Patient values and preferences

For this recommendation, we placed high value on NIV's beneficial impact on delaying hospital readmission and improving survival. Tolerance to high-intensity ventilation was also considered to be important for the widespread applicability of this treatment. Considering that high-intensity NIV was a prerequisite for success in recent clinical trials,[5,7] less emphasis was placed on the impact of NIV on costs and burden of utilization of long-term NIV.

Details of included studies

High versus low-intensity NIV

Dreher et al.[39] compared the effects of high versus low-intensity NIV on physiological outcomes and HRQoL in 13 patients with stable COPD and chronic hypercapnic respiratory failure ($PaCO_2 > 45$ mmHg) who were already on NIV and on LTOT. The aim of high-intensity ventilation was to maximally reduce $PaCO_2$ and this was done following a careful, in-hospital titration procedure. On average, an IPAP of 28 cmH_2O and an EPAP of 4.5 cmH_2O were used at a mean breathing frequency of 17.5 breaths/min. In comparison, the corresponding ventilatory parameters during low-intensity ventilation were: IPAP = 15 cmH_2O, EPAP = 4 cmH_2O, and breathing frequency of 8.0 breaths/min. Each ventilation strategy was applied for 6 weeks and all patients received nocturnal oxygen. $PaCO_2$ during nocturnal ventilation was the primary outcome. Other outcome measures included daytime $PaCO_2$ at rest while breathing oxygen, Borg dyspnea score immediately after a 6-min walking test, and HRQoL using the SRI. Significantly improved nighttime $PaCO_2$ while on ventilation was seen with high- compared to low-intensity NIV (mean difference of 9 mmHg) and this was related to larger tidal volume. In contrast, no between-treatment differences in daytime $PaCO_2$, 6-min walking distance, and HRQoL were observed. However, Borg dyspnea score immediately after a 6-min walking test was significantly improved in the high- compared to low-intensity NIV. Interestingly, adherence was significantly higher with high-intensity NIV by a mean of 3.6 hours per night.

Lukacsovits et al.[54] compared the short-term effects of high versus low-intensity NIV on $PaCO_2$, work of breathing, non-invasive determination of cardiac output, and Borg dyspnea score at rest while receiving ventilatory support in 15 patients with COPD and chronic hypercapnic respiratory failure ($PaCO_2 \geq 50$ mmHg). Low-intensity ventilation was delivered according to a local protocol aiming to reduce $PaCO_2$ by > 10%, achieving a VT of 6- ml/kg while reducing transdiaphragmatic pressure during tidal breathing by 50% of baseline value. These objectives were achieved with a mean IPAP of 17.7 cmH_2O and mean EPAP of 4 cmH_2O. High-intensity NIV was aimed at achieving the maximally tolerated pressure, at least 50% greater than with low-intensity NIV. This resulted in a mean IPAP of 27.6 cmH_2O and mean EPAP of 4 cmH_2O, thereby obtaining clear differences in the mean IPAP between the 2 ventilatory strategies. Each ventilatory strategy was applied for 30 minutes. High-intensity NIV improved breathing pattern, reduced work of breathing and $PaCO_2$ at the end of the ventilatory period compared to low-intensity NIV. However, no between-group differences in dyspnea were found. More air leakage and greater reductions in cardiac output were seen with high-pressure ventilation. This short-term physiological study did not allow any conclusion with regard to the superiority of 1 ventilatory strategy over the other but nevertheless, pointed out possible adverse effects of high-pressure NIV in patients with COPD.

Duiverman et al.[53] compared the effects of 6 weeks of high and low-intensity NIV on cardiac and pulmonary function in patients with COPD and chronic hypercapnic respiratory failure in a randomized, open-label, 2-treatment period crossover design. Fourteen patients with GOLD stage 3 or 4 COPD who had symptoms of chronic respiratory failure and either ≥ 2 severe acute exacerbations with acute hypercapnic respiratory failure (pH <7.35) and/or a daytime $PaCO_2 \geq 50$ mmHg and/or nocturnal $PaCO_2 \geq 52$ mmHg or a rise in $PtCO_2 \geq 7.5$ mmHg during the night were randomized in accordance with the German CPGs for Home Mechanical Ventilation in patients with stable COPD.[60] NIV was titrated in-hospital; high-intensity NIV aimed at establishing normocapnia or the lowest $PaCO_2$ value possible, according to patient's tolerance. A back-up breathing rate just above the spontaneous breathing frequency during sleep was used. This resulted in a mean IPAP of 23.6 cmH_2O and EPAP of 4–6 cmH_2O. Low-intensity NIV used an IPAP ≤ 14 cmH_2O and breathing frequency of ≤ 12 breaths/min. The primary outcome was percent change in cardiac output at rest, during spontaneous breathing after 6 weeks of treatment. Other outcome measures included the assessment of HRQoL (SRI, CAT), daytime $PaCO_2$, nt-proBNP, lung function, and 6-min walking distance. Six weeks of either high-intensity or low-intensity NIV did not affect cardiac output. This study was not powered for many of the outcomes but suggested a benefit over time of both high and low-intensity NIV on HRQoL and physiological parameters. There were no significant differences between the 2 strategies for daytime $PaCO_2$, night $PtCO_2$, FEV_1, HRQoL, and 6-min walking test.

PICO 3: When applying long-term NIV to patients with COPD, does volume-assured pressure-preset NIV compared to standard pressure-preset NIV improve:

1. **Dyspnea**
2. **HRQoL**
3. **Daytime $PaCO_2$**

Recommendation:

We **do not recommend** the use of volume-assured pressure-preset NIV over standard pressure-preset NIV in patients with COPD and chronic hypercapnic respiratory failure. (*strong recommendation, low certainty evidence*)

Clinical remarks

- Standard pressure-preset NIV (often referred to as pressure support ventilation) is the most commonly used mode of ventilation to treat chronic hypercapnic respiratory failure in patients with COPD.