Viewpoint: Turning the Air Blue

Why Home-NIV Should Begin in the Hospital, Not at Home

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Chronic hypercapnic respiratory failure (CHRF) due to COPD is associated with increased risk for hospitalizations and mortality.[1 2] Home nocturnal non-invasive ventilation (homeNIV) reduces hospitalizations and mortality.[3]

The initiation of homeNIV in the outpatient settings has been shown to be beneficial in patients with CHRF due to COPD.[2] Kohnlein et al. recruited patients with chronic hypoxemic respiratory failure and CHRF, defined as $PaCO_2$>52mmHg, from the clinic. The 1-year mortality decreased from 33% to 10% with homeNIV. Murphy and colleagues also demonstrated that homeNIV in patients that have persistent hypercapnia 2-4 weeks after hospital discharge reduces the chance of re-hospitalization or death within one year from 80.4% to 63.4%.[1] In both randomized controlled trials (RCTs), homeNIV was initiated in outpatient settings but participants underwent in-hospital acclimation and titration of the device. The recently published American Thoracic Society(ATS) guidelines recommend initiating homeNIV in the outpatient settings and advise against initiating HomeNIV upon hospital discharge for hypercapnic respiratory failure due to COPD.[4] However, the delay in initiating homeNIV for several weeks post-discharge leaves the patients vulnerable for re-hospitalizations during the immediate post-discharge period. Approximately 20% of patients hospitalized with COPD are re-hospitalized within one month.[5] The highest risk for re-hospitalization is two days after discharge.[6] Among those hospitalized with hypercapnic respiratory failure due to COPD, 40% will be re-hospitalized within 30 days.[7] It would make sense that homeNIV to be initiated upon discharge. Moreover, hospital staying may facilitate longer and several homeNIV education sessions relative to the education provided in a singe outpatient session at post-discharge follow-up. These are the reasons that several US academic centers initiate homeNIV upon discharge.[7-9] Why, then, do ATS guidelines recommend against the initiation of homeNIV upon discharge? The intention of the ATS guidelines is to avoid over-utilization of homeNIV and prolonging patient hospital stay to trend $PaCO_2$ and confirm CHRF. The rationale for this recommendation is based on two points described below. We also provide

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counterarguments explaining why homeNIV should be initiated in selected patients upon hospital discharge from the hospital following hypercapnic respiratory failure due to COPD.

1. *Can chronic hypercapnic respiratory failure be identified upon discharge?*

The ATS guidelines argue that patients with hypercapnia upon discharge may no longer be hypercapnic 2-4 weeks after hospital discharge. The rationale is primarily driven by findings of RTCs showing that the $PaCO_2$ may normalize in some patients without intervention when it is measured again at least 2-4 weeks after discharge in outpatient settings.[1 10] The Struik trial included patients hospitalized with COPD that had hypercapnia after discontinuation of non-invasive or invasive ventilation for at least 48 hours. Participants in that trials were randomized to homeNIV or control (no homeNIV).[10] In the control group, 26% of the participants experienced spontaneous resolution of hypercapnia within 3 months after discharge. One could argue that perhaps more time is needed to ensure that the state of the acute respiratory failure has resolved. However, the study design allowed the inclusion of patients with acute hypercapnic respiratory failure, not just those with acute-on-chronic. According to the publication baseline table, the mean pH in the control group was 7.39 with a standard deviation of 0.04 indicating that approximately 16% of participants had acidemia. Some of the participants who experienced spontaneous resolution of hypercapnia in the control group had acute hypercapnic respiratory failure. Furthermore, the Struik study showed that among hospitalized patients who still had hypercapnia after discontinuation of ventilatory support for at least 48 hours, $PaCO_2$ did not drop by more than 8 mmHg one year after hospitalization in 95% of them. Therefore, a $PaCO_2 \geq 60$mmHg upon discharge will not drop to lower than 52mmHg, which is the cut-off used in most of RTCs that showed benefit from homeNIV, in 95% of the cases because $PaCO_2$ cannot drop more than 8 mmHg (60-8=52 mmHg). These patients should be considered as having CHRF and be initiated on homeNIV upon discharge.

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Counterpoint: ***Hospitalized patients who are discontinued from invasive or non-invasive ventilatory support for at least 48 hours and have a $PaCO_2$>60 mmHg are likely have CHRF and may benefit from homeNIV.***

2. *Does initiating homeNIV upon discharge improve outcomes, including hospitalizations and mortality?*

ATS guidelines argue that although pooled data of RCTs might suggest potential benefit from initiating homeNIV upon discharge, initiating homeNIV upon discharge does not improve patient-important outcomes.[4] The rationale of this argument is based on the Struik study, which did not demonstrate any benefit in terms of re-hospitalization or death.[10] However, there are two limitations of the study: i) as mentioned above, the study design allowed inclusion of patients with acute hypercapnic respiratory failure who likely do not benefit from homeNIV and ii) despite randomization, there was a selection bias. The intervention group included patients with more severe disease, as 53% of the participants were on oral glucocorticosteroids compared to 38% in the control group. Although there is no RCT showing that homeNIV initiated upon discharge reduces hospitalizations in the 2-4-week post-discharge period, observation studies have shown benefit.[3] In addition, a recent claim data study showed that initiating homeNIV early was associated with reduction in mortality and Medicare expenditures. Patients with COPD who were prescribed homeNIV within 15 days of CHRF diagnosis had a $3,412 reduction in expenditures relative to patients did not receive homeNIV, and cost decreased by $2,072 more if homeNIV was prescribed with 7 days of CHRF diagnosis.

Counterpoint: ***Existing literature suggests that initiating homeNIV upon hospital discharge*** **following hypercapnic respiratory failure due to COPD may be beneficial.**

Although homeNIV implementation is rather a complicated process that requires close monitoring and follow-up, initiating homeNIV early in CHRF is critical because it is an intervention with huge

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impact. I propose that future guidelines should not discourage the initiation of homeNIV upon discharge in selected patients for the following reasons:

1. CHRF can be identified 48 hours after mechanical ventilator support is discontinued during hospital stay,
2. Initiating HomeNIV upon discharge may prevent re-hospitalizations during the most vulnerable period, immediately after discharge, for hypercapnia due to COPD.

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