16 Predictors of Failure

Why predictors of failure rather than predictors of success? Because we believe that it is the failure of NIV, above all by culpably and unduly delaying intubation, which determines the outcome of the patient; on the other hand knowing that a patient has a good possibility of success should reassure us but certainly not let us lower our guard.

It should be immediately clarified that the so-called predictors, or perhaps more accurately factors associated with failure, differ greatly between acute hypercapnic respiratory failure due to a pump impairment and hypoxic respiratory failure due to parenchymal problems. As demonstrated by Demoule et al. (2006), a failed attempt at NIV in the former situation is not associated with a higher mortality rate, even if the patient needs intubation, whereas in the case of pure hypoxia, a failed trial of NIV lowers the probability of survival.

16.1 Hypercapnic Respiratory Failure

Table 16.1 lists the possible predictors of failure of NIV during an episode of hypercapnic respiratory failure.

They include clinical parameters, blood-gas values, and mixed indicators. The indices of severity of status on admission to hospital (e.g., SAPS or APACHE) were considered to have a discrete correlation with the outcome of NIV in some studies, whereas no significant correlation was found in others. In any case, it is clear that less severely ill patients (i.e., those with a SAPS II score <30–35 and an APACHE II score <15–20) will have a better outcome. The state of the sensorium is another variable to consider, although taking into account that even comatose patients can be ventilated successfully; the important point is to monitor this index frequently, using the most specific scale possible, such as the Kelly scale.

The possibility of removing bronchial secretions effectively, the tolerance of the NIV, and the presence of massive air losses have been sporadically associated with failure of NIV although it is difficult to determine a threshold level requiring

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Table 16.1 Factors associated with failure of NIV

Acute hypercapnic respiratory failure
• Minimal (<0.02) or no change in pH after 1–2 h
• Minimal or no reduction in respiratory rate after 1–2 h
• High severity score at commencement of NIV (i.e. SAPS II>30- APACHE II>20)
• Scarce collaboration or poor tolerance
• Incapacity to remove secretions effectively
Acute hypoxic respiratory failure
• Minimal or no change in the PaO_2/FiO_2 ratio after 1–2 h
• Age >40 years
• High severity score at commencement of NIV (i.e. SAPS II>34)
• Presence of ARDS, CAP and/or sepsis

attention, since most of the studies considered these problems in a dichotomous manner (yes/no).

There is certainly more concordance concerning blood-gas indicators. The pH is the first index to consider, since any changes in the level of $PaCO_2$ are found only later. The absolute value of pH at the time of starting NIV is not necessarily associated with the final outcome since only a few studies have shown a substantial difference between successes and failures.

Certainly, it is intuitive that a patient with a pH <7.25 will be more difficult to ventilate than one with a pH of ~7.30. The single most effective predictor of failure of NIV is definitely change in pH after 1 h of ventilation. A minimal increase (<0.02), no change or, even worse, a decrease in the pH value as the acute response to a trial with NIV is an indicator of almost certain failure.

This does not necessarily mean you have to "wave the white flag" and surrender, but great care must be taken when continuing NIV, perhaps with variations in the parameters, in order not to reach an irreversible clinical condition: the NIV should not be continued for more than another 30–60 min and close monitoring is essential.

The so-called mixed indicators, which take into account several variables, represent an interesting, alternative approach. Certainly the most original and scientifically valid study on this issue is that by Confalonieri et al. (2005), who collected data from more than 1,000 patients and used them to stratify the risk of failure of NIV into three levels corresponding to the colors of a traffic light. The red light, indicating the highest risk of around 70 %, was associated with a pH on admission of <7.25 with an APACHE II score ≥29, a respiratory rate ≥30 breaths per minute, and a score of <11 on the Glasgow Coma Scale. A pH <7.25 after 2 h of ventilation was an indicator of almost certain failure (>90 %). Less severe levels of each of the listed parameters lowered the risk of failure in a manner almost proportional to the number of altered factors and the degree of lesser severity.

It is important to note that while a worsening in the first hours of ventilation is almost always associated with failure of NIV, the opposite—success in those who have dramatic improvement in their clinical conditions after a brief trial—does not hold true. Some years ago, Moretti et al. (2000) showed that a substantial proportion of "early responders" (about 15–20 %) are destined to worsen over time and, therefore, to be intubated or even to die, despite the initial success. The main factors associated with these late failures are comorbidities, in particular hyperglycemia.

So far we have only described and discussed the literature, but these indicators can only provide a rational orientation for our choices, they certainly are not objective guidelines. The success of NIV, just as its failure, depends above all on all those human and organizational variables discussed previously, such as familiarity with the technique, training, environment in which the ventilation takes place, and the number of clinicians involved, factors which cannot easily be quantified and even less so summarized in tables or flow-charts.

16.2 Hypoxic Respiratory Failure

This section of the chapter is much shorter, given the paucity of studies. In fact, there are only four studies focusing on this subject, perhaps because the literature on the use of NIV in hypoxic respiratory failure is much scarcer than that on hypercapnic forms.

In our opinion, the problem of predictors of failure in this field is much more important than in exacerbations of COPD because while the time factor is important in this latter case it is not critical, whereas in the case of the hypoxic patient a delay in instituting alternative forms of ventilation other than NIV can be fatal for the patient. Thus, the speed of decision after a brief trial of NIV is a factor of utmost importance. The decision must be yes or no; "let's see what happens in a while" is not an acceptable choice.

The multicenter study by Antonelli and colleagues in 2001, which involved almost 6,000 patients, showed that age over 40 years, a SAPS II score $\geq$35, the presence of community acquired pneumonia, ARDS and a PaO_2/FiO_2 ratio $\leq$146 after 1 h of NIV were factors independently associated with failure (Antonelli et al. 2001).

Subsequently the same authors focused on patients with ARDS and showed that in this group a SAPS II score $\geq$34 and a PaO_2/FiO_2 ratio $\leq$175 after 1 h were the only independent predictors of failure of NIV (Antonelli et al. 2007). Furthermore, their study showed that patients who were intubated were, on average, older and required higher levels of external PEEP and/or Pressure Support.

In a relatively small, consecutive series of hypoxic patients, Rana et al. (2006) demonstrated that the presence of shock, metabolic acidosis, and a low PaO_2/FiO_2 ratio were factors predicting failure of NIV. Demoule et al. (2006), analyzing data from 70 French intensive care units, concluded that the failure of NIV in hypoxic patients was correlated with a high mortality (OR of 3.24), once again confirming that one must be very prudent when treating such patients with NIV.

In conclusion, there are easily measurable clinical factors that can rapidly alert a clinician to the possible failure of NIV and lead him to a quick decision to intubate the patient. However, we do note that the umbrella term of hypoxia covers numerous pathologies with very different pathogenic mechanisms and their responses to NIV could, therefore, be markedly different. For example, as already said earlier, a given PaO_2/FiO_2 ratio in a patient with acute pulmonary edema has a completely different meaning from the same ratio in a patient with ARDS.

Suggested Reading

Ambrosino N, Foglio K, Rubini F et al (1995) Non-invasive mechanical ventilation in acute respiratory failure due to chronic obstructive pulmonary disease: correlates for success. Thorax 50(7):755–757

Antonelli M, Conti G, Moro ML (2001) Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Med 27(11):1718–1728

Antonelli M, Conti G, Esquinas A et al (2007) 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 35(1):18–25

Carlucci A, Richard JC (2001) Noninvasive versus conventional mechanical ventilation. An epidemiological survey. Am J Respir Crit Care Med 163(4):874–880

Carlucci A, Delmastro M, Rubini F et al (2003) Changes in the practice of non-invasive ventilation in treating COPD patients over 8 years. Intensive Care Med 29(3):419–425

Confalonieri M, Garuti G, Cattaruzza MS et al (2005) Italian noninvasive positive pressure ventilation (NPPV) study group. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. Eur Respir J 25:348–355

Demoule A, Girou E, Richard JC et al (2006) Benefits and risks of success or failure of noninvasive ventilation. Intensive Care Med 32(11):1756–1765

Meduri GU, Abou-Shala N, Fox RC et al (1991) Noninvasive face mask mechanical ventilation in patients with acute hypercapnic respiratory failure. Chest 100(2):445–454

Moretti M, Cilione C, Tampieri A et al (2000) Incidence and causes of non-invasive mechanical ventilation failure after initial success. Thorax 55(10):819–825

Nava S, Carlucci A (2002) Non-invasive pressure support ventilation in acute hypoxemic respiratory failure: common strategy for different pathologies? Intensive Care Med 28(9):1205–1207

Nava S, Ceriana P (2004) Causes of failure of noninvasive mechanical ventilation. Respir Care 49(3):295–303

Rana S, Jenad H, Gay PC et al (2006) Failure of non-invasive ventilation in patients with acute lung injury: observational cohort study. Crit Care 10(3):R79

Soo Hoo GW, Santiago S, Williams AJ (1994) Nasal mechanical ventilation for hypercapnic respiratory failure in chronic obstructive pulmonary disease: determinants of success and failure. Crit Care Med 22(8):1253–1261