Home NIV for COPD: The devil is in the detail

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The data supporting the benefits of home non-invasive ventilation (NIV) in patients with severe chronic obstructive pulmonary disease (COPD) has been accumulating over the last decade. Historically, there was debate about the potential benefits of home NIV in this patient population with early small scale studies in specialist centres demonstrating physiological changes[1-3] but these small studies did not translate into clinical benefit in the initial large scale randomised clinical trials[4, 5]. Two pivotal trials made clear the potential improvements in overall and admission-free survival in patients with moderately severe chronic hypercapnic respiratory failure and NIV titrated to control hypoventilation[6, 7]. Analysis of the data highlighted the importance of both population selection and optimal delivery and timing of the intervention. It is clear that home NIV is only a valuable treatment for selected patients with COPD and that the intervention itself must be delivered to target control of hypercapnic respiratory failure. Further analysis of the current clinical trial data has further demonstrated clinically meaningful differences in patient relevant outcomes including exacerbations and mortality[8] as well as system benefits such as health care costs[9, 10].

The optimal delivery of home NIV is also controversial with some advocating for the use of detailed physiological monitoring to minimise patient ventilator asynchrony and others championing a more parsimonious approach[11-13]. Recent studies have provided clear data that not only does the change in daytime pCO2 relate to a range of important outcomes but that it trumps the control of sleep hypoventilation when predicting long-term survival[14]. It is therefore important that home NIV is delivered in expert centres as the provision of a device without the ability to optimise the intervention, including concordance to treatment, is unlikely to improve outcomes.

In patients treated with home NIV, as with the management of COPD in general, there is an increasing recognition of the importance of phenotypes and, in particular, treatable traits[15]. With recent data suggesting the potential to use biologic therapy to improve outcomes from acute exacerbations of COPD[16]. Phenotyping has also been explored in patients treated with home NIV. Janssens and colleagues used a single centre cohort of patients on home NIV for COPD to identify 2 distinct phenotypes of patient; respiratory and systemic[17]. These 2 groups had different clinical characteristics and outcomes that could be classified using a simple algorithm. Pepin et al also explored phenotypes of patients with COPD initiated on home NIV by using cluster analysis on 54,545 patients identified from a national database[18]. This work identified 4 clusters of patients, each with different characteristics and health trajectories. These 4 clusters where characterised by those initiated on home NIV 1: in the ambulatory setting or after a single exacerbation; 2: after 2 or more severe exacerbations in the last 6 months; 3: after repeat severe exacerbations in the last year; and 4: after many long-lasting/slow recovering exacerbations. Whilst not specifically addressed in either of the above studies on phenotyping the presence of obstructive sleep apnoea (OSA) in patients with COPD and respiratory failure has been shown to have a perhaps paradoxical effect on outcomes, with an improved survival compared to patients initiating on home NIV with COPD alone[19]. The reasons for this are speculative but may relate to the earlier development of hypercapnia occurring with more preserved spirometry in those with co-morbid OSA.

In this issue of Thorax, Pepin et al provide more data on the benefits of home NIV in patients with severe COPD and how they impact in the different phenotypic clusters [TBC in press]. The study uses the same national database, which has near comprehensive coverage within France, to examine the impact of home NIV on COPD relevant outcomes (severe exacerbation & death) using a multi-state model (without exacerbation, severe exacerbation and death). The clear

strength of this work is the robust statistical methodology and large dataset (49,503 patients starting home NIV between 2015 and 2019 with outcome data until December 2020) with minimal missing data allowing for adjustment of many potential confounders. Of note the authors excluded any patient that completed <3 months of home NIV therapy on the basis that this was an insufficient duration to impact long term outcomes. The major limitations of the study are the lack of granularity on some important patient and treatment characteristics, most notably the ventilator settings, adherence to treatment and assessment of respiratory failure, which as outlined earlier are integral to the understanding of the delivery of home NIV as a treatment. However, even with these limitations there are several important messages within this study.

The data again confirms the potential for home NIV to improve survival in patients with severe COPD with significant reductions in transition to death from both without exacerbation (hazard ratio [HR] 0.88, 95% confidence interval [CI] 0.83–0.93) and severe exacerbation (HR 0.84, 95% CI 0.79–0.91) states. Although there was not an impact on transition from without exacerbation to severe exacerbation (HR 0.98, 95% CI 0.95–1.00) in the unselected cohort, there was impact in, the largest subgroup, cluster 1 (HR 0.88, 95% CI 0.85–0.92), confirming the importance of patient selection. These data help clinicians working in field by further strengthening the data on the ability of home NIV to improve survival in patients with severe COPD when few other therapies are available which can modulate this outcome. Furthermore, it helps to allow assessment of individual benefit of therapy so that patient and clinicians can discuss whether the undoubted burden of home NIV is sufficient to warrant treatment initiation and continuation.

These data further support clinicians to be confident that home NIV can be used in patients with severe COPD to improve patient relevant outcomes including mortality with ongoing work to allow individualised treatment decisions to ensure patient selection is optimal.

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