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REVIEW

The RICU during the COVID Pandemic

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ABSTRACT

The respiratory intermediate care unit (RICU) is logistically a «step up» or «step down» unit between the intensive care unit (ICU) and general hospitalization. It is efficiency in terms of «avoided cost». During the pandemic, RICU increased exponentially with the aim of avoiding ICU congestion with coronavirus disease 2019 (COVID-19) patients. These units must be attended by a multidisciplinary professional team with presence and assistance 24 hours a day and must be prepared with adequate monitoring for a quick scale in case of deterioration. The high flow nasal cannula (HFNC) increases ventilator-free days and reduces hospital stays. Awake prone position significantly reduced the incidence of treatment failure. Conscious sedation is used to increase the tolerance to non-invasive ventilation (NIV). In the treatment with HFNC, obesity, immunosuppression and elevated inflammatory markers were associated with a higher failure rate. With everything learned so far, there should be no hospital without RICU.

Keywords: RICU. COVID-19. NIRS. Awake prone. Conscious sedation.

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic that caused coronavirus disease 2019 (COVID-19) began in Wuhan, China, and became a global pandemic on March 11, 2020[1]. COVID-19 has spread rapidly throughout the world despite the significant efforts (quarantine, social distancing) made to try to contain it[2]. Globally, by 19 August 2022, there have been 591.683.619 confirmed cases of COVID-19, including 6.443.306 deaths, reported to WHO[3].

Until the advent of mass vaccination worldwide[4], one-third of hospitalized patients developed acute respiratory distress syndrome (ARDS) requiring advanced respiratory treatment[5].

Large differences in outcomes and respiratory disease management have been reported for different countries as pandemics evolved – e.g., the mortality of these patients in China is two times higher than those in Europe[6]. Independently, worldwide healthcare systems and workers have faced surges of infected patients who need hospital care; COVID-19 forced hospitals to review their care strategies, team management, and logistics organization.

In many hospitals, before the pandemic, there were monitoring beds for respiratory patients, such as patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) requiring non-invasive ventilation (NIV), or with neuromuscular diseases where NIV was started, also in terms of early discharges from intensive care units (ICU), for weaning or tracheostomy decannulation. However, only a few hospitals had specific NIV units, known as respiratory intermediate care units (RICU). The RICU is logistically a "step up" or "step down" unit between the ICU and general hospitalization, also admitting patients from the emergency department[7] (Fig. 1). This unit allows easy and dynamic management of patients, rapid development of treatment algorithms and implementation of new care protocols[8,9]. Additionally, RICU promotes earlier discharge of some ICU patients, is an alternative to ICU for patients who only require intensive monitoring, specific support, or procedures[10,11], and significantly reduces ICU mortality in hospitals with RICU compared to hospitals without RICU[12]. The implantation of the RICU is not yet universal in our environment and there are still many patients who, without needing it, must receive care in the ICU due to the lack of a highly complex RICU, with the consequent increase in care costs and limitation in the use of the adequate resources in each case. The study conducted by Heili et al[10], which analyzes the costs of an RICU to determine the annual cost associated with its complexity and its potential efficiency in terms of "avoided cost", showed that a cost of 500.000 $/year can be avoided by reducing days of stay in the ICU. The development of RICU is possible because the ratios of nurses, doctors and physiotherapists per patient are higher than those in general wards.

Recently, some studies reported positive results on non-invasive respiratory strategies (NIRS) in patients with COVID-19 in RICU[13-15]. During the pandemic, RICU increased exponentially with the aim of avoiding ICU congestion. This was a major challenge as NIRS treatments were initiated in severe and very severe patients outside the ICU as there were no ICU beds available[16-17]. Belgium faced a considerable challenge, as it was one of the most severely affected countries during the first waves of the pandemic,

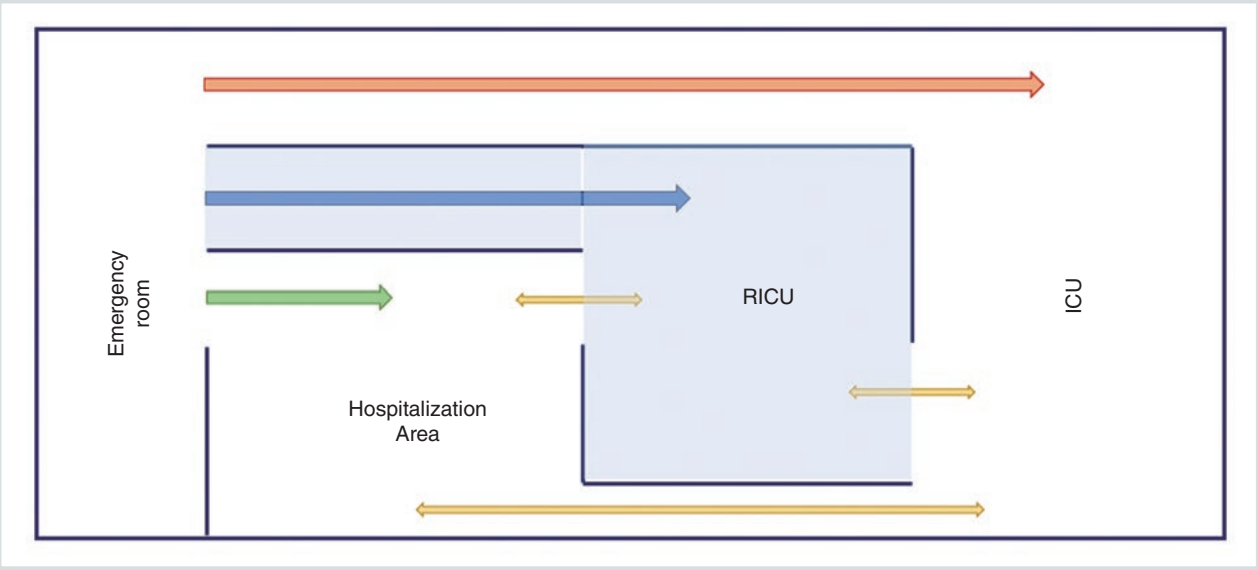

Figure 1. Example of the versatility of an RICU, where patients can access directly from the emergency room, hospitalization floor as a step up, and they can enter from ICU units as a step down.
ICU: intensive care unit; RICU: respiratory intermediate care unit.

with overcrowded hospitals and the highest mortality rate per capita in the world[18].

Before the COVID-19 pandemic, there were no exact recommendations in favor of the use of NIRS in hypoxemic failure, associated with pulmonary infectious processes of viral origin (SARS, Middle East Respiratory Syndrome [MERS]), but, after the experience accumulated since 2020, it has been seen that these techniques can be considered an option for managing and avoiding invasive mechanical ventilation (IMV) in many cases. In most studies with hypoxemic patients, it was found that high flow oxygen therapy (HFNC) is a clear alternative to conventional oxygen therapy, with a decrease in mortality[17]. Multiple studies have shown that after the need for NIRS in patients with hypoxemic failure with COVID-19 outside the ICU, it was feasible[18,19], and with positive results[17,19,20].

Between 5-10% of patients with SARS-CoV-2 (COVID-19) infection develop severe acute respiratory failure, which in most cases presents with hypoxemia and in more severe cases, with the development of ARDS. In these patients, orotracheal intubation (OTI) can condition an increase in mortality, reaching up to 50% according to some series. In a meta-analysis where more than 50.000 patients were included, with data from the first wave of the pandemic, between March and May, it was concluded that OTI could be avoided in a high percentage of cases, using various respiratory support strategies, such as HFNC, NIV, and continuous positive airway pressure (CPAP)[21].

According to these data, non-invasive techniques could avoid IMV in up to 70% of patients with COVID-19. In addition to being well tolerated, these procedures have presented an acceptable level of failure, defined as

death, or requiring IMV, which ranges between 20% and 30%.

Efficacy of NIRS, specifically CPAP, of up to 83% in avoiding OTI-IMV has been described[17]. In clinical trials, this efficacy is around 65-70%: 66.6% with CPAP[22]; 65.7% with HNFC[23]; 70% with CPAP (HENIVOT)[24]. In other observational studies, an efficacy of NIRS in avoiding OTI-IMV of around 40% is described: 37% with CPAP[18]; 40% with CPAP[25].

The essential criteria, based on expert consensus, collected by the Spanish (Cinesi et al.)[26] and the European (Chalmers et al.)[27] pneumology societies for escalation from conventional oxygen therapy (COT) to NIRS in hypoxemic acute respiratory failure secondary to COVID-19 pneumonia is the need for a fraction of inspired oxygen (FiO_2) ≥ 0.40 (conventional nasal cannula flow ≥ 5 liters/min, simple mask at flow ≥ 5 liters/min, Venturi mask at FiO_2 ≥ 0 .40 and flow ≥ 12 liters/min, reservoir mask at a flow of 10 to > 15 liters/min) to maintain oxygen saturation (SpO_2) ≥ 92%[26], or SpO_2 ≥ 9 4%[27].

The objective of this document is to report on what has been learned during the COVID-19 pandemic in the NIRS in RICU, in terms of structure, organization models, the different non-invasive treatments, progression scores or poor prognosis and mortality.

INFECTION PREVENTION RECOMMENDATIONS FOR HEALTHCARE WORKERS

The application of NIV techniques entails an increased risk of contagion for health professionals since, during the performance of these procedures, a dispersion of aerosols from the patient's air can occur, which may contain viruses[28]. They are aerosol-generating procedures with the potential to transmit infection, so health personnel must take extreme precautions[29].

The measures that are recommended to minimize this risk are, the placement of viral and bacterial filters in the appropriate places, in case of using NIRS, covering the patient's face with a surgical mask, and being careful when handling the ventilatory systems at the time of depressurization during disconnection, at which time high flows of gas containing high concentrations of viral particles can be generated[30].

With these measures, the World Health Organization (WHO) states that, when used by adequately trained personnel, they do not increase the dispersion of infectious particles, so they should not be associated with an increase in airborne transmission of the disease[31].

ADMISSION CRITERIA TO RICU

Clinical[22,26,27]:

- Moderate-severe dyspnea with work of breathing and use of accessory muscles or paradoxical abdominal movement.
- Tachypnea greater than 24 rpm.
- Absence of multi-organ failure (APACHE < 20).

Gasometers[22,26,27]:

- Partial pressure of arterial oxygen (PaO_2)/ FiO_2 < 200 (or the need to administer an FiO_2 > 0.4 to achieve an SpO_2 > 92%).

- Acute ventilatory failure (pH < 7.35 with partial pressure of arterial carbon dioxide ($PaCO_2$) > 45 mm Hg).

INFRASTRUCTURE

There has been discussion after the pandemic about what could be the best distribution in an RICU. There are two clearly defined models: the open RICU, where there is a direct view of all patients by the nursing staff, or the closed RICU (ideally with negative pressure)[32] where patients are monitored by telemetry and camera. The first has the advantage of continuous vision or proximity for speed of action, but the second has the advantage of providing greater privacy and allows the possibility of infectious isolation. With all this, probably the best alternative is a mixed arrangement with open beds facing the nursing control and at least two closed rooms for isolation. Additionally, we are currently in a situation in which the COVID-19 contagion pattern has been defined by airborne transmission, and its incidence is falling, so it is very difficult for hospitals to have two units available (COVID and not COVID), with which the mixed infrastructure could be the best option so that both pathologies can coexist without risk of contagion (Fig. 2).

These units must be prepared with adequate monitoring for a quick scale in case of deterioration[33]. Monitoring should include non-invasive methods that allow continuous assessment of respiratory and cardiac function and frequent assessment of vital signs, with the primary goal of early detection of NIV failure[34].

STAFF

These units must be attended by a multidisciplinary professional team. The direction must be exercised by medical specialized in pulmonology. Likewise, there must be a person who exercises coordination or nursing supervision[35].

The necessary medical staff is one physician for every six patients and the nursing staff of each shift must be one person for a maximum of four patients, with presence and assistance in the RICU 24 hours a day.

In the RICU the medical staff does not need to be in the unit 24 hours a day, but the shift must be in person at the hospital. In general, care in the afternoon and at night could be integrated into the pulmonology shifts.

Physiotherapy staff. The recommended ratio is one person for every six beds, ideally in morning and afternoon shifts. It is also necessary to have auxiliary nursing staff and health assistants, especially for the mobilization and changes of the position of patients.

NON-INVASIVE RESPIRATORY SUPPORT TREATMENTS

In the pre-COVID-19 era, HFNC was shown to be superior to COT in avoiding OTI, but without improving mortality in patients with ARDS[21]. In the COVID-19 era, HFNC has been widely used with favorable results in observational studies, with an average success rate of 60%[11,36-39], and its use has also been recommended by some guidelines during the pandemic[26,27,40]. Failure rates appear to be lower

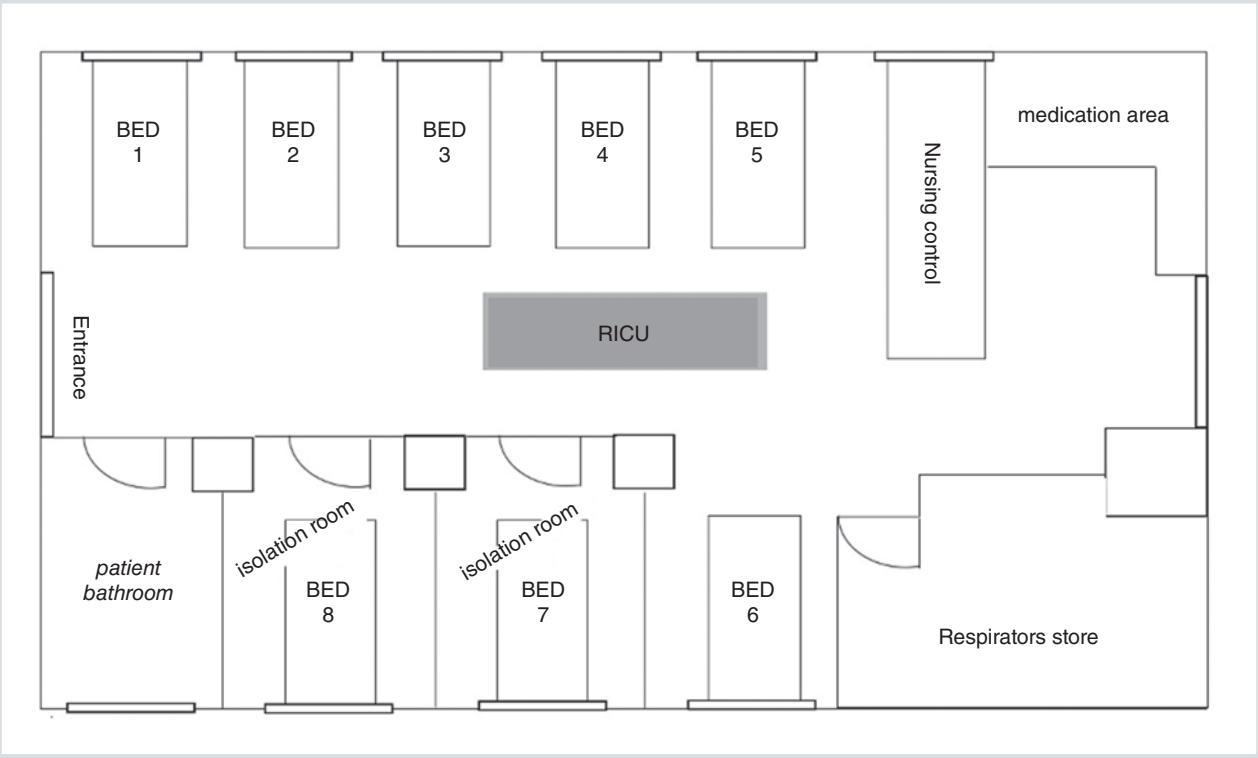

Figure 2. Example of a mixed model respiratory intermediate care unit.

in patients with PaO_2/FiO_2 > 200 compared with those with PaO_2/FiO_2 ≤ 200[27].

NIV delivered with a mask or 'helmet' was superior to COT for patients with ARDS in the pre-COVID-19 era[21] and has been used widely during the pandemic, but also irregularly in centers, probably depending on the implementation of this therapy or the existence of RICU[16,18,41,42]. In a pre-COVID-19 study, helmet-delivered NIV was superior to mask-delivered NIV, likely due to more continuous use[43] and fewer air leaks[44], greater comfort, and increased more "protective" ventilation. During the current COVID-19 pandemic, a significant number of studies have used helmet CPAP[13,17,45-48] and have shown high success rates. A randomized controlled trial (RCT) failed to demonstrate a significant difference in the number of days without ventilation support within 28 days between helmet NIV and HFNC in patients with PaO_2/FiO_2 ≤ 200, although the rate of OTI was significantly lower in the helmet NIV group[49]. In addition, contrary to what was believed at the beginning of the pandemic, the use of HFNC at ICU admission in adult patients with ARDS related to COVID-19 led to an increase in ventilator-free days and a reduction in the duration of hospital stay[50].

According to some proposed algorithms, COT may be the first step for patients with fractional inspired oxygen (FiO_2) requirements

that are not very high (i.e., 21% to 40%) to achieve adequate oxygenation and respiratory rate (RR) goals (SpO_2 of 93% – 96%) and RR < 30)[51]. For higher patient FiO_2 requirements (FiO_2 > 0.4) and RR, HFNC or higher NIV/CPAP may be required. In the absence of RCTs in patients with COVID-19 pneumonia, some suggestions can be made on an individual basis.

Sometimes patients with COVID-19 and severe hypoxemia have great difficulty weaning from NIRS, secondary to desaturations and increased work of breathing, which ultimately leads to rapid clinical worsening and is not without risk. Therefore, a point to consider with these measures is the possibility of combining the different therapies to obtain the specific benefits of each of them. In this group of patients with hypoxemia without hypercapnia, the combination of therapies (HFNC+ NIV/CPAP) could be an alternative to therapies alone.

COMPLEMENTARY TREATMENTS

Prone position awake

Based on pre-COVID and COVID-19 experiences, awake pronation in patients receiving NIRS may improve gas exchange and probably reduce the likelihood of deterioration and the need for OTI[52]. Several physiological mechanisms could explain the possible beneficial clinical effects of awake pronation during NIRS, such as a more homogeneous distribution of pleural pressure in the lung regions and less changes in transpulmonary pressure, better oxygenation through a reduction of ventilation-perfusion mismatch and alveolar shunting facilitated drainage of secretions through repositioning of the patient[53]. Despite this rationale and the positive findings from physiological studies, only a few RCTs addressing this issue have been published. In a recent large, randomized, controlled, multinational meta-trial of 1126 COVID-19 patients undergoing HFNC by acute hypoxemic respiratory failure (AHRF), awake prone position significantly reduced the incidence of treatment failure defined as the proportion of patients intubated or they died within 28 days of inclusion[54]. Several drawbacks must be considered for a successful application of prone positioning protocols in patients with COVID-19 admitted to the RICU; the compliance of non-sedated patients to maintain prolonged prone sessions, the additional work for nurses and therapists to facilitate the pronation procedure and improve treatment compliance, and the difficulties in maintaining adequate continuous monitoring of cardiopulmonary parameters and in treating emergent OTI are some of the main limitations. Very recently, it has been shown that the improvement in oxygen saturation obtained with the prone position during NIV was achieved at the expense of a worsening of the patient's comfort score and an increase in the fraction of diaphragmatic thickening[55].

Conscious sedation

Conscious sedation has had an exponential growth in its use in RICUs, especially after the multidisciplinary medical management of patients with NIRS during the pandemic. Its fundamental objective is to improve tolerance to NIRS, since rejection by the patient can lead to interruption and the need for OTI. Distress,

due to pain, fear/anxiety, dyspnea, or delirium is common among critically ill patients; distress may manifest clinically as agitation that is often associated with ventilator asynchrony and vital sign abnormalities[56]. Prior to the COVID pandemic, there were very few studies dealing with awake sedation of patients with NIV to improve their adherence to treatment. This is probably because sedation has not been perceived as a major problem or opportunity within the broader context of NIV use or has not been systematically studied[57]. A general aspect of poor tolerance to NIV could be related to the patient-device interface. The choice of interface can influence the need for sedation. Patient acceptance is greater with less restrictive interfaces, such as the helmet, and is less well tolerated as facial pressure increases (total-face, oronasal...). Regarding ventilation modes, Bi-level Positive Airway Pressure (BiPAP) is more difficult to tolerate than CPAP, as it has different pressures in inspiration and expiration, compared to CPAP, but both can generate anxiety and require sedation to improve tolerance. On the contrary, the HFNC is usually better tolerated without requiring sedation for its use[58,59]. Patient acceptance and compliance with NIV are essential to its success. Achieving patient acceptance and compliance is a multidisciplinary exercise (nursing, medicine…), in which the expertise and competence of staff are one of the main influences[60]. The use of sedation in NIV is aimed at preventing NIV failure and is based on the clinical management of discomfort, anxiety, agitation, pain, dyspnea, delirium, and the patient's disappointed expectations. A nonpharmacologic attempt to calm the patient should always be made before administering sedatives. In patients under NIV, sedation should be closely monitored to watch for signs of NIV failure. Sedation in NIV patients, if used appropriately, improves comfort and reduces the possibility of NIV failure. There are no preferences for any drug to date[61]. The goal of NIV sedation is to keep the patient comfortable with minimal sedation. We would establish a start of sedation in patients with Richmond agitation and sedation scale (RASS) 1 or + to reach RASS –2 or 0[62].

Are there evidence-based reasons to prefer specific sedative drugs during NIV?

There is no strong data favoring any one drug, drug class, or protocol over all others. Given the pathophysiology of NIV failure, at least three aspects could be influenced by the choice of sedative drugs: upper airway patency, respiratory depression, and the affective dimension of dyspnea. The most common drugs for sedation in NIV, Propofol, midazolam, opioids, dexmedetomidine and ketamine were compared, without finding that any of them was better than the others in all areas of sedation, so at the present time the decision to the use of each of them must be based fundamentally on the experience of the professional who cares for the patient[63]. Dexmedetomidine must be commented on, since it has been one of the most used sedatives in Spain for the management of COVID patients who have required NIV. Dexmedetomidine is a highly selective, centrally acting alpha-2 agonist with anxiolytic, sedative, and some analgesic effects. According to the US Food and Drug Administration (FDA)-approved product information, dexmedetomidine is indicated for initial sedation of mechanically ventilated patients for up to 24 hours. The rationale for the 24-hour limit is that prolonged use may increase the

risk of withdrawal effects (e.g., hypertension). One of the most important details of this drug is that it does not present respiratory depression[64]. A meta-analysis of seven studies with a total of 1624 patients reported a mean reduction in the duration of mechanical ventilation by 22% and in hospital stay by 14%. However, the quality of the evidence ranged from low to very low, which limits the interpretation of the analysis. All seven studies included medical and surgical patients and patients at low to moderate risk of mortality[65].

Another study looked at the effect of early sedation with dexmedetomidine compared to usual care. It was associated with lower 90-day mortality compared with usual care in patients > 65 years of age (OR 0.83 [95% interval 0.68-1.00], with a 97.7% probability of reduced mortality in disease severity categories. In contrast, the probability of increased mortality in patients ≤ 65 years was 98.5% (OR 1.26 [95% interval 1.02-1.56], i.e., early sedation with dexmedetomidine exhibited a high probability of reduced mortality at 90 days in older patients, whereas a high probability of increased mortality at 90 days was observed in younger patients[66].

POOR PROGNOSIS SCORES

Several factors have been associated with the failure of noninvasive respiratory therapy in patients with COVID-19 pneumonia. In the case of treatment with HFNC, obesity, immunosuppression and elevated inflammatory markers were associated with a higher failure rate[67]. Additionally, comorbidities such as hypertension and chronic kidney disease as well as bacterial co-infections may predict worse treatment outcomes[68].

The development of failure predictor scores has improved the identification of patients at risk of noninvasive therapy failure, ultimately reducing the delay of orotracheal intubation in nonresponders.

In this regard, the Heart rate, Acidosis, Consciousness, Oxygenation, and Respiratory rate (HACOR) score is an easy and useful tool that can serve as a rapid approach for predicting HFNC failure measured at the first hour of initiation of the therapy. Results around 5.5-6 present good diagnostic accuracy of patients who had a higher risk of intubation and hospital mortality[69].

The ROX index (pulse oximetry/fraction of inspired oxygen/respiratory rate), another useful scale in assessing the efficacy of HFNC, has been widely used in COVID-19 pneumonia. Chandel et al.[70] demonstrated that a ROX index > 3.0 at 2, 6 and 12 hours after initiating HFNC therapy had a sensitivity of 85.3% for identifying that HFNC therapy was being successful. However, Vega et al.[71] established a cut-off point of 5.99 in the ROX index as the most suitable (sensitivity = 62%; specificity = 96%; p = 0.0008) for assessing the response to HFNC therapy at 12 h. In view of the difficulty in establishing a standard cut-off point, maybe the measurement of the evolutionary curve in the ROX index over the first hours after initiation of HFNC therapy, can offer a closer approximation to the effectiveness of HFNC.

The HACOR score has proven useful in the treatment with CPAP or NIV. In the case of CPAP, a value > 5 within one hour of initiating

treatment predicts failure of CPAP with 82.03% accuracy in SARS-CoV-2 pneumonia, although its effectiveness is very similar to that demonstrated by the PaO_2/FiO_2 ratio (81.25%)[72].

In the Randomized evaluation of COVID-19 therapy–respiratory support (RECOVERY-RS) clinical trial, Perkins et al.[22] reported a CPAP failure rate of 36.3%. Although assessing risk factors for CPAP failure was not raised as a primary or secondary objective, age (> 50 years), symptom days before initiating therapy (< 7 days) and obesity (body mass index [BMI] > 35) could be associated with a higher failure rate, although studies focused on answering these questions are needed.

MORTALITY/THERAPEUTIC LIMIT

There are scarce data regarding mortality in subjects with severe COVID-19, particularly in the RICU. Mortality varies widely among published series, ranging from 8 to 30%[11,14]. In observational studies, the mortality was associated with male sex, older age, leukocytosis, high lactate dehydrogenase level, cardiac injury, hyperglycemia, and high-dose corticosteroid at admission.

In a cohort of patients admitted to the RICU of a monographic hospital[83] mortality risk was associated with older age, a shorter time from symptom onset to RICU admission, lower PaO_2/FIO_2 and ROX index, and higher lactate dehydrogenase levels.

Special mention should be made of patients with do-not-intubation order, where NIRS is established as the therapeutic ceiling. These subjects tend to be older and presented with more comorbidity and sequential organ failure assessment (SOFA) and Simplified acute physiology score II (SAPS II) higher than other patients. It is not surprising that they have a higher mortality rate, which can reach as high as 54%[73]. In this regard, it is important to establish the objectives and feasibility of the treatment to prioritize the comfort.

CONCLUSIONS

1. If a hospital does not have an RICU, patients with acute respiratory failure may be cared for in an environment that is not adequately calibrated for their disease, either in terms of undercare (for example, ward) or overcare at a high cost greater than what is really needed (for example, ICU). Also, at discharge, some patients who do not require an ICU stay may be transferred to an environment that, again, is not good enough to handle them (e.g., ward) or may remain in an environment (ICU) too long that provides more care, and higher cost, than is needed.

2. It has been shown that ill acute hypoxemic COVID-19 patients can be successfully managed outside the ICU using non-invasive modalities; Until now, most RICUs have cared for very low-risk hypercapnic or hypoxemic patients.

With everything learned so far, there should be no hospital without RICU.

FUNDING

None to declare.

CONFLICT OF INTEREST

None to declare.

ETHICAL DISCLOSURES

This work has been carried out under a rigorous bibliographic search, and with the aim of helping health managers who want to improve the care of their patients through an RICU.

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