Gabriela Ferreyra and V. Marco Ranieri

Noninvasive ventilation in hypoxemic respiratory insufficiency

Introduction

Since its introduction into clinical practice, noninvasive ventilation (NIV) has been a major advantage in the management of acute respiratory failure caused by chronic obstructive pulmonary disease (1, 2, 3) and sleep hypoventilation disorders (4).

In recent years, there has been an increase in this technique as a first-line ventilation modality in the acute care setting (5). However, although NIV has showed to be effective in acute respiratory failure, there is still a controversy over its benefits in hypoxemic respiratory failure.

Hypoxemic respiratory failure is defined as a condition in which the respiratory system fails in its gas exchange function of oxygenation, PaO_2/FIO_2 less than 200, respiratory rate greater than 35 breaths per minute and active contraction of the accessory muscles of respiration (6). Patients who develop hypoxemic respiratory failure, requiring endotracheal intubation and sedation, show a high rate of ventilator-associated pneumonia (6), prolonging mechanical ventilation with increased morbidity and mortality (7). Therefore, NIV has recently been proposed in patients with hypoxemic respiratory failure to avoid endotracheal intubation, decrease ICU and hospital length of stay and mortality through respiratory muscle unloading and gas exchange improvement.

Is NIV effective and safe in all forms of hypoxemic respiratory failure?

In patients with various forms of hypoxemic respiratory failure, the beneficial effects of NIV remain controversial. An international consensus conference held in 2001 analysed data on the use of NIV in patients with acute respiratory failure (8) from several studies. This expert analysis concluded that based on current data, the use of NIV does not consistently improve clinical outcomes in patients with hypoxemic respiratory failure, and therefore cannot be recommended at this time. Although some select patient populations may have benefits, the conference committee's main concern was that larger controlled studies are still required to determine the potential benefit and safety of using this type of ventilation and thereby avoiding endotracheal intubation during hypoxemic acute respiratory failure. Currently, five years after the original consensus conference analysis, two surveys have re-examined the use of NIV outside clinical trials and have confirmed that NIV success varies in different types of hypoxemic respiratory failure. Specifically, Schettino et al. (9) recorded data over one year examining the use of NIV in a standard medical care routine in the

ICU, emergency ward, and general medical-surgical units. More than 449 patients with acute respiratory failure were enrolled in this study; NIV prevented intubation in 62% of the patients and was correlated with improved survival. Examination of different pathologies found that NIV successfully prevented intubation in patients with cardiogenic pulmonary oedema (82%) and COPD exacerbation (76%). However, due to other causes, it was much less successful during hypoxemic respiratory failure, which had the lowest rate of prevented intubation (40%). Moreover, intubated patients in this category had a high mortality rate (64%). A more recent prospective survey evaluated the use of NIV over three weeks in 70 French intensive care units. Among patients receiving NIV, only 38% subsequently required endotracheal intubation, showing that NIV prevented ETI in 62% of patients, which is similar to previous result (9, 10, 11). However, NIV failure in hypoxemic patients was lower (54%) than in the former study (5).

Early studies in patients with hypoxemic respiratory failure from heterogeneous categories were promising (12, 13), although improvements in outcome were only observed when hypercapnia was present (14). Subsequently, the comparison of NIV and conventional ventilation in acute hypoxemic, not hypercapnic, respiratory failure due to various causes was studied in a randomised controlled trial. Only 31% of the NIV group needed intubation. More patients in the conventional group had serious complications. Nonetheless, mortality was not different in both groups (6). On the contrary, in a similar population treated with continuous positive airway pressure (CPAP), there were no improved outcomes in comparison with the patients in the oxygen group. Moreover, higher rates of adverse events were found in the CPAP group (15).

The application of NIV in patients with acute cardiogenic pulmonary oedema (ACPE) has showed beneficial effects in comparison with standard treatment (16–18). However, higher myocardial infarction rate was associated with noninvasive positive pressure ventilation (NPPV) in one of the studies (19). In contrast, most recently several studies have shown that neither continuous positive airway pressure (CPAP) nor NPPV had an effect on new myocardial infarction rates (9, 20, 21). Several meta-analyses and systematic reviews (20, 22–25) have been performed over the last few years to confirm the overall beneficial effect of NIV on clinical outcomes and to determine whether CPAP and NPPV is more advantageous in the treatment of respiratory failure due to ACPE. Overall, NIV was associated with a significant reduction in the need for invasive mechanical ventilation, and decreased mortality in comparison with standard therapy. However, although a trend towards less mortality was shown with NPPV alone, it did not result in a significant reduction, which was probably due to the low power related to the limited number of patients in the studies (20, 23).

The superior effect of NPPV in comparison with CPAP in patients with hypercapnic ACPE, through the investigation of its potential superiority due to respiratory muscle unloading, has been further analysed in the meta-analysis published by Winck et al. (20). The authors performed a subgroup analysis by dividing patients according to their $PaCO_2$ levels (below or above 50 mmHg), finding that NPPV again showed only a small trend towards a decreased mortality rate and a reduced need of ETI. However, because these results did not reach significance the authors conclude that there is no superiority of NPPV, even in the more severe hypercapnic ACPE patients ($PaCO_2$ above 50 mmHg).

To date, the extended literature suggests that both modes are safe and efficient ways to improve clinical outcomes in cardiogenic pulmonary oedema; although the simplicity of CPAP makes it the logical choice as a first-line technique. However, if the patient fails to improve or experiences accessory muscle overload, NPPV should be applied. Moreover, the literature suggests that in patients with cardiogenic pulmonary oedema it is both safe and effective to use NIV in the emergency ward (9, 26).

Other forms of hypoxemic respiratory failure

There is a significant debate concerning the precise indications for NIV in patients with hypoxemic respiratory failure not due to cardiogenic pulmonary oedema or chronic obstructive pulmonary disease (27).

In a recent meta-analysis, Keenan et al. evaluated the effect of NIV in patients with hypoxemic

respiratory failure of various causes. NIV was associated with a reduction of endotracheal intubation, ICU length of stay and mortality rate. Similar results were found in an interim analysis when patients with cardiogenic pulmonary oedema and COPD were excluded. Notwithstanding, because of the few studies and the heterogeneity found in the population analysed, strong conclusions could not be reached. The authors suggest that some selected populations such as patients with immunosuppression (28) or specific postoperative conditions (29, 30) had the best outcomes (27).

Several studies reported SAPS II > 31 or 32, PaO_2/FiO_2 < 175 to 200 as indicators of noninvasive ventilation failure (9, 11, 31, 32). Accordingly, patients with hypoxemic respiratory failure and SAPS II < 31 or 32, PaO_2/FiO_2 > 175 to 200, would be better candidates for successful NIV.

Is it safe and effective to use NIV in patients with ALI/ARDS and pneumonia?

Whether to use NIV in these patients has been a matter of debate. A recent physiologic study with acute respiratory distress syndrome (ARDS) patients demonstrated a reduction of muscle effort and improved oxygenation when noninvasive pressure support combined with positive end expiratory pressure was applied (33). Moreover, clinical improvements in patients with ARDS and pneumonia were reported with the use of NIV in earlier randomised and non-randomised studies (12, 34). One of the first cohort studies analysing NIV in patients with ALI/ARDS showed that 66 % of the patients could avoid intubation when NIV was used as a first intervention prior to endotracheal intubation (12). Furthermore, in selected patients with community-acquired pneumonia, NIV was associated with a reduction in intubation rate (34). However, most recently, Pneumonia and ARDS have been identified as independent risk factors for NIV failure. Intubation rates in patients with ARDS and community-acquired pneumonia were 51 % and 50 % respectively (31). Honrubia et al. found similar results in another RCT. Patients received either NPPV or conventional invasive ventilation. The intubation rate was lower in the NIV group, but no further benefits were confirmed. Despite a tendency towards reduction in mortality (23 % in the noninvasive group and 39 % in the conventional group), it did not reach significance. In addition, in a subgroup analysis all the patients with pneumonia failed NIV and 66 % died in the ICU (35). The poor outcome of patients with pneumonia is consistent with previous studies (11, 14, 36).

Despite these trials, different results have been observed in another study. Ferrer et al. conducted a randomised trial in patients with acute hypoxemic respiratory failure compared with oxygen therapy; NIV decreased the need for intubation, incidence of septic shock and ICU mortality. Interestingly, a separate analysis showed a significant reduction of the intubation rate in patients with pneumonia, which was not the case in patients with ARDS where NIV was associated with an increased risk of intubation (37).

In a recent multi-centre survey, the application of NIV as a first-line intervention was investigated in selected patients with early ARDS (32). The study was conducted over a period of 25 months and included 147 patients with sepsis as the primary cause of ARDS. The authors reported that 54 % of ARDS patients avoided intubation. Patients who required intubation had an ICU mortality of 53 %. However, the overall ICU mortality including patients with NIV success and failure was 28 %, lower than recently published literature about prediction of death in ARDS patients (38). This data is not consistent with other published studies (9). One important difference in this trial is that applied PEEP levels were higher (12 cmH_2O) than in the former study (5 cmH_2O). Predictive values of NIV failure were higher SAPS II, older age, and higher levels of ventilator pressure. The authors suggest that ARDS patients with SAPS II < 34 and a PaO_2/FiO_2 > 175 are likely to benefit from the use of NIV.

Immunocompromised patients

Hilbert et al. in a RCT comparing NIV with standard therapy in immunosuppressed patients with type 1 respiratory failure have shown a reduction not only in intubation rate but also in mortality. Fewer patients in the NIV group than in the standard treatment group required endotracheal intubation and had serious complications. Moreover, ICU and hospital mortality were lower in the treatment group (28).

Surgical patients

Several early studies on the use of NIV as CPAP or NPPV to prevent or treat hypoxemic respiratory failure in postoperative patients reported physiologic benefits in the first stage of hypoxemia (39–41). However, clinical outcomes were less clear. In recent years, randomised controlled trials have also reported improvement in clinical outcomes. CPAP, when used prophylactically after thoracoabdominal aneurysm repair was shown to reduce pulmonary complications and length of hospital stay (42). Similarly, Squadrone et al. evaluated the effectiveness of continuous positive airway pressure in patients with early hypoxemia after major abdominal surgery in comparison with oxygen and standard therapy. Pneumonia and intubation rate were lower in the CPAP group and a trend toward shorter ICU stay was reported. Three patients died in hospital among the group of patients who received oxygen alone, but none in the treatment group died (43).

NIV has also been applied to prevent hypoxemia after cardiac surgery, with improvement in lung function and oxygenation (40, 41). Pasquina et al. conducted a study comparing CPAP and NPPV. Less atelectasis were found in the NPPV group. However, the absence of a control group with standard therapy did not allow for a conclusion (44). To date, there is no data to support that NIV or CPAP improve clinical outcomes in cardiac surgery. On the contrary, in the postoperative setting of patients with hypoxemic respiratory failure after lung resection, comparing NIV with standard therapy, a reduction of intubation rate and mortality was reported in 50 % of the patients in the control group versus 20 % in the NIV group. The investigators recommended NIV to improve survival in such patients (30).

Comparable benefits were reported in a randomised controlled trial of NIV in comparison with standard therapy with oxygen administration in solid organ transplantation (29). There was a faster improvement in oxygenation and a reduction in intubation rate with NIV in comparison with standard therapy. However, mortality did not differ between groups.

Weaning and postextubation respiratory failure

NPPV as a weaning strategy

Weaning failure and reintubation are considered risk factors for higher pneumonia and mortality rates (7). Favourable impact has been described in several studies on the use of NIV as a mode of early extubation (45, 46).

Lately, in a heterogeneous population of patients, two RCTs have demonstrated beneficial effects of NIV compared to standard therapy in preventing respiratory failure after extubation in high-risk patients. There was a lower rate of intubation, and a trend to lower mortality when NIV was applied for at least 48 hours (47). In a similar study, comparing prophylactic NIV with conventional therapy for at least 24 hours, the authors reported a reduction of respiratory failure and lower ICU mortality in the treatment group (48). A recent meta-analysis evaluated the role of NIV in facilitating early extubation. NIV compared to invasive mechanical ventilation resulted in decreased ventilator-associated pneumonia, shorter hospital length of stay and less mortality; however, most of the studies included in the meta-analysis had a high percentage of COPD patients (49). Therefore, information about hypoxemic, not hypercapnic, patients remains less ambiguous.

The use of NIV when extubation failure is already established has been less clear over the years. Promising results of NIV on postextubation failure with the application of NIV were suggested at the international consensus conference (8). However, there was not enough evidence to recommend NIV in this population, suggesting the need for further studies. Recently, two randomised trials were conducted in this field. Keenan et al. published the first randomised controlled trial examining the use of NIV in comparison with standard therapy in a heterogeneous population of patients who developed acute respiratory failure after extubation. There was no difference in the rates of reintubation and hospital mortality for both groups. However, the criterion for reintubation was not hypoxemia but other clinical signs (50). Similar results were observed by Esteban et al. in a larger multi-centre randomised controlled trial evaluating NIV versus conventional therapy in postextubation respiratory failure. There was

no difference in reintubation rate in the control and NIV groups. Moreover, there no further benefit was found in the subgroup analysis of hypoxemic patients. In addition, patients who failed NIV and were reintubated had a higher mortality rate than the control group. What is of interest is that the time from the development of respiratory distress to the reintubation was higher in the NIV group (51).

Comments

Broad literature on the use of NIV in an acute setting has emerged over the last years in the fervour to avoid endotracheal intubation, ventilator-associated pneumonia and hospital mortality. NIV was shown to play an important role as an adjunctive therapy to standard treatment in many forms of acute respiratory failure. However, the question whether NIV is safe and efficient in an overall population of patients with hypoxemic respiratory failure remains unanswered.

The setting and how NIV is applied, as well as the heterogeneity of the population studied, may have influenced the effectiveness of noninvasive ventilation in different studies.

NIV as a ventilatory mode to prevent or treat early stages of hypoxemia in the postoperative abdominal period is supported by published articles and a meta-analysis.

Selected patient populations, such as immuno-compromised patients (28), and postoperative respiratory failure (29, 30) have shown clinical benefits.

The question of whether to use NIV in patients with ARDS and pneumonia remains unanswered. Although a recent survey reported that half of the treated patients with ARDS avoided endotracheal intubation, further studies are needed to confirm the benefit of NIV as a ventilatory mode in this challenging population of patients.

Recent data from everyday practice outside the clinical trials in one survey has shown that although well-trained respiratory staff was involved, a high percentage of patients with hypoxemic respiratory failure failed to improve clinical outcome and had a mortality rate when noninvasive ventilation was applied (9). This data is consistent with the statement of the consensus conference held in 2001 (8). Noninvasive ventilation, although attractive in the intensive care unit setting, cannot be recommended as a first-line therapy for an overall population with hypoxemic respiratory failure.

The authors

Gabriela Ferreyra
V. Marco Ranieri, MD, Prof.
Dipartimento di Anestesia e Rianimazione | Università di Torino | Ospedale S. Giovanni Battista-Molinette | Torino, Italy

Address for correspondence
V. Marco Ranieri
Università di Torino
Dipartimento di Anestesia e Rianimazione
Ospedale S. Giovanni Battista-Molinette
Corso Dogliotti 14
10126 Torino, Italy
e-mail: marco.ranieri@unito.it

References

1. Brochard L, Isabey D, Piquet J, Amaro P, Mancebo J, Messadi AA et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. N Engl J Med. 1990;323(22): 1523–30.
2. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. Lancet. 2000;355(9219):1931–5.
3. Keenan SP, Sinuff T, Cook DJ, Hill NS. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. Ann Intern Med. 2003;138(11):861–70.
4. Kerby GR, Mayer LS, Pingleton SK. Nocturnal positive pressure ventilation via nasal mask. Am Rev Respir Dis. 1987;135(3):738–40.
5. Demoule A, Girou E, Richard JC, Taille S, Brochard L. Increased use of noninvasive ventilation in French intensive care units. Intensive Care Med. 2006;32(11): 1747–55.
6. Antonelli M, Conti G, Rocco M, Bufi M, De Blasi RA, Vivino G et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med. 1998;339(7):429–35.
7. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest. 1997;112(1):186–92.
8. Evans TW. International Consensus Conferences in Intensive Care Medicine: non-invasive positive pressure ventilation in acute respiratory failure.Organised jointly

by the American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, and the Societe de Reanimation de Langue Francaise, and approved by the ATS Board of Directors, December 2000. Intensive Care Med. 2001; 27(1):166–78.
9. Schettino G, Altobelli N, Kacmarek RM. Noninvasive positive-pressure ventilation in acute respiratory failure outside clinical trials: experience at the Massachusetts General Hospital. Crit Care Med. 2008; 36(2):441–7.
10. Antro C, Merico F, Urbino R, Gai V. Non-invasive ventilation as a first-line treatment for acute respiratory failure: "real life" experience in the emergency department. Emerg Med J. 2005;22(11):772–7.
11. Demoule A, Girou E, Richard JC, Taille S, Brochard L. Benefits and risks of success or failure of noninvasive ventilation. Intensive Care Med. 2006;32(11):1756–65.
12. Rocker GM, Mackenzie MG, Williams B, Logan PM. Noninvasive positive pressure ventilation: successful outcome in patients with acute lung injury/ARDS. Chest. 1999;115(1):173–7.
13. Pennock BE, Crawshaw L, Kaplan PD. Noninvasive nasal mask ventilation for acute respiratory failure. Institution of a new therapeutic technology for routine use. Chest. 1994;105(2):441–4.
14. Wysocki M, Tric L, Wolff MA, Millet H, Herman B. Noninvasive pressure support ventilation in patients with acute respiratory failure. A randomized comparison with conventional therapy. Chest. 1995;107(3):761–8.
15. Delclaux C, L'Her E, Alberti C, Mancebo J, Abroug F, Conti G et al. Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: A randomized controlled trial. Jama. 2000;284(18):2352–60.
16. Masip J, Betbese AJ, Paez J, Vecilla F, Canizares R, Padro J et al. Non-invasive pressure support ventilation versus conventional oxygen therapy in acute cardiogenic pulmonary oedema: a randomised trial. Lancet. 2000; 356(9248):2126–32.
17. Nava S, Carbone G, DiBattista N, Bellone A, Baiardi P, Cosentini R et al. Noninvasive ventilation in cardiogenic pulmonary edema: a multicenter randomized trial. Am J Respir Crit Care Med. 2003;168(12):1432–7.
18. L'Her E, Duquesne F, Girou E, de Rosiere XD, Le Conte P, Renault S et al. Noninvasive continuous positive airway pressure in elderly cardiogenic pulmonary edema patients. Intensive Care Med. 2004;30(5):882–8.
19. Mehta S, Jay GD, Woolard RH, Hipona RA, Connolly EM, Cimini DM et al. Randomized, prospective trial of bilevel versus continuous positive airway pressure in acute pulmonary edema. Crit Care Med. 1997;25(4):620–8.
20. Winck JC, Azevedo LF, Costa-Pereira A, Antonelli M, Wyatt JC. Efficacy and safety of non-invasive ventilation in the treatment of acute cardiogenic pulmonary edema – a systematic review and meta-analysis. Crit Care. 2006; 10(2):R69.
21. Ferrari G, Olliveri F, De Filippi G, Milan A, Apra F, Boccuzzi A et al. Noninvasive positive airway pressure and risk of myocardial infarction in acute cardiogenic pulmonary edema: continuous positive airway pressure vs noninvasive positive pressure ventilation. Chest. 2007; 132(6):1804–9.
22. Masip J, Roque M, Sanchez B, Fernandez R, Subirana M, Exposito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. Jama. 2005;294(24):3124–30.
23. Peter JV, Moran JL, Phillips-Hughes J, Graham P, Bersten AD. Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis. Lancet. 2006; 367(9517):1155–63.
24. Ho KM, Wong K. A comparison of continuous and bi-level positive airway pressure non-invasive ventilation in patients with acute cardiogenic pulmonary oedema: a meta-analysis. Crit Care. 2006;10(2):R49.
25. Moritz F, Brousse B, Gellee B, Chajara A, L'Her E, Hellot MF et al. Continuous positive airway pressure versus bilevel noninvasive ventilation in acute cardiogenic pulmonary edema: a randomized multicenter trial. Ann Emerg Med. 2007;50(6):666–75, 675 e1.
26. Collins SP, Mielniczuk LM, Whittingham HA, Boseley ME, Schramm DR, Storrow AB. The use of noninvasive ventilation in emergency department patients with acute cardiogenic pulmonary edema: a systematic review. Ann Emerg Med. 2006;48(3):260–9, 269 e1–4.
27. Keenan SP, Sinuff T, Cook DJ, Hill NS. Does noninvasive positive pressure ventilation improve outcome in acute hypoxemic respiratory failure? A systematic review. Crit Care Med. 2004;32(12):2516–23.
28. Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. N Engl J Med. 2001; 344(7):481–7.
29. Antonelli M, Conti G, Bufi M, Costa MG, Lappa A, Rocco M et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. Jama. 2000;283(2): 235–41.
30. Auriant I, Jallot A, Herve P, Cerrina J, Le Roy Ladurie F, Fournier JL et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. Am J Respir Crit Care Med. 2001;164(7): 1231–5.
31. Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Med. 2001;27(11):1718–28.

32. Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med. 2007;35(1):18–25.
33. L'Her E, Deye N, Lellouche F, Taille S, Demoule A, Fraticelli A et al. Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med. 2005;172(9):1112–8.
34. Confalonieri M, Potena A, Carbone G, Porta RD, Tolley EA, Umberto Meduri G. Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. Am J Respir Crit Care Med. 1999;160 (5 Pt 1):1585–91.
35. Honrubia T, Garcia Lopez FJ, Franco N, Mas M, Guevara M, Daguerre M et al. Noninvasive vs conventional mechanical ventilation in acute respiratory failure: a multicenter, randomized controlled trial. Chest. 2005;128(6):3916–24.
36. Jolliet P, Abajo B, Pasquina P, Chevrolet JC. Non-invasive pressure support ventilation in severe community-acquired pneumonia. Intensive Care Med. 2001;27(5): 812–21.
37. Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, Torres A. Noninvasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. Am J Respir Crit Care Med. 2003;168(12):1438–44.
38. Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M et al. Incidence and outcomes of acute lung injury. N Engl J Med. 2005;353(16):1685–93.
39. Lindner KH, Lotz P, Ahnefeld FW. Continuous positive airway pressure effect on functional residual capacity, vital capacity and its subdivisions. Chest. 1987;92(1): 66–70.
40. Kindgen-Milles D, Buhl R, Loer SA, Muller E. Nasal CPAP therapy: effects of different CPAP levels on pressure transmission into the trachea and pulmonary oxygen transfer. Acta Anaesthesiol Scand. 2002;46(7):860–5.
41. Matte P, Jacquet L, Van Dyck M, Goenen M. Effects of conventional physiotherapy, continuous positive airway pressure and non-invasive ventilatory support with bilevel positive airway pressure after coronary artery bypass grafting. Acta Anaesthesiol Scand. 2000;44(1): 75–81.
42. Kindgen-Milles D, Muller E, Buhl R, Bohner H, Ritter D, Sandmann W et al. Nasal-continuous positive airway pressure reduces pulmonary morbidity and length of hospital stay following thoracoabdominal aortic surgery. Chest. 2005;128(2):821–8.
43. Squadrone V, Coha M, Cerutti E, Schellino MM, Biolino P, Occella P et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. Jama. 2005;293(5):589–95.
44. Pasquina P, Merlani P, Granier JM, Ricou B. Continuous positive airway pressure versus noninvasive pressure support ventilation to treat atelectasis after cardiac surgery. Anesth Analg. 2004;99(4):1001–8, table of contents.
45. Nava S, Ambrosino N, Clini E, Prato M, Orlando G, Vitacca M et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized, controlled trial. Ann Intern Med. 1998;128(9):721–8.
46. Girault C, Daudenthun I, Chevron V, Tamion F, Leroy J, Bonmarchand G. Noninvasive ventilation as a systematic extubation and weaning technique in acute-on-chronic respiratory failure: a prospective, randomized controlled study. Am J Respir Crit Care Med. 1999;160(1):86–92.
47. Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med. 2005;33(11):2465–70.
48. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. Am J Respir Crit Care Med. 2006;173(2):164–70.
49. Burns KE, Adhikari NK, Meade MO. A meta-analysis of noninvasive weaning to facilitate liberation from mechanical ventilation. Can J Anaesth. 2006;53(3): 305–15.
50. Keenan SP, Powers C, McCormack DG, Block G. Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. Jama. 2002;287(24):3238–44.
51. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguia C, Gonzalez M et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. N Engl J Med. 2004;350(24):2452–60.

Gabriela Ferreyra and V. Marco Ranieri

Rolf Dembinski and Ralf Kuhlen

Weaning: Protocols vs. clinically driven

Introduction to the topic

Depending on its duration mechanical ventilation affects morbidity and mortality of patients in the intensive care unit due to life-threatening complications (1). Most important, mechanical ventilation may cause severe lung injury due to pulmonary baro- and volutrauma (2) and is associated with the occurrence of nosocomial pneumonia (3). The incidence of these complications increases with every day passing on mechanical ventilation (4) resulting in concomitant increased mortality (5). Vice versa, complications of mechanical ventilation usually prolong the ventilation period due to gas exchange disorders. Consequently, all efforts should be made from the start to shorten the duration of mechanical ventilation as much as possible.

However, even when the reason for the onset of mechanical ventilation has been treated successfully and severe complications have been avoided or adequately treated, discontinuation after prolonged mechanical ventilation often cannot be performed instantaneously due to weakness of the respiratory musculature. Therefore, a certain time period is necessary for ventilator withdrawal to accustom patients to breathing without mechanical assistance, a process referred to as weaning from mechanical ventilation.

In patients ventilated for longer than 24 hours about 40–92 % of the duration of mechanical ventilation is dedicated to weaning (1, 6, 7). However, reasons for prolonged weaning are not only related to medical problems such as gas exchange disorders and/or muscle weakness but are also associated with logistic problems such as the clinicians' delay in recognizing the ability of a patient to have mechanical ventilation discontinued. The latter issue has been strikingly disclosed in studies demonstrating a reintubation rate of only 60 % in patients self-extubated during mechanical ventilation (8). This is probably due to the fact that no single factor or measurement is able to predict successful discontinuation from mechanical ventilation (9). Moreover, it should not be forgotten that extubation failure as well is accompanied with increased mortality (10).

In contrast to single parameters, the completion of a combination of several discrete criteria has been shown to improve the likelihood of successful discontinuation from mechanical ventilation (11). Therefore, it is suggested to screen a bundle of parameters frequently in all ventilated patients to provide early identification of patients who are 'ready to wean'. In all patients complying with these requirements successful spontaneous breathing trials have been demonstrated to further increase the probability of successful discontinuation from ventilation (12–14). Thus, daily spontaneous breathing trials are recommended in patients who are ready to wean.

With the aim of simplifying this screening process, increasing efficiency, and decreasing physicians' workload, most experts in the field recommend the use of

weaning protocols (see fig. 1). This position seems to be maintained by the results of several clinical trials in which weaning protocols revealed beneficial effects compared to usual care (15–17). However, other studies failed to reveal improvements of outcome parameters after implementation of weaning protocols (18). Thus, there is ongoing controversy about the impact of weaning protocols compared to clinical decision making based on more or less standardised parameters. The following contribution highlights the most important arguments alleged within this discussion.

Controversial position 1: Weaning by protocols

Weaning protocols are mainly compiled on the basis of statistically significant results. Up until today four major randomised controlled trials including a total number of more than 1,000 patients revealed a significant reduction of the duration of mechanical ventilation due to weaning protocols (15–17, 19).

In the first of these studies presented by Wesley Ely and colleagues in 1996 daily screening followed by spontaneous breathing trials in medical and coronary intensive care units reduced the du-

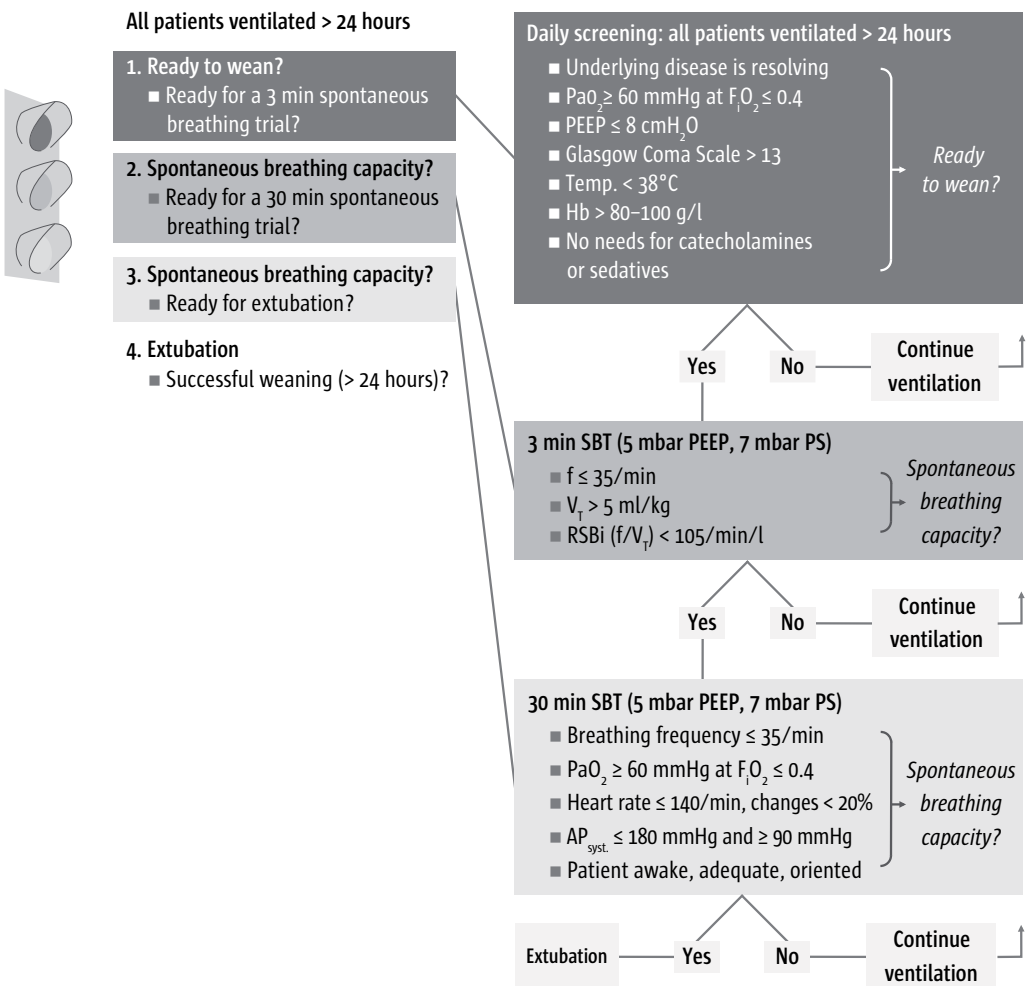

Fig. 1 SBT: Spontaneous breathing trial, RSBi: Rapid shallow breathing index, $AP_{syst.}$: Systolic arterial blood pressure