Ventilation

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Contents

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Learning Objectives

In this chapter the reader will learn the physiological effects and the commonly accepted indications for noninvasive respiratory support (high flow nasal cannulae [HFNC], noninvasive mechanical ventilation [NIMV]) and invasive mechanical ventilation (IMV), with special consideration to the elderly patient, whenever there is specific information in the literature regarding this age group.

Practical Implications

HFNC are increasingly used for the treatment of acute hypoxemic respiratory failure (AHRF), acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and other conditions associated with risk of hypoxemia.

Unlike standard oxygen therapy (SOT), HFNC provide a higher airflow rate, higher fraction of inspired oxygen (FiO_2), and effectively heated and humidified air.

Physiological effects include provision of some level of positive end expiratory pressure, improved oxygenation, reduced anatomical dead space, better patient comfort, and less dryness.

When compared to SOT, HFNC decreases the need for intubation and escalation of respiratory support in AHRF.

Patients with AHRF being treated with HFNC should be closely monitored to identify signs of failure and the need for intubation. There are studies supporting the use of the ROX index ($[SpO_2/FiO_2]$/RR) to predict the likelihood of intubation in patients requiring HFNC.

NIMV is used for the treatment of AECOPD. In elderly patients it has been shown that NIMV, as compared to standard medical treatment, is associated with a significant decrease in the proportion of patients meeting criteria for tracheal intubation.

NIMV is also used for the treatment of acute cardiogenic pulmonary edema (ACPE) where, as compared to SOT, it is associated with a reduction in hospital mortality, intubation rate and ICU length of stay, and a quicker symptomatic improvement and better tolerance.

In AHRF, NIMV reduces the intubation rate and hospital mortality, as compared to SOT.

In ARDS, success rates of NIMV in mild, moderate, and severe ARDS are 78%, 58%, and 53%, respectively, according to the LUNG SAFE study. The use of NIMV was in that study independently associated with increased ICU (but not hospital) mortality. Using propensity score, ICU mortality was greater in the NIMV versus the IMV group only in patients with PaO_2/FiO_2 ratio <150. Thus, consideration should be given to the high mortality rate of patients with ARDS failing treatment with NIMV, and to the association between the initial use of NIMV and mortality in ARDS, at least for patients with more impaired oxygenation (e.g., PaO_2/FiO_2 < 150). The conclusions of the LUNG SAFE study may partly pertain to the elderly, as median age was between 66 and 63 years.

18.1 Introduction

Different forms of respiratory support can be used to treat oxygenation and ventilation failure of the lungs. We will discuss here the role of HFNC, NIMV, and IMV for the treatment of acute respiratory failure (ARF) in the elderly. We will also address ventilation issues in patients with AHRF and COVID-19 pertaining to elderly patients. Most of the published literature does not deal directly with elderly patients, but often a large proportion of patients included in the different studies are >65 years of age, and conclusions can to some extent be applied to the treatment of the elderly patient population.

18.2 High Flow Nasal Cannulae

HFNC are increasingly used for the treatment of AHRF and AECOPD and prevention of post-extubation respiratory failure, preintubation oxygenation, sleep apnea, acute heart failure, and hypoxemia in the context of do-not-intubate (DNI) orders [1].

Unlike standard oxygen therapy (SOT), HFNC provide a higher airflow rate, higher fraction of inspired oxygen (FiO2), and effectively heated and humidified air.

Physiological effects include provision of some level of positive end expiratory pressure (PEEP), improved oxygenation, reduced anatomical dead space, better patient comfort, and less dryness [2–4]. Due to the higher airflow rate delivered, the FiO2 provided is more predictable than with SOT [5–7]. As a result of providing high FiO2 and low level of PEEP, oxygenation increases with HFNC [4, 7–15]. HFNC also increases tidal volume (Vt) and decreases respiratory rate (RR) [11], thus decreasing the work of breathing.

18.3 HFNC in AHRF

A number of studies have shown that HFNC improves oxygenation and enhances patient comfort, but whether its use attains other benefits as compared to SOT or NIMV is less clear. The outcome benefits of treatment with HFNC have been analyzed in different meta-analysis.

Nedel et al. evaluated nine studies that assessed HFNC in critically ill subjects with AHRF or at risk for this complication [16]. They found that HFNC was associated with nonsignificant reduction in the incidence of IMV compared with NIMV (odds ratio [OR] 0.83, 95% confidence interval [CI] 0.57–1.20) or SOT (OR 0.49, 95% CI 0.22–1.08), nor was it associated with reduction in ICU mortality compared with NIMV (OR 0.72, 95% CI 0.23–2.21) or with SOT (OR 0.69, 95% CI 0.33–1.42). There was a trend toward better oxygenation compared with SOT but a worse gas exchange compared with NIMV.

Another meta-analysis of randomized controlled trials that compared HFNC and SOT or nasal continuous positive airway pressure (nCPAP) in children with acute lower respiratory infection reported treatment failure as an outcome [17]. HFNC significantly reduced treatment failure (risk ratio [RR] 0.49, 95% CI 0.40–0.60) in children with mild hypoxemia (arterial pulse oximetry [SpO_2] >90% on room air), but in infants of 1–6 months of age with severe hypoxemia (SpO_2 < 90% on room air or SpO_2 > 90% on supplemental oxygen), HFNC was associated with an increased risk of treatment failure compared with nCPAP (risk ratio [RR] 1.77, 95% CI 1.17–2.67). No significant differences were found in intubation rates or mortality between HFNC and SOT or nCPAP. HFNC had a significantly lower risk of nasal trauma compared with nCPAP (RR 0.35, 95% CI 0.16–0.77).

In a more recent meta-analysis, Lewis et al. [18] included 51 studies in which treatment was initiated either after extubation or before mechanical ventilation in adults admitted to the ICU. The authors concluded that HFNC, versus SOT, may lead to less treatment failure (low-certainty evidence) but probably with little or no difference in mortality (moderate-certainty evidence). HFNC versus NIMV found no evidence of a difference in treatment failure, either being used post-extubation or before IMV (low-certainty evidence), nor was it associated with difference in in-hospital mortality (low-certainty evidence).

Thus, HFNC has been shown to enhance patient comfort and improve oxygenation, and may lead to less treatment failure when compared to SOT, but probably makes little or no difference when compared to NIMV, conclusions supported in general by low or very low certainty. There is not enough evidence to support the use of HFNC to achieve other benefits such as decrease in mortality or decrease in intubation rates.

The recommendation based on the available evidence is that HFNC is preferred to SOT for the treatment of AHRF [18]. When compared to SOT, HFNC decreases the need for intubation and escalation of respiratory support. It also has a greater improvement in oxygenation, but it provides no benefit in mortality, length of stay, dyspnea, or patient comfort [19–24]. There is not enough data to compare HFNC with NIMV for treatment of AHRF [18]. Patient comfort is greater with HFNC, but there is not enough evidence to support a benefit in other outcomes such as intubation rate, mortality, or length of stay [25, 26].

18.4 Other Indications for HFNC

HFNC is used for preoxygenation before and during intubation. However, studies have not shown consistent benefit in clinically relevant outcomes [27–30], and therefore practice guidelines give no recommendation as to the use of HFNC for the intubation procedure [1].

HFNC is also used in post-extubation respiratory failure. In patients at low risk for extubation failure, SOT often suffices to maintain oxygenation. One clinical trial showed reduction in re-intubation rate as compared to SOT [31], but no difference was reported in another study [32]. Thus, HFNC is not routinely recommended for the prevention of post-extubation respiratory failure in patients with low risk for re-intubation.

In patients at high risk for re-intubation, clinical trials show that HFNC is superior to SOT for the prevention of post-extubation respiratory failure [4, 33–36]. However, no differences are shown when HFNC is compared to NIMV [36–38]. Current guidelines thus indicate a conditional recommendation for the use of HFNC (versus SOT) in patients at high risk for re-intubation. NIMV should be used instead according to routine practice of the particular institution [1].

In the postoperative setting, HFNC can be used for the treatment or prevention of respiratory failure. Some patients, but not all, should receive HFNC in the postoperative period, such as obese and high-risk patients following cardiothoracic surgery [1, 11, 18, 32, 39–48].

Other common uses of HFNC include oxygenation during bronchoscopy, in patients with tracheostomy being weaned off the ventilator, and in combination with NIMV for oxygenation support.

18.5 Failure of HFNC in AHRF

Patients with AHRF being treated with HFNC should be closely monitored to identify signs of failure and the need for intubation. There are studies supporting the use of the ROX index to predict the likelihood of intubation in patients requiring HFNC [15]. The acronym ROX stands for respiratory rate and oxygenation. It is calculated as the ratio of (SpO_2/FiO_2) to respiratory rate (RR): ([SpO_2/FiO_2]/RR). The ROX index remains to be validated and is not currently routinely used to guide the clinical decision of intubation.

Roca et al. studied 157 patients with severe pneumonia treated with HFNC, of whom 44 (28.0%) required MV [49]. The ROX index measured at 12 hours after initiation of HFNC had the best accuracy (area under the receiver operating characteristic curve [AUC] 0.74) for the prediction of the need for MV, with the best cut-off value of 4.88. In a more recent multicenter prospective observational cohort study of patients with pneumonia treated with HFNC [50], among the 191 patients treated with HFNC in the validation cohort, 68 (35.6%) required intubation. The prediction accuracy of the ROX index increased over time. ROX index ≥4.88 measured at 2 (hazard ratio [HR] 0.434; 95% CI 0.264–0.715), 6 (HR 0.304; 95% CI 0.182–0.509), or 12 hours (HR 0.291; 95% CI 0.161–0.524) after HFNC initiation was consistently associated with a lower risk for intubation. ROX indices <2.85, < 3.47, and <3.85 at 2, 6, and 12 hours of HFNC initiation, respectively, were predictors of HFNC failure. Patients who failed presented a lower increase in the values of the ROX index over the 12 hours. Among the components of the index, SpO_2/FiO_2 was more predictive than RR. In a retrospective analysis of patients with COVID-19 pneumonia, the ROX index was tested in 120 patients receiving HFNC [51], of whom 35 patients (29%) failed HFNC and required intubation. ROX index at 12 h was the best predictor of intubation, with an AUC of 0.792 and a cut-off value of 5.99, with specificity 96% and sensitivity 62%. The ROX index has also been tested in other conditions. For instance, in 171 chest trauma patients receiving SOT, 49 (28.6%) of whom required endotracheal intubation, a threshold value of 12.85 (sensitivity 82, specificity 89) over the first 24 h predicted endotracheal intubation [52]. According to these data, the ROX index may be useful in assessing treatment failure in patients with different conditions, but different threshold values may be optimal in different conditions.

18.6 Development of NIMV

First used as the iron lung in the polio epidemics [53], NIMV later evolved when delivering intermittent positive pressure ventilation, and continuous positive airway pressure via a rubber face mask to treat different respiratory conditions became feasible [54, 55]. In 1981 Sullivan et al. described the successful use of continuous positive airway pressure (CPAP) via nasal mask in the management of obstructive sleep apnea [56] that was later used to treat respiratory failure from neuromuscular disease and nocturnal hypoventilation [57]. Subsequently, a Consensus Conference agreed on the role of NIMV in the management of patients with ARF [58–61]. NIMV is currently recommended for the treatment of various forms of ARF as detailed below. Specific indications for the elderly, when available, will be commented.

18.7 NIMV for the Treatment of AECOPD

AECOPD is one of the leading causes of hospitalizations. Pathophysiological changes during AECOPD include increased airflow resistance resulting in incomplete expiration, dynamic hyperinflation, and subsequent reduced diaphragm strength and respiratory muscle fatigue [62–64]. Reduced respiratory reserve in the elderly aggravates these physiological changes. NIMV is not the first line of treatment in AECOPD, but it is rather used in severe cases to prevent progression of the respiratory failure [65]. NIMV unloads the respiratory muscles and improves oxygenation and ventilation [25].

A trial of NIMV is recommended for AECOPD since it has shown a significant decrease in mortality, length of stay, intubation rate, and improvement in gas exchange [18, 59, 60, 66–76]. The recommended modality in this setting is bilevel positive airway pressure (BPAP). The benefit of BPAP in AECOPD extends from mild to severe COPD exacerbation and therefore should be used in all range of severities [69].

A national audit by Roberts et al. [77] of 10,000 COPD admissions showed that in patients with acidosis, mortality was higher if they received NIMV versus those who did not. However, this could be due to the late use of NIMV in patients already deteriorated or to the use of NIMV in cases of non-respiratory acidosis.

Whereas NIMV is recommended in the management of AECOPD, little evidence existed at the time of those recommendations [78, 79] to advocate its use in the elderly, and the guidelines had little evidence for the use of NIMV in the elderly with AECOPD [80].

Later studies proved the safety and efficacy of NIMV for the treatment of AECOPD in elderly patients. In a clinical trial on the treatment of AECOPD with NIMV, 82 patients aged >75 years [81] were randomized to receive NIMV or standard medical treatment (SMT). Treatment was associated with a significant decrease in the proportion of patients meeting criteria for tracheal intubation (7.3 versus 63.4%, in the treated and control groups, respectively), and a reduction in mortality rate (OR 0.40; 95% CI 0.19–0.83). Interestingly, 22 of 41 patients in the SMT group and DNI orders received NIMV as a rescue therapy. The mortality rate in this subgroup was comparable to the group receiving NIMV (OR 0.60, 95% CI 0.18–1.92), and significantly lower when compared with patients receiving intubation (OR 4.03,

95% CI 2.35–6.94). Balami et al. conducted a prospective study of 36 patients >65 years of age with AECOPD [82]. Mean age was 77.4 years. Only 2 patients (6%) could not be started on NIMV because of lack of tolerance, and treatment was successful in 27 of 34 patients treated (79%), whereas it did not succeed in 21%. Another indirect evidence that NIMV is effective in elderly patients is the finding that when patients ≥75 years of age are compared to younger patients, there are no differences in intubation or mortality rates [83], suggesting that NIMV is also safe and effective in the elderly population.

It is important to underline the clinical impact of a specialized NIMV team to optimize treatment success. A lower risk of death and intubation and a shorter ICU and hospital stay have been shown in patients treated with a dedicated NIMV team compared to management by ICU doctors and nurses working independently [84].

18.8 NIMV for the Treatment of Acute Cardiogenic Pulmonary Edema

Acute cardiogenic pulmonary edema (ACPE) is a leading cause of hospitalization for the elderly [85] and is associated with a high mortality rate. Reported in-hospital and 1-year mortality rates are 12% and 40%, respectively [86, 87]. In ACPE, the increase in extravascular lung fluid results in reduced lung volume and respiratory system compliance, increased airway resistance, and increased work of breathing. Noninvasive ventilation in ACPE prevents alveolar collapse, reduces alveolar edema, improves lung compliance [87], and decreases preload and afterload, thus reducing the work of breathing, increasing cardiac output, and improving oxygenation [65, 87, 88].

Systematic reviews and meta-analysis demonstrated a reduction in the rate of intubation and mortality in patients that received NIM [89]. Although a non-inferiority study questioned the role of NIMV in the management of ACPE, showing no difference in short-term mortality or need for intubation between the NIMV and standard therapy groups, several subsequent studies concluded that the use of NIMV in treating ACPE decreased the rate of intubation and in-hospital mortality [90–94]. However, results regarding mortality have not been entirely consistent between clinical trials [89, 90, 95–101].

There are few studies focused specifically on the elderly population, but given that the mean age of patients admitted for acute heart failure is greater than 70 years, many of the previous studies are thought to be applicable to this population. A study designed to investigate the clinical efficacy of NIMV in ACPE in patients greater than 75 years of age demonstrated early clinical improvement with a reduction in the rate of intubation and 48-hour mortality without sustained benefit during their hospital stay [101].

18.9 NIMV for the Treatment of AHRF

There is conflicting evidence about whether NIMV is beneficial to patients with AHRF not due to ACPE [102–110]. A prospective observational study on the use of NIMV in patients with AHRF reported a failure rate of 61% in patients with septic shock and 23% in patients without sepsis [111]. A meta-analysis of 11 studies (exclud-

ing patients with AECOPD or ACPE) showed that NIMV reduced the intubation rate (RR 0.59, 95% CI 0.44–0.79) and hospital mortality (RR 0.46; 95% CI 0.24–0.87) compared with SOT [109]. The wide confidence intervals reported suggest variable benefit among patients. A network meta-analysis studied 25 clinical trials comparing noninvasive treatments (NIMV or HFNC) with SOT in patients with AHRF [25]. Mortality was lower in patients treated with helmet or face mask NIMV compared with SOT. All three noninvasive modalities (helmet NIMV, face mask NIMV, HFNC) reduced intubation rates. High heterogeneity and risk of bias suggest caution when interpreting the results of this meta-analysis. In addition, a mortality benefit was not observed in patients with more severe impairment of oxygenation (PaO2/FiO2 < 200 mm Hg). In another meta-analysis of 29 randomized trials of mixed population of patients with AHRF comparing NIMV versus HFNC [112], it was found that HFNC resulted in lower mortality (RR 0.44, 95% CI 0.24–0.79), intubation rate (RR 0.71, 95% CI 0.53–0.95), and possibly hospital-acquired pneumonia (RR 0.46, 95% CI 0.15–1.45) and improved patient comfort.

The LUNG SAFE study provided important insights into the effects of treatment with NIMV in patients with ARDS [113]. Of 2813 patients with ARDS, 436 (15.5%) were managed with NIMV on days 1 and 2 following fulfillment of diagnostic criteria. The use of NIMV in moderate and severe forms of ARDS was surprising as the recommendations for NIMV in ARDS suggest that its use be restricted to mild ARDS [114]. However, success rates of NIMV in mild, moderate, and severe ARDS were not low (78%, 58%, and 53%, respectively). Hospital mortality in patients with NIMV success and failure was 16.1% and 45.4%, respectively. Importantly, the use of NIMV was independently associated with increased ICU (HR 1.446, 95% CI, 1.159–1.805), but not hospital, mortality. However, using propensity score, ICU mortality was greater in the NIMV versus the IMV group only in patients with PaO_2/FiO_2 ratio <150 (36.2% with NIMV compared with 24.7% with IMV). Thus, consideration should be given to the high mortality rate of patients with ARDS failing treatment with NIMV, and to the association between the initial use of NIMV and mortality in ARDS, at least for patients with more impaired oxygenation (e.g., $PaO2/FiO_2$ < 150). The conclusions of the LUNG SAFE study do not pertain necessarily to the elderly patient population. However the median (IQR) age of patients with NIMV success or failure was, respectively, 66.5 [52–77] and 63.0 [53–73] years, indicating that elderly patients were notably represented in this study.

In immunocompromised patients, NIMV is suggested as first option for treatment of patients with mild or moderate AHRF [115–117]. Several studies [118–122], but not all [123], have suggested improved mortality by using NIMV in these patients.

18.10 Noninvasive Mechanical Ventilation for Weaning from Mechanical Ventilation

Different clinical trials and a meta-analysis have shown that patients weaned with NIMV after extubation demonstrate reduced mortality, less ventilator-associated pneumonia, and shorter ICU and hospital stay, without increasing the risk of weaning failure or re-intubation [124–131].

In a Cochrane systematic review, 16 trials comparing extubation and immediate application of NIMV with continued invasive weaning in adults on mechanical ven-

tilation were studied, involving 994 participants, most of them with COPD [132]. The use of NIMV was associated with reduced mortality (RR 0.53, 95% CI 0.36–0.80), weaning failure (RR 0.63, 95% CI 0.42–0.96), ventilator-associated pneumonia (RR 0.25, 95% CI 0.15–0.43), length of stay in the ICU (mean difference [MD] −5.59 days, 95% CI −7.90 to −3.28) and in hospital (MD -6.04 days, 95% CI −9.22 to −2.87), and total duration of mechanical ventilation (MD −5.64 days, 95% CI −9.50 to −1.77). This indication for NIMV mainly applies to hypercapnic respiratory failure, and patients included in the studies are generally old. For instance, in the study by Ferrer et al. [126], mean age was 70 years.

18.11 NIMV for Post-extubation Support

NIMV can be used after extubation in patients at low risk for post-extubation respiratory failure. In this scenario, NIMV provides no benefit compared to SOT. In patients at high risk for post-extubation respiratory failure, some studies do not show reduction in re-intubation rate or mortality [133–136], whereas others suggest a decrease in the re-intubation rate [131, 132, 136–140].

18.12 NIMV in the Postoperative Setting

Changes in respiratory function in the postoperative period, including depressed respiratory drive, decreased Vt because of postoperative pain, recumbent atelectasis, etc., place the patient at increased risk of ARF. The elderly is at increased risk for these changes, as muscle function may already be deteriorated.

NIMV is not recommended in all postoperative patients for the prevention of ARF. The general indication of NIMV in the postoperative period is for the treatment of patients who develop AHRF and fail to respond to HFNC [141–143].

18.13 Invasive Mechanical Ventilation

ARDS represents a high proportion of patients receiving mechanical ventilation in the ICU. Among 29,144 ICU patients, 10.4% fulfilled the criteria for the diagnosis of ARDS, and ARDS represented 23.4% of patients requiring mechanical ventilation [144]. In line with those results [144], in a large prospective study, among 7944 patients requiring mechanical ventilation for >24 hours, 986 (12.3%) had hypoxemic respiratory failure ($PaO_2/FiO_2 < 300$), and 731 (9.1%) met criteria for ARDS [145].

Mortality of AHRF and ARDS is high. In the LUNG SAFE study, hospital mortality was 34.9%, 40.3%, and 46.1% for patients with mild, moderate, and severe ARDS, respectively [144]. Parhar et al. reported that hospital mortality for mild, moderate, and severe ARDS was, respectively, 26.5%, 31.8%, and 60.0%, whereas 3-year mortality was 43.5%, 46.9%, and 71.1% [145].

How ARDS is diagnosed and managed seems to be suboptimal. First, the syndrome is recognized only in part of the patients fulfilling the diagnostic criteria, ranging from 51.3% in mild to 79% in severe ARDS [144]. Second, modifiable mortality

risk factors related with mechanical ventilation settings are not always measured or set according to current recommendations. In 18,302 patients receiving mechanical ventilation for various indications [146], Vt decreased over time from a mean (SD) of 9.3 (2.3) to 8.2 (2.0) mL/kg predicted body weight between 2004 and 2010. However, in the more recent LUNG SAFE study [144], less than two-thirds of 2377 patients with ARDS received a tidal volume ≤8 mL/kg of predicted body weight. Plateau airway pressure was measured only in 40.1% of patients with ARDS, and prone positioning was used in 16.3% of patients with severe ARDS [144]. In addition, it has been shown that mechanical power is associated with increased 28-day hospital and 3-year mortality [145]. This finding is of importance, since modifiable determinants of mechanical power associated with lower survival include plateau pressure and driving pressure.

Description on how mechanical ventilation is used may apply to the elderly population only to some extent. For instance, in a large prospective study of 731 patients with ARDS [145], median (IQR) age was 60 (49–69) years; in 3022 ARDS patients [144], mean (95% CI) age was 61.5 (60.9–62.1). In another study of 18,302 patients [146], mean (SD) age was 59 (17), 59 (17), and 61 (17) years in three different study periods (1998, 2004, and 2010, respectively). However, it seems reasonable to assume that conclusions as to under recognition of ARDS and suboptimal treatment in terms of attaining low plateau and delta pressures, and low tidal volume, and using prone positioning as indicated, will also apply to the elderly patient population.

18.14 Invasive Versus Noninvasive Ventilation for Patients with COVID-19 and ARF

Clinical experience indicates that many patients can be supported with noninvasive oxygen therapy (either HFNC or NIMV) only to require tracheal intubation and IMV some time later in worse clinical conditions. Whether late intubation worsens prognosis is not known. Mortality of patients with COVID-19 and AHRF seems to be decreasing over time [147, 148], and it has been proposed that the decrease in mortality could be related to less frequency in the use of tracheal intubation as first therapy in patients with COVID-19 and AHRF. Other factors can certainly contribute to the decreased mortality, including routine use of corticosteroids, the use of HFNC, lung-protective ventilation strategies, better sedation, better attention to the treatment of delirium, and avoidance of unproven therapies [149].

In an ancillary analysis of the COVID-ICU study, Dres et al. [150] studied 1199 elderly patients admitted to the ICU, 62% of whom were intubated on day 1 and an additional 16% were intubated during their ICU stay. Those two groups did not differ in their PaO2/FiO2 ratio or other characteristics, suggesting that the decision to intubate was based just on clinical judgment. However, using Inverse Probability Weighting Treatment and propensity score analysis, mortality was higher in patients intubated on day 1 (42% versus 28%).

In a large multicenter cohort of 13,301 patients with the diagnosis of COVID-19 admitted to 126 ICUs in Brazil, younger age, absence of frailty, and the use of noninvasive respiratory support (NIRS) as first support strategy were independently associated with improved outcomes [151]. Among all patients, 18% received some form of NIRS (either NIMV, HFOT, or both), and 13% received IMV. However,

there was a time pattern from the first to the last period of time analyzed: some form of NIRS (NIMV or HFOT) increased from 8.3% to 25%, whereas only IMV decreased markedly from 25% to 6.5% of all patients. Among those patients receiving some form of NIRS, there were significant changes: only NIMV from 92% to 79%, only HFOT from 4.4% to 6%, and both NIVM and HFOT from 3.3% to 15.0%. Thus, patients were less often intubated to receive IMV, and among those not intubated, the use of only NIMV decreased, whereas the use of HFOT or a combination of NIMV and HFOT increased over time. In addition, patients who suffered failure of NIRS did not show a greater mortality in comparison to those intubated directly [151]. In conclusion, HFNC has been used during the COVID-19 outbreak [51, 152–154]. The use of first some form of NIRS, probably HFNC, rather than quickly deciding IMV in patients with COVID-19 and AHRF, does not seem to be unwarranted, even in elderly patients [150, 151].

If HFNC is chosen, close monitoring is required for the early identification of signs of failure that would indicate the requirement of IMV [152]. Roca et al. [49] identified patients at high risk of HFNC failure if ROX <4.88 at 12 hours. This threshold was confirmed also in COVID-19 patients [155, 156] who showed, however, higher intubation rates than in other studies [153, 154, 157]. Panadero et al. conducted a retrospective, observational single-center study of 196 patients with COVID-19 and bilateral pneumonia, 40 of whom were treated with HFNC [156]. The intubation rate at day 30 was 52.5%, and overall mortality was 22.5%. Patients that required intubation, as compared to patients who did not, presented a significantly lower PaO2/FiO2 (93.7 ± 6.7 vs. 113.4 ± 6.6) and a significantly lower ROX index (4.0 ± 1.0 vs. 5.0 ± 1.6). A ROX index <4.94 measured 2 to 6 h after the start of therapy was associated with increased risk of intubation (HR 4.03, 95% CI 1.18–13.7). In another study, Vega et al. [51] tested whether the ROX index is an accurate predictor of HFNC failure for COVID-19 patients treated outside the ICU. In a multicenter retrospective observational study, 120 patients with confirmed COVID-19 treated with HFNC were included, of whom 35 (29%) failed HFNC and required intubation. The 12-hour ROX index was the best predictor of intubation according to an area under the ROC curve of 0.792 (95% CI 0.691–0.893), with a threshold of 5.99 (specificity 96%, sensitivity 62%). Thus, the ROX index seems useful to predict failure of treatment with HFNC, although the best discriminative value differs from the previously reported for patients with other types of AHRF. Previous small single-center studies in patients with COVID-19, probably with greater disease severity, reported lower values for the ROX index (4.95 and 5.40) during the first 6 hours of treatment [155, 156].

18.15 Liberation from Mechanical Ventilation in the Elderly

Physiological and anatomical respiratory peculiarities in the elderly make the weaning process different as compared to younger adults. Different studies have investigated factors involved in weaning in patients ≥75 years of age. Decreased elastic recoil of the lung and the chest wall, ventilation-perfusion mismatch, and diminished muscle strength are among the age-related respiratory physiological changes in the elderly. Of interest, studies reviewing weaning in the elderly did not identify age in itself as an independent risk factor for difficult weaning, but severity of acute illness instead influences weaning [158–163].

It has been shown that the probability of meeting weaning criteria and successful weaning decreases with age [159], but independent predictors of weaning were comorbidity, severity of illness, rapid shallow breathing (the ratio between the respiratory frequency to the tidal volume), and lung static compliance, not age. Negative fluid balance and lower central venous pressure have also been shown to be related to weaning success [162].

In another study [163], after adjusting for the APACHE II score, patients ≥75 years of age passed a spontaneous breathing trial earlier than younger patients, further indicating that age in itself is not a risk factor for delayed extubation. Same results on the lack of independent relationship between age and weaning were obtained by Hifumi et al. [158] in a retrospective study in patients with community-acquired pneumonia. Another study [160] found that the presence of emphysematous changes in chest CT and low serum albumin concentration, but not age, were associated with difficult weaning.

A number of measures have been proposed to expedite weaning, including less use of benzodiazepines to decrease the risk of delirium [164, 165], and early rehabilitation and prevention of immobility [166]. Daily spontaneous breathing trial to test for readiness for extubation (one the inciting event has resolved) is crucial to shorten the time spent on mechanical ventilation [167]. Daily awakening trials have been associated with fewer days on mechanical ventilation, better cognitive function, and decreased long-term mortality [164, 165]. Cader et al. [161] studied 41 elderly intubated patients who had been mechanically ventilated for at least 48 h and showed that providing inspiratory muscle training resulted in increased maximal inspiratory pressure and reduction in the weaning time by 1.7 days. In addition, physical therapy and occupational therapy during spontaneous awakening trials to patients who had been intubated for more than 48 hours had beneficial effects and found decreased incidence of delirium and shortened time spent in mechanical ventilation [166, 168].

Conclusions

Recommendations for the use of various form of respiratory support (NIMV, HFNC, IMV) exist for different forms of ARF. However, studies in elderly patients are scarce and insufficient to emit recommendations for this specific age group. Patients included in studies on NIMV for the treatment of AECOPD and ACPE represent to some extent the aged group and could reasonably be extrapolated to the elderly. This is less the case for studies on the use of IMV for the treatment of AHRF and ARDS. Thus, studies on respiratory support for the elderly are required, particularly for the treatment of AHRF.

Take-Home Message

- Different forms of respiratory support (SOT, CPAP, HFNC, NIMV, IMV) are available to treat ARF of different etiologies.
- It is important to know the specific indications (and the supporting evidence) of these therapies in the various conditions associated with (or risk of) ARF.
- Early identification of signs of failure of any of these therapies is crucial for optimal patient management, to make timely decisions to escalate therapy. Failure to do so is associated with increased mortality.

- The elderly population is often underrepresented in clinical trials; thus the physiological peculiarities of the elderly patient should be considered when applying the results of clinical trials to the elderly.

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