**Causes of mortality** need to be stated but they were not reported in any of the studies.

### Conclusion

In conclusion, even if NIRT have been shown to be effective tools in preventing ETI in COVID-19 acute respiratory failure, further studies designed to address important neglected issues are needed to better tailor each treatment for each individual case performed by each individual team; management should not be altered on the basis of expert opinion only! It is essential that researchers performing observational studies include relevant indicators like the ones we pointed out even during pandemics.

## References

- Hall M, Pritchard M, Dankwa EA, Baillie JK, Carson G, Citarella BW, et al. ISARIC Clinical Data Report 20 November 2020; 2020.
- Vianello A, Arcaro G, Molena B, Turato C, Sukthi A, Guarnieri G, et al. High-flow nasal cannula oxygen therapy to treat patients with hypoxemic acute respiratory failure consequent to SARS-CoV-2 infection. *Thorax*. 2020;75:998–1000.
- Oranger M, Gonzalez-Bermejo J, Dacosta-Noble P, Llontop C, Guerder A, Trosini-Desert V, et al. Continuous positive airway pressure to avoid intubation in SARS-CoV-2 pneumonia: a two-period retrospective case-control study. *Eur Respir J*. 2020. <http://dx.doi.org/10.1183/13993003.01692-2020>.
- Franco C, Facciolo N, Tonelli R, Dongilli R, Vianello A, Pisani L, et al. Feasibility and clinical impact of out-of-ICU noninvasive respiratory support in patients with COVID-19-related pneumonia. *Eur Respir J*. 2020;56.
- Alviset S, Riller Q, Aboab J, Dilworth K, Billy PA, Lombardi Y, et al. Continuous Positive Airway Pressure (CPAP) face-mask ventilation is an easy and cheap option to manage a massive influx of patients presenting acute respiratory failure during the SARS-CoV-2 outbreak: a retrospective cohort study. *PLOS ONE*. 2020;15:e0240645.
- Ma X, Yin F, Zhang J, Peng H, Guan H, Gong P. Risk factors associated with failure of high-flow nasal cannula oxygen therapy in patients with severe COVID-19 in Wuhan, China; 2020. <https://assets.researchsquare.com/files/rs-41316/v1/6386e958-e597-4be4-b6f2-32ada8a5eb38pdf>.
- Pagano A, Porta G, Bosso G, Allegorico E, Serra C, Dello Vicario F, et al. Non-invasive CPAP in mild and moderate ARDS secondary to SARS-CoV-2. *Respir Physiol Neurobiol*. 2020;280:103489.
- Nightingale R, Nwosu N, Kutubudin F, Fletcher T, Lewis J, Frost F, et al. Is continuous positive airway pressure (CPAP) a new standard of care for type 1 respiratory failure in COVID-19 patients? A retrospective observational study of a dedicated COVID-19 CPAP service. *BMJ Open Respir Res*. 2020;7.
- Gaulton TG, Bellani G, Foti G, Frazer MJ, Fuchs BD, Cereda M. Early clinical experience in using helmet continuous positive airway pressure and high-flow nasal cannula in overweight and obese patients with acute hypoxemic respiratory failure from coronavirus disease 2019. *Crit Care Explor*. 2020;2:e0216.
- Faraone A, Beltrame C, Crociani A, Carrai P, Lovicu E, Filetti S, et al. Effectiveness and safety of noninvasive positive pressure ventilation in the treatment of COVID-19-associated acute hypoxemic respiratory failure: a single center, non-ICU setting experience. *Intern Emerg Med*. 2020. Published on line 22 Nov.
- Noeman-Ahmed Y, Gokaraju S, Powrie DJ, Amran DA, El Sayed I, Roshdy A. Predictors of CPAP outcome in hospitalized COVID-19 patients. *Respirology*. 2020;25:1316–9.
- Burns GP, Lane ND, Tedd HM, Deutsch E, Douglas F, West SD, et al. Improved survival following ward-based non-invasive pressure support for severe hypoxia in a cohort of frail patients with COVID-19: retrospective analysis from a UK teaching hospital. *BMJ Open Respir Res*. 2020;7.
- Aliberti S, Radovanovic D, Billi F, Sotgiu G, Costanzo M, Pilocane T, et al. Helmet CPAP treatment in patients with COVID-19 pneumonia: a multicentre cohort study. *Eur Respir J*. 2020;56.
- Patel M, Gangemi A, Marron R, Chowdhury J, Yousef I, Zheng M, et al. Retrospective analysis of high flow nasal therapy in COVID-19-related moderate-to-severe hypoxaemic respiratory failure. *BMJ Open Respir Res*. 2020;7.
- Guy T, Creac'hcadec A, Ricordel C, Sale A, Arnouat B, Bizec JL, et al. High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. *Eur Respir J*. 2020;56.
- Calligaro GL, Lalla U, Audley G, Gina P, Miller MG, Mendelson M, et al. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: a multi-centre prospective observational study. *EClinicalMedicine*. 2020;100570.
- Wang K, Zhao W, Li J, Shu W, Duan J. The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China. *Ann Intensive Care*. 2020;10:37.
- Xia J, Zhang Y, Ni L, Chen L, Zhou C, Gao C, et al. High-flow nasal oxygen in coronavirus disease 2019 patients with acute hypoxemic respiratory failure: a multicenter, retrospective cohort study. *Crit Care Med*. 2020;48:e1079–86.
- Brusasco C, Corradi F, Di Domenico A, Raggi F, Timossi G, Santori G, et al. Continuous positive airway pressure in Covid-19 patients with moderate-to-severe respiratory failure. *Eur Respir J*. 2020. Published online 8 Oct.
- Di Domenico SL, Coen D, Bergamaschi M, Albertini V, Ghezzi L, Cazzaniga MM, et al. Clinical characteristics and respiratory support of 310 COVID-19 patients, diagnosed at the emergency room: a single-center retrospective study. *Intern Emerg Med*. 2020. Published online 11 Nov:1–10.
- Duca A, Memaj I, Zanardi F, Preti C, Alesi A, Della Bella L, et al. Severity of respiratory failure and outcome of patients needing a ventilatory support in the Emergency Department during Italian novel coronavirus SARS-CoV2 outbreak: preliminary data on the role of Helmet CPAP and Non-Invasive Positive Pressure Ventilation. *EClinicalMedicine*. 2020;24:100419.
- Demoule A, Vieillard Baron A, Darmon M, Beurton A, Geri G, Voiriot G, et al. High-flow nasal cannula in critically ill patients with severe COVID-19. *Am J Respir Crit Care Med*. 2020;202:1039–42.
- Coppadoro A, Benini A, Fruscio R, Verga L, Mazzola P, Carbone M, et al. Helmet CPAP to treat hypoxic pneumonia outside the ICU: an observational study during the COVID19 outbreak. *ResearchSquare pre-print*. 2020.
- Aliberti S, Amati F, Pappalettera M, Di Pasquale M, D'Adda A, Mantero M, et al. COVID-19 multidisciplinary high dependency unit: the Milan model. *Respir Res*. 2020;21:260.

João Carlos Winck<sup>a,\*</sup>, Raffaele Scala<sup>b</sup>

<sup>a</sup> Faculty of Medicine, Porto University, Portugal

<sup>b</sup> Pulmonology and Respiratory Intensive Care Unit, S Donato Hospital, Arezzo, Italy

\* Corresponding author.

E-mail address: jcwinc@mail.telepac.pt (J.C. Winck).