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# Early ward-based acute noninvasive ventilation: a paper that changed practice

## Landmark papers in respiratory medicine

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Noninvasive ventilation (NIV) is now an established evidence-based treatment for acute hypercapnic respiratory failure (AHRF), predominantly for defined patients admitted with exacerbations of chronic obstructive pulmonary disease (COPD), but also a range of other conditions including obesity-related respiratory failure and chest wall deformities requiring an acute hospital admission. Over the past two decades, there has been a significant shift towards greater use of NIV in place of invasive mechanical ventilation (IMV) in this group of patients. Here we set out to discuss a landmark paper in this respect: the report of the YONIV trial (Yorkshire Noninvasive Ventilation Trial), published in June 2000, which addressed the key practical questions around the early use of ward-based NIV at the time [1]. A recent narrative review on the epidemiology of NIV for acute respiratory failure in COPD patients concluded that this dramatic increase in NIV use is probably due to the increased experience of the medical teams, treating sicker patients with comorbidities and utilising NIV outside the intensive care unit (ICU), further confirming the pivotal role of the original trial enabling the early use of acute NIV on medical wards [2].

## The 1990s question: is NIV feasible in the "real world"?

Evidence about the effect of noninvasive positive pressure ventilation, particularly in exacerbations of COPD, has been accumulating since the early 1990s. NIV was shown to improve the hypercapnic ventilatory response (respiratory drive), improve gas exchange, reduce the work of breathing and unloading inspiratory muscles [3, 4].

However, there remained a big question about the wider applicability of NIV in the "real world", *i.e.* outside centres with considerable expertise in respiratory physiology. The initial response was seen to be good, but the 30-day mortality did not show a significant improvement [5]. Also, there were concerns that application of NIV in the emergency department may delay tracheal intubation and the initiation of mechanical ventilation in some patients with acute respiratory distress. The logistical problem of assessing patients for encephalopathy, agitation and loss of alertness while they wore nasal masks was thought to have contributed to a delay in the clinical recognition of the need for intubation [6].

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**The landmark YONIV trial addressed key practical questions surrounding the early use of ward-based noninvasive ventilation, which is now an established evidence-based treatment for acute hypercapnic respiratory failure** http://ow.ly/BDC530iWhne

## The 1990s question: can NIV be performed successfully outside the ICU?

The evidence for the successful use of NIV in ICU patients with acute exacerbations of COPD to avoid endotracheal intubation and complications associated with IMV was steadily firming up in the 1990s. Patients enrolled in such studies had known COPD, or a high probability of the disease (on the basis of the clinical history, physical examination and chest film), with respiratory acidosis and an elevated bicarbonate level. It was being established that in selected patients with acute exacerbations of COPD (in the ICU), NIV can reduce the need for endotracheal intubation, the length of the hospital stay, and the in-hospital mortality rate [7]. However, the availability of ICU beds varies from country to country and it was increasingly being acknowledged that the inability to use NIV on general wards could delay its use and that even a short delay might make NIV fail.

## The YONIV trial: early ward-based acute NIV

The YONIV trial aimed to find out whether the introduction of NIV, early after the admission to a general respiratory ward, was effective at reducing the need for intubation and the mortality associated with acute exacerbations of COPD [1]. It was a prospective, multicentre randomised controlled study (involving 14 UK hospitals over 22 months) comparing NIV with standard therapy in patients with mild-to-moderate acidosis during an acute exacerbation of COPD. NIV was administered on the ward with a simple noninvasive ventilator and a standardised predefined protocol. A total of 236 patients were recruited, 118 received standard therapy alone and 118 received additional NIV. The two groups had similar characteristics at enrolment. The use of NIV significantly reduced the need for intubation as defined by the failure criteria. 32 (27%) out of 118 patients in the standard therapy group failed compared with 18 (15%) patients in the NIV group ($p=0.02$). In-hospital mortality was also reduced by NIV: 24 (20%) out of 118 patients died in the standard group compared with 12 (10%) out of 118 in the NIV group ($p=0.05$). In both groups, the pH, arterial carbon dioxide tension and respiratory rate improved at 4 h ($p<0.01$). However, NIV led to a more rapid improvement in pH in the first hour ($p=0.02$) and a greater fall in respiratory rate at 4 h ($p=0.035$). The duration of breathlessness was also reduced by NIV ($p=0.025$).

This trial directly addressed the two biggest questions the respiratory and critical care community faced at the time: "is NIV feasible in the real world?" and "can NIV be performed successfully outside the ICU?". It demonstrated that the early use of NIV for mildly and moderately acidotic patients with COPD in a general ward setting leads to more rapid improvement of physiological variables, a reduction in the need for IMV (with objective criteria), and a reduction in in-hospital mortality.

## Summary and prospect

Early ward-based NIV has been the bedrock for the expansion of acute NIV services across countries. 15 years after the publication of YONIV, an international survey including a sample of hospitals from five continents focusing on ward-based NIV for AHRF has shown that acute exacerbations of COPD are the most common indication for NIV use outside the ICU (94%) and that NIV outside the ICU has become a growing phenomenon [8]. Although patients can be extensively monitored in the "safe" ICU environment, a shortage of intensive care beds, managing less severe cases of AHRF in other units, and increased experience and evidence in the use of NIV outside the ICU may have led to this trend. The survey concluded that the use of NIV in general wards was effective, common and gradually increasing. Improvements in staff training and introduction of protocols could help to make this technique safer and more common when applied in a general ward setting [9, 10].

It has been shown that caring for a higher volume of NIV patients in ICU may develop local expertise and lead to better NIV outcomes [11]. We have seen similar effects of patient volume on local expertise when analysing temporal trends at a single, large ward-based NIV unit, recording that more severely ill acute hypercapnic respiratory failure patients are being treated with no significant change in mortality [12]. Ward-based NIV is consistently emerging as a sustainable tool to deal with acute exacerbations of COPD as well as other patients with ventilatory insufficiency leading to hospital admissions due to respiratory failure, who are now living longer with various comorbidities.

Even in the USA, where NIV was almost exclusively used in ICUs in the 1990s, an observational cohort study based at eight acute care hospitals in Massachusetts found that, although only a fifth of acute NIV patients were started on general wards, the NIV utilisation rate was highest for general wards (73%), most likely reflecting the higher proportion of patients with a "do-not-intubate" status in general wards compared with critical care units [13].

In the context of limited availability of ICU beds, some clinicians may consider that admission of debilitated patients with an underlying end-stage chronic illness, like those with COPD, may merely deprive other critically ill candidates who could benefit more from ICU resources. So the question is no longer "should we use NIV in 'do-not-intubate' patients?", the answer is obviously "Yes", NIV should at least be offered to these patients, especially when the underlying cause of the AHRF is reversible, but rather "how can we apply NIV to 'do-not-intubate'

patients without drifting toward unreasonable care?"[14].

Finally, there is accumulating evidence of improved admission-free survival through administration of post-acute home nocturnal NIV in selected patients in the largest segment of acute NIV recipients (those with persistent hypercapnia following an acute exacerbation of COPD are the ones that benefit) [15]. The expansion of ward-based NIV, enabled largely by YONIV and similar trials, is on the verge of seeing a step change in improving outcomes in people living with COPD.

## Conflict of interest

R. Mukherjee reports non-financial support from ResMed (training for physiologists and physiotherapists in the NIV unit that he leads), grants from the National Institute for Health Research (NIHR), UK (as a co-investigator in a NIHR-funded systematic review of cost-effectiveness and clinical effectiveness of NIV in stable COPD), and grants from the HOT-HMV trial (Birmingham site principal investigator of the HOT-HMV in COPD trial), all outside the submitted work. R. Nenna has nothing to disclose. A. Turner reports personal fees from ResMed (for chairing a meeting on NIV in COPD), and grants from the National Institute for Health Research (NIHR), UK (as the principal investigator in a NIHR-funded systematic review of cost-effectiveness and clinical effectiveness of NIV in stable COPD), all outside the submitted work.

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