



Glossary

ARF: Acute respiratory failure

CHF: Congestive heart failure

COPD: Chronic obstructive pulmonary disease

CPAP: Continuous positive airway pressure

CPE: Cardiogenic pulmonary oedema

DNI: "Do not intubate" order

NIV: Non-invasive ventilation

SARS: Severe acute respiratory syndrome

Non-invasive ventilation: a year in review

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Educational aims

- To present four innovative papers from the field on non-invasive ventilation published in 2004 and to discuss the important points and conclusions from each.

Summary

This paper summarises the findings of four important papers that have been published over the last year.

The first paper reports data on the success rate of NIV in patients with early onset of ARF due to SARS. Furthermore, the paper discusses how NIV may be used in patients affected by highly contagious diseases in a way which is safe for healthcare workers.

The second paper concentrates on dying at end-stage disease and the limits of medical care. It studies the use of NIV treatment in patients with CHF and COPD affected by ARF who have signed a DNI order.

The next article investigates the use of both CPAP and NIV delivered by face mask in patients with CPE, when compared with the use of oxygen alone, and their effect on physiological parameters and avoiding intubation.

Finally, the last paper reviewed reports on the use of NIV to treat an episode of post-extubation respiratory failure in "unselected" patients.

This review article aims to keep the reader updated on the most recent and some of the important advancements in this field over the last year.

NIV has been increasingly used as a ventilatory strategy both for ARF and chronic respiratory failure. Consequently, its use has been recommended as first-line treatment in certain patients [1]. In 2004, >100 peer-reviewed papers were published in this field, making it difficult to select only four manuscripts to specifically discuss in this review. The four reviews chosen may not

necessarily be the "best" from the year; however, they are all innovative in some way. Only studies dealing with the treatment of ARF are presented; in particular, those conducted in patients with lung failure (hypoxic respiratory failure), since there is a consensus that NIV should be used as a gold standard for an episode of pump failure (hypercapnic respiratory failure) [1, 2].

SARS

The first paper presented here deals with a specific disease which had a dramatic outbreak in the Far East.

Severe acute respiratory syndrome (SARS) was first defined by the World Health Organization in March 2003. Its clinical course can be stormy, with up to 25% of cases progressing to acute respiratory failure (ARF) and requiring mechanical ventilation. Due to the fear of leakage from the mask interface, with subsequent transmission of SARS to healthcare workers, the rate of non-invasive mechanical ventilation (NIV) use for these patients was very low and not recommended.

In a retrospective observational study performed in Hong Kong [3], NIV was applied to 20 out of 87 patients admitted to the hospital with a confirmed diagnosis of SARS (coronavirus was positive in 95% of patients) and ARF. On account of a possible risk of aerosol generation, resulting from leakage at the interface during NIV, stringent infection-control measures were implemented. NIV was started 9.6 days from the symptom onset and the mean duration of

ventilation was 85 hours. Endotracheal intubation was avoided in 14 (70%) patients, in whom the length of intensive care unit stay was shorter and the chest radiography score within 24 hours of NIV lower when compared with patients that needed to be intubated. Changes in some physiological variables, such as a reduction in respiratory rate and a decrease in oxygen requirement within 24 hours of NIV, were predictors of NIV success. Interestingly, no infections were observed among the 105 healthcare workers caring for the patients receiving NIV, who underwent coronavirus serology.

Clearly, this study does not fit the criteria of evidence-based medicine, due to the small number of patients, its retrospective nature and the lack of a control group. However, it should be considered that the outbreak of the disease was dramatic and very fast in its emergence and also in its diminution (mid March to the end of April in Hong Kong), which did not give the authors time to organise a randomised, controlled trial. Similar results were also obtained by HAN *et al.* [4] who were working in the same geographical area.

Photo shows researchers from the Chinese University, Hong Kong.

Key points

▶ These preliminary data demonstrate that the success rate of NIV in patients with early onset of ARF due to SARS is comparable to that observed in early acute respiratory distress syndrome or acute lung injury.

▶ Using stringent and severe control measures, NIV may be used in patients affected by highly contagious diseases such as SARS, in a way which is safe for healthcare workers.





FRAGONARD, Alexandre-Évariste
(1780–1850)
*Cardinal Mazarin at the
Deathbed of Eustache Le Sueur.*

End of life

The problems associated with dying at end-stage disease and the limits of medical care have become some of the consuming interests of the media, especially in the light of recent high-profile cases (*e.g.* individuals travelling to other countries where euthanasia is sanctioned). A few governments, health agencies and religious communities have recently taken positions on the issues of withholding and/or withdrawing life-support therapies, physician-assisted suicide and euthanasia. In general, the “shared decision” (*i.e.* a decision mutually reached by hospital staff, the patient (if they retain a decision-making capacity) and the relatives) is regarded as the best approach for determining end-of-life care strategies.

Some preliminary reports have shown that NIV may offer a dignified and comfortable ventilatory approach in the management of patients who have decided to forego intubation (“do not intubate” or DNI). Despite this, the use of NIV for terminally ill patients has aroused controversy, since it has been suggested that this modality of ventilation violates the biomedical principle of “first do not harm”.

In a multicentre prospective cohort study, LEVY *et al.* [5] expanded knowledge on this topic by studying 114 patients with ARF and a DNI status. Of these patients, 20% had advance directives and had declared their wishes prior to admission,

while the remainder had their DNI status established following admission. A rather unexpectedly large proportion of patients (43%) survived to discharge. The variables associated with survival were a higher baseline arterial carbon dioxide tension and the diagnosis of congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD), whereas those patients with pneumonia, cancer and other primary diagnoses had roughly a 1 in 4 chance. A stronger cough and being awake at the time of NIV instigation were also associated with a better survival.

Bearing in mind that these patients had a DNI order, the first consideration from this study may be the following: “Is the cause of ARF potentially reversible or not?” If yes, as in the case of cardiogenic pulmonary oedema (CPE) or COPD exacerbation, the first-line treatment, if the patient is willing to receive it, should be NIV. Another important consideration is that signing a DNI order does not necessarily mean that you want to die “right away” (actually, the overall survival rate was ~50%), but, instead, means that you want to avoid unnecessary pain and discomfort. This was also recently confirmed by other investigations [6, 7].

The effects of NIV on dyspnoea, quality of life and survival beyond acute hospitalisation deserve further studies, despite a single observational study which clearly showed that the use of NIV as a palliative measure can reduce the degree of breathlessness [8].

Key points

- ▶ Patients with CHF and COPD affected by ARF, possibly sustained by a reversible cause, may be successfully treated with NIV when they have signed a DNI order and are willing to receive a non-invasive form of ventilation.
- ▶ A DNI order is not necessarily associated with a very high mortality rate.



Key points

- ▶ In patients with CPE, both CPAP and NIV delivered by face mask are equally useful in rapidly improving some physiological parameters and avoiding intubation compared with the use of oxygen alone.
- ▶ The use of NIV and CPAP should be recommended in the major guidelines for the treatment of CPE, since, so far, only oxygen therapy has been considered as first-line treatment.

CPAP

The best therapy for treating an episode of ARF due to CPE is still a controversial matter. For example, the use of continuous positive airway pressure (CPAP) is not yet judged as standard in the guidelines of the American Heart Association or the European Society of Cardiology, or in most textbooks of medicine. As an alternative to CPAP, NIV combines additional inspiratory pressure assistance above the baseline continuous pressure, which has been shown *per se* to improve oxygenation and reduce left ventricular pre- and afterload in patients with CPE. So far, most randomised controlled trials have compared either oxygen therapy *versus* CPAP or oxygen therapy *versus* NIV, so there was a need for a simultaneous comparison among oxygen, NIV and CPAP.

PARK *et al.* [9] randomly assigned 80 patients with severe CPE into three treatment groups. Treatment with CPAP or NIV resulted in a significant improvement in oxygenation, dyspnoea, and respiratory and heart rates compared with oxygen alone. Endotracheal intubation was necessary in 42% of the patients in the oxygen-alone group, but only in 7% of the patient in other groups ($p < 0.001$). Interestingly, there was no increase in the incidence of acute myocardial infarction in the groups undergoing the two modalities of ventilation. Mortality at 15 days was higher in the oxygen group, but this difference disappeared at hospital discharge.

This study showed that there is no difference in the clinical outcome between CPAP and NIV delivered by face mask, while the use of oxygen alone was associated with a higher intubation rate. Therefore, PARK *et al.* [9] suggested that “a positive intrathoracic pressure must be seen as a non-pharmacologic form of treatment for CPE, rather than a supportive measure”. Another important message from the study is that only a small portion of patients with CPE (~20%) were, in fact, enrolled in the study, because the remaining were judged not “so sick” to be ventilated. Finally, this study failed to investigate the potential different clinical outcome between hypercapnic and non-hypercapnic patients. In 2004, the results of two other randomised controlled trials were published in the same field [10, 11].

Educational questions

1. Which one of the following statements is true:
 - a) NIV is the first-line treatment for patients with ARF due to a SARS infection.
 - b) NIV is contraindicated in the treatment of patients with ARF due to a SARS infection.
 - c) NIV may be used in the treatment of patients with ARF due to a SARS infection only employing stringent infection-control measures.
 - d) NIV may be used in the treatment of patients with ARF due to a SARS infection only in the People's Republic of China.
2. What is a DNI order?
 - a) It is the will of a patient who has decided to forego intubation (do not intubate).
 - b) It is the will of a patient who has decided to forego any form of aggressive intervention (*i.e.* intubation, resuscitation, defibrillation) (do not intervene).
 - c) It is the will of a patient who has decided to forego NIV (do not initiate).
 - d) It is the will of a patient who has decided to not be disturbed (do not irritate me).
3. Which of the following statements is true:
 - a) CPAP is better tolerated than NIV during an episode of ARF due to CPE.
 - b) The use of NIV is associated with a high rate of myocardial infarction during an episode of ARF due to CPE.
 - c) Patients treated with NIV, CPAP or oxygen for an episode of ARF due to CPE showed similar mortality rates at hospital discharge.
 - d) Oxygen and NIV are presently included in the major guidelines for the treatment of CPE.
4. What did the study by ESTEBAN *et al.* [12] show:
 - a) That the use of NIV to treat an episode of post-extubation hypercapnic respiratory failure may be harmful.
 - b) That the use of NIV to treat an episode of post-extubation hypercapnic respiratory failure in “unselected” patients may be harmful.
 - c) That the use of NIV is recommended only to treat an episode of post-extubation hypercapnic respiratory failure, but not of hypoxic.
 - d) That Spain never won any World or European football championships.

Post-extubation respiratory failure

The last study for discussion deals with a very peculiar aspect of NIV: its application to treat an episode of post-extubation respiratory failure.

After a successful weaning trial, the patient is usually extubated, since he/she is considered to be ready for unsupported breathing. Nevertheless, the documented need for reintubation ranges 13–19%, and the mortality rate in this subset of patients is considerably higher than in those not requiring a new intubation. On the basis of few non-randomised studies, NIV has been deemed to be a promising therapy after failure of extubation, despite the unfavourable results of a small randomised controlled trial.

In a multicentre (37 centres worldwide) study [12], patients who were electively extubated after at least 48 hours of mechanical ventilation, and who had respiratory failure within the following 2 days, were randomly assigned to either NIV (114 patients) or standard medical therapy (107 patients). The rate of reintubation was similar in the two groups, whereas the rate of death in the intensive care unit was higher in the NIV group than in the standard therapy one (25 versus 14%; relative risk 1.78). The median time from respiratory failure to reintubation was longer in the NIV group, and it was possible that this delay in

Key points

- ▶ The use of NIV to treat an episode of post-extubation respiratory failure in “unselected” patients may be harmful.
- ▶ The potential usefulness of NIV in the subset of patients developing “hypercapnic” post-extubation failure still remains to be determined.

reintubation was the reason for the significant increase in the risk of death. ESTEBAN *et al.* [12] concluded that NIV is not effective in averting the need for reintubation and may, in fact, be harmful, despite also stating that “selected patients in specialised centers may benefit from this therapy”.

Has this study really “killed” the use of NIV in this situation? As a matter of fact, in this study, NIV was applied only when ARF became overt, whilst it has also been shown that there is a clearly identified subset of patients (*i.e.* those with comorbidities, increased work of breathing at the time of extubation, CHF, excess of secretions, repeated weaning failure and upper airways obstruction) at a high risk of reintubation, where the preventive use of NIV may be theoretically indicated. Therefore, considering that NIV should not presently be used to “treat” an episode of post-extubation respiratory failure, it may eventually be used to “prevent” the occurrence of this complication.

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Suggested answers

1. c
2. a
3. c
4. b