Review

trd Tuberculosis & Respiratory Diseases

Home High-Flow Nasal Cannula in Patients with Chronic Respiratory Failure: A Literature Review and Suggestions for Clinical Practice

https://doi.org/10.4046/trd.2024.0196
ISSN: 1738-3536(Print)/
2005-6184(Online)
Tuberc Respir Dis 2025;88:264-277

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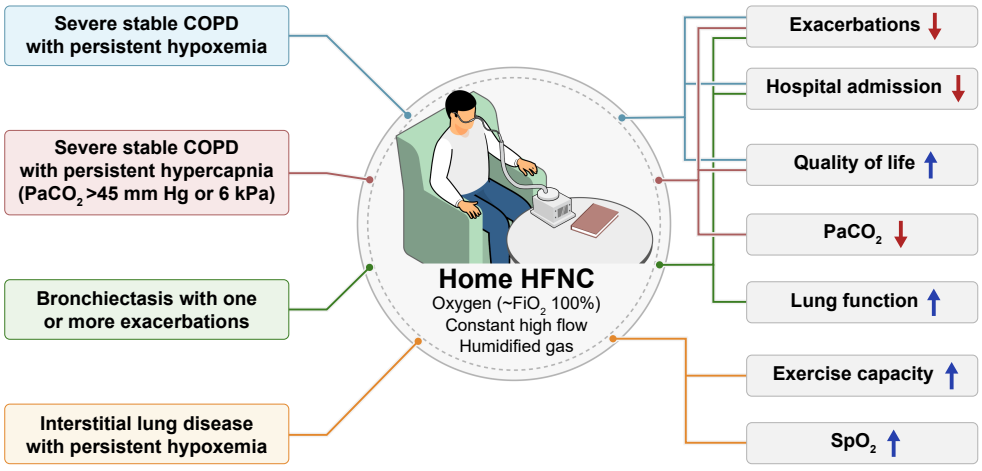

HFNC = high flow nasal cannula
COPD = chronic obstructive pulmonary disease

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Received Dec. 22, 2024
Revised Feb. 8, 2025
Accepted Feb. 12, 2025
Published online Feb. 18, 2025

Abstract

High-flow nasal cannula (HFNC) is a noninvasive respiratory support system that delivers air that is heated at 31°C–38°C, humidified 100%, and oxygen-enriched at a constant high flow rate of 15–60 L/min. Because of its numerous physiological benefits, convenience, and minimal side effects, HFNC has been increasingly used over the past decade in patients with acute hypoxemic respiratory failure, yet the clinical benefits of long-term HFNC remain uncertain. Several studies have suggested its potential use as an alternative home oxygen therapy for patients with chronic stable lung diseases,

such as chronic obstructive pulmonary disease (COPD), interstitial lung disease, and bronchiectasis. The use of long-term home HFNC in patients with chronic respiratory failure is an emerging area with promising potential. Despite limited clinical research, this review aims to describe the physiology of HFNC use and summarize the current evidence on its long-term application, to provide healthcare providers with insights and perspectives on the potential role of long-term home HFNC.

Keywords: High-Flow Nasal Cannula; Home; Oxygen; Chronic Lung Disease

Introduction

Oxygen therapy has been a cornerstone in the management of hypoxemia, and in supporting patients at risk of this condition[1]. Conventional oxygen therapy (COT), involving the delivery of oxygen via nasal cannula or face mask, has been the traditional frontline treatment for both acute and chronic hypoxemia[2]. However, the inadequate heating and humidification of the gas mean that its capacity to deliver oxygen is limited to flow rates of up to 15 L/min, which as flow rates increase, can cause patient discomfort[2].

High-flow nasal cannula (HFNC) oxygen therapy represents an advanced approach that can deliver oxygen at higher flow rates (above 15 L/min), while ensuring adequate heating and humidification[3]. Since the publication in 2015 by the FLORALI study group of the landmark randomized controlled trial (RCT), HFNC has gained considerable attention as an innovative, noninvasive respiratory support method[3,4]. Compared to COT, HFNC offers greater comfort and improved efficiency[5], and recent guidelines have endorsed HFNC over COT to manage hypoxemic acute respiratory failure[6,7].

In contrast to established international guidelines for long-term oxygen therapy (LTOT) and noninvasive ventilation (NIV)[8,9], the evidence supporting the use of HFNC in long-term home settings, particularly for hypercapnic respiratory failure, remains limited. While some studies have reported that long-term HFNC reduces exacerbation rates in patients with chronic airway diseases, such as chronic obstructive pulmonary disease (COPD)[10-12], other studies, including systematic meta-analyses, have yielded inconsistent findings[13-15]. These discrepancies may stem from the inclusion of heterogeneous study populations, combining acute and chronic patients, as well as short-term and long-term treatment protocols.

Although the benefits of home HFNC may not apply uniformly across all chronic respiratory patients, there may be specific subgroups that stand to benefit more from HFNC, compared to LTOT or NIV. This article reviews the existing literature to evaluate the role of HFNC in home oxygen therapy (Tables 1, 2)[10,11,16-36], and proposes optimal settings for its long-term use at home, based on findings from previous research (Table 3)[9,34,37].

Literature Search and Selection

The literature was searched in PubMed for relevant articles published in English up to June 2024. The indexing terms used were 'high flow nasal cannula' OR 'high flow therapy' OR 'high flow oxygen therapy' OR 'high flow nasal oxygen' OR 'nasal high flow' OR 'HFNC.' The terms 'home' OR 'domiciliary' OR 'long-term' were also used to retrieve publications that were focused on patients undergoing long-term HFNC therapy. Eligible studies included clinical research articles, reviews, meta-analyses, and case reports, while editorials were excluded. The full text of each searched article was reviewed by the authors, and finally, relevant articles were selected.

Physiology of HFNC

The HFNC system consists of a flow generator (e.g., air-oxygen blender with a flow meter), an active heated humidifier, a single-limb heated circuit, and a nasal cannula[38]. It can deliver flow rates of up to 60 L/min, and reliably achieve a fraction of inspired oxygen (FiO_2) of up to 100%. This system provides several physiological benefits that include improved mucociliary clearance, dead space washout, reduced work of breathing (WOB), and increased positive airway pressures[39,40].

1. Higher and more stable FiO_2

Alveolar oxygen delivery depends on the flow rate of supplemental oxygen, FiO_2, and the patient's spontaneous inspiratory demand[41]. Low-flow oxygen devices, such as nasal cannula or masks, can deliver oxygen

Table 1. Clinical studies of home HFNC on patients with stable COPD

Study	Patient groups	No. of patients	Study design	HFNC setting	Results
Rea et al. (2010)[10]	Stable COPD or bronchiectasis	108	Randomized, open-labeled, controlled trial: HFNC+usual care vs. usual care (12 mo)	Flow 20–25 L/min HFNC use 1.6±0.67 hr/day Temperature 37°C	↓ Exacerbation rate ↑ Time to first exacerbation ↑ QoL and lung function
Braunlich et al. (2015)[24]	Stable COPD with daytime hypercapnia ($PaCO_2$ ≥50 mm Hg)	11	Prospective cross-over study: HFNC vs. NIV (6/6 wk, at least 5 hr/day)	Flow 20 L/min (HFNC group) Device use >5 hr/day	Both HFNC and NIV reduced $PaCO_2$
Fraser et al. (2016)[26]	Stable COPD in LTOT	30	Randomized cross-over study: HFNC vs. LTOT (20 min for each)	Flow 30 L/min	↓ TcO_2, $TcCO_2$, RR, I:E ratio ↑ Vt and EELV
Pisani et al. (2017)[21]	Stable hypercapnic COPD	14	Randomized cross-over study	HFNC 20 L/min vs. 30 L/min vs. NIV (for every 30 min)	↓ RR, intrinsic PEEP and PTPdi More pronounced effects with mouth closed
Braunlich et al. (2018)[22]	Stable hypercapnic COPD ($PaCO_2$ >45 mm Hg)	36	Comparison between four conditions (different flow rates and nasal prong positions)	A: 20 L/min (two prongs inside) B: 40 L/min (two prongs inside) C: 40 L/min (one outside, open) D: 40 L/min (one outside, closed)	Greater reductions in $PaCO_2$ with higher flow rates and air leakages (D > C > B > A)
Nagata et al. (2018)[16]	Stable hypercapnic COPD	32	Randomized, cross-over study (9 hospitals): HFNC+LTOT vs. LTOT (6 wk for each)	Flow 29.2±1.9 L/min (A) Flow 30.3±4.6 L/min (B) HFNC use 7.1±1.3 hr/day (A) HFNC use 8.6±2.9 hr/day (B)	Improved $PaCO_2$, pH, and nocturnal $PtcCO_2$ ↑ QoL
Storgaard et al. (2018)[18]	COPD with hypoxemic respiratory failure in LTOT	200	Randomized clinical trial: HFNC+LTOT vs. LTOT (12 mo)	Flow 20 L/min HFNC use 6 hr/day	↓ AECOPD, hospital admission, and $PaCO_2$ ↑ mMRC, QoL, and 6MWT Similar mortality rates
Braunlich et al. (2019)[23]	Stable COPD with daytime hypercapnia ($PaCO_2$ ≥50 mm Hg)	94	Randomized, cross-over study (13 hospitals): HFNC vs. NIV (6 wk for each)	Flow 19.8±0.6 L/min HFNC use 5.2±3.3 hr/day NIV use 3.9±2.5 hr/day	Both HFNC and NIV reduced $PaCO_2$ and improved QoL
Weinreich et al. (2019)[27]	Advanced COPD patients with chronic hypoxic failure	100	*Post hoc* analysis from an RCT[18]: patients with 0 or 1 exacerbation vs. those with ≥2 exacerbations in the preceding year	HFNC use 6.1 vs. 6.0 hr/day	↓ Exacerbation & hospitalization rates in those with ≥2 exacerbations in the preceding year

Table 1. Continued

Study	Patient groups	No. of patients	Study design	HFNC setting	Results
Storgaard et al. (2020)[19]	COPD with hypoxemic and hypercapnic failure ($PaCO_2$ >45 mm Hg)	74	*Post hoc* analysis from an RCT[18]: 31 HFNC plus LTOT vs. 43 LTOT for 12 mo	Flow 20 L/min HFNC use 8 hr/day	↓ $PaCO_2$ (more effective for those with higher baseline $PaCO_2$) ↓ Exacerbation rate ↓ Hospital admission rate
Pisani et al. (2020)[20]	COPD (±OSA) with hypercapnia who recovered from AECOPD	50	One-arm study with patients with pH >7.35 and $PaCO_2$ >45 mm Hg	Temp 31°C, up to 37°C FiO_2 for SpO_2 target 92%–94% Flow 33.5±3.2 L/min HFNC use >8 hr/day (day and night)	↓ $PaCO_2$ for 72 hr (in pure COPD not in overlap [COPD/OSA]) More effective in those with lower baseline pH
Nagata et al. (2022)[17]	Stable COPD (GOLD 2–4; $PaCO_2$ >45 mm Hg and pH >7.35)	104	Multicenter RCT: 49 HFNC+LTOT vs. 60 LTOT for 12 mo	Temperature 37°C Flow 28.5±4.57 L/min HFNC use 7.3±3.0 hr/day	↓ AECOPD (moderate/severe) ↑ QoL (SGRQ) ↑ SpO_2
Weinreich et al. (2023)[25]	COPD with hypoxic or hypercapnic respiratory failure or both	33	LTOT plus HFNC vs. LTOT plus NIV for 12 mo	Not described	Both HFNC and NIV reduced hospitalization rates HFNC is more tolerable than NIV at the very end of COPD.
Milne et al. (2022)[32]	COPD on LTOT (cost-effectiveness study)	99	55 HFNC+LTOT vs. 44 LTOT	Not described	↑ Cost saving
Sorenssen et al. (2021)[11]	COPD with chronic hypoxic failure (cost-effectiveness study)	200	HFNC+usual care (LTOT) vs. usual care	Not described	↑ Health-related QoL ICER of £3,605 per QALY gained
Groessl et al. (2023)[33]	COPD on LTOT (cost-effectiveness study)	200 (data from an RCT[18])	QALYs using health utility values associated with acute exacerbations	Not described	↑ Healthcare benefit ↑ Cost saving

HFNC: high-flow nasal cannula; COPD: chronic obstructive pulmonary disease; QoL: quality of life; $PaCO_2$, partial pressure of carbon dioxide; NIV: noninvasive ventilation; LTOT: long-term oxygen treatment; TcO_2: transcutaneous O_2; $TcCO_2$: transcutaneous CO_2; RR: respiratory rate; I: inspiration; E: expiration; Vt: tidal volume; EELV: end-expiratory lung volume; PEEP: positive end-expiratory pressure; PTPdi: trans-diaphragmatic pressure–time product; $PtcCO_2$: transcutaneous PCO_2; AECOPD: acute exacerbation of COPD; mMRC: modified Medical Research Council; 6MWT: 6-minute walk test; RCT: randomized controlled trial; OSA: obstructive sleep apnea; FiO_2: fraction of inspired oxygen; SpO_2: saturation of partial pressure oxygen; GOLD: Global Initiative for Chronic Obstructive Lung Disease; SGRQ: St. George's Respiratory Questionnaire; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year.

at a maximum of 15 L/min. In these systems, room air containing 21% FiO_2 dilutes the high FiO_2 provided by the oxygen device[42]. In contrast, HFNC devices can meet or exceed the patient's inspiratory flow demand, which increases from 30 L/min at rest, to up to 100 L/min during respiratory failure[43]. By delivering flows higher than the patient's inspiratory demand, HFNC minimizes room air entrainment, enabling the accurate delivery of high FiO_2.

2. Dead space washout

By effectively removing expired gas from the upper

Table 2. Clinical studies of home HFNC on patients with bronchiectasis and ILD

Study	Patient groups	No. of patients	Study design	HFNC setting	Results
Hasani et al. (2008)[34]	Bronchiectasis	10	Physiology study: mucociliary clearance of (99 m)Tc-labelled polystyrene tracer particles	Flow 20–25 L/min HFNC use >3 hr/day Temperature 37°C	High flow via humidification system improved mucociliary clearance
Good et al. (2021)[28]	Bronchiectasis with 2 or more exacerbations in the previous year and daily sputum production	45	A *post hoc* analysis of a previous RCT (by Rea et al.[10]): HFNC vs. usual care (12 mo)	Temperature 37°C Flow 20–25 L/min HFNC use 1.7 hr/day	↓ Exacerbation rate ↑ Pulmonary function ↑ QoL (SGRQ)
Crimi et al. (2022)[29]	Bronchiectasis with a severe exacerbation in the previous year	40	Retrospective study: HFNC vs. optimized medical treatment (12 mo)	Temperature 34°C or 37°C Flow 20 (initial)–40 L/min HFNC use >6 hr/day (night) SpO_2 ≥92%	↓ Exacerbation rate ↓ Hospitalization ↑ Pulmonary function
Hui et al. (2020)[35]	Cancer involving the lungs without hypoxemia	44	Patients with SpO_2 >90% at rest: High-flow oxygen vs. high-flow air vs. low-flow oxygen vs. low-low air Symptom-limited cycle ergometry	High-flow air ~70 L/min High-flow oxygen 100% Low-flow oxygen and air 2 L/min Temp 35°C and 37°C	↓ Exertional dyspnea (Borg dyspnea intensity) ↑ Exercise capacity
Weinreich et al. (2022)[30]	ILD on AOT or LTOT	10	A retrospective, cross-over study: HFNC (6 wk) vs. observation (6 wk)	Temperature 37°C Flow 30 L/min HFNC use 6.5 hr/day (night)	↑ Walking distance ↓ Dyspnea (mMRC) ↑ Minimum SpO_2 during 6MWT
Harada et al. (2022)[36]	Stable IPF with desaturation during 6MWT (not home setting)	24	Randomized, open-labeled, cross-over study (a single center): 12 HFNC vs. 12 VM Symptom-limited cycle ergometry	HFNC 37°C, 60 L/min (flow), 50% (FiO_2) VM: 12 L/min and 50%	↑ Exercise duration ↑ Minimum SpO_2 ↓ Leg fatigue
Yanagita et al. (2024)[31]	Stable ILD (not home setting)	25	Three-treatment cross-over study: room air vs. HFNC (FiO_2 0.21) vs. HFNC with oxygen (FiO_2 0.60) Constant-load cycle ergometry.	Temp 34°C Humidification 100% Flow 40 L/min	↑ Exercise duration ↑ SpO_2

HFNC: high-flow nasal cannula; ILD: interstitial lung disease; RCT: randomized controlled trial; QoL: quality of life; SGRQ: St. George's Respiratory Questionnaire; SpO_2: saturation of partial pressure oxygen; AOT: ambulatory oxygen treatment; LTOT: long-term oxygen treatment; mMRC: modified Medical Research Council; 6MWT: 6-minute walk test; IPF: idiopathic pulmonary fibrosis; VM: venturi mask; FiO_2: fraction of inspired oxygen.

Table 3. Suggestions for home (long-term) HFNC

1. Indications (based on limited data)
Stable COPD with persistent hypoxemia
Alternating HFNC (night) and LTOT (daytime) is suggested.
RCTs demonstrated that compared to usual care (or LTOT) only, HFNC plus usual care decreased acute exacerbations and hospital admissions and improved quality of life.
Stable COPD with persistent hypercapnia ($PaCO_2$ >45 mm Hg or 6 kPa)
HFNC showed no significant difference in $PaCO_2$ reduction, compared to NIV.
HFNC plus LTOT decreased acute exacerbations and $PaCO_2$ and improved quality of life, compared to LTOT only.
However, home NIV should be considered the first option for COPD patients with hypercapnia in accordance with the guidelines[37]; home HFNC may serve as an alternative for COPD patients with mild to moderate hypercapnia.
Bronchiectasis with one or more exacerbations in the previous year
Small studies demonstrated that compared to usual care, HFNC decreased acute exacerbations and hospital admissions and improved lung function.
ILD with persistent hypoxemia
Short-term studies using cycle ergometry demonstrated that compared to traditional oxygen therapy, HFNC improved exercise capacity and SpO_2.
Currently, there are no studies on the long-term effects of HFNC.
2. Contraindications
No absolute contraindications, except for cases with poor adherence.*
3. Prescription
Home HFNC therapy should be prescribed by physicians.
The following HFNC settings should be stated in the prescription:
Flow (L/min), FiO_2 (%), oxygenation target (SpO_2), and a minimum time for HFNC use (6 hr/day)
For LTOT during the hours without HFNC, a separate prescription should be made by physicians according to the guidelines[9,34].
4. Settings
Nasal cannula size
Cross-sectional area should be no more than 50 % of the nares, or OD should be no more than 2/3 of the nares (according to the manufacturer's instructions).
Large-sized cannula may decrease nuisance from high flow and decrease noise. However, it can hinder the effective flush of CO_2.
Flow
A flow rate of 20–40 L/min was used in most studies on long-term HFNC.
Flow rates should be titrated from 15–20 L/min (initial flow) up to 20–40 L/min (if tolerated).
Higher flows should be avoided for home HFNC treatment, as they can decrease adherence.†
FiO_2 and target oxygenation
When the desired flow rate is reached, titrate FiO_2 until the target SpO_2 is obtained.
Target SpO_2 is equivalent to that of LTOT by the guidelines.‡
A home HFNC requires a large amount of oxygen supply, compared to conventional nasal cannulas.
Temperature
Target temperature is usually 37°C.
If 37°C is not tolerated, temperature can start from 31°C to 35°C.
Time of use
Daily use of HFNC of >6 hr/day should be encouraged.
5. Maintenance and follow-up visit
Maintenance of device (according to the manufacturer's instructions)
Patients/caregivers should be instructed about daily cleaning and maintenance of the equipment, in accordance with the manufacturer's instructions.
Do not fill with tap water (not boiled) or bottled water stored in warm conditions.
Filter and water chamber should be changed every 2 to 3 months.
Nasal cannula (with long tube) should be changed monthly.
A cotton pad or wipe containing alcohol can be used to disinfect the cannula between uses.
Nurses or providers need to check the condition of equipment regularly, as in the case of a home mechanical ventilator.
Follow-up
Regular follow-ups (outpatient visits) should be planned to check patient's condition.
During the regular follow-ups, appropriateness of flow rate and FiO_2, as well as adherence, should also be checked.

*However, caution may be necessary when applying home HFNC to patients with head trauma: there is a case report of tension pneumocephalus[68]. †For pediatric patients, a more delicate adjustment of flow rate and cannula size is needed. The use of inappropriately large-sized cannula or high flow rate may be associated with barotrauma. ‡Care should be taken when increasing FiO_2, as it can worsen existing hypercapnia in patients with COPD.
HFNC: high-flow nasal cannula; COPD: chronic obstructive pulmonary disease; LTOT: long-term oxygen treatment; $PaCO_2$, partial pressure of carbon dioxide; RCT: randomized controlled trial; NIV: noninvasive ventilation; ILD: interstitial lung disease; SpO_2: saturation of partial pressure oxygen; FiO_2: fraction of inspired oxygen; OD: outer diameter.

airways, HFNC reduces anatomical dead space[41]. This mechanism flushes out CO_2, creates an oxygen reservoir, increases alveolar ventilation, and reduces CO_2 rebreathing, leading to improved oxygenation[44]. The reduction of anatomical dead space is proportional to the increase in flow rate. Additionally, HFNC has been shown to improve thoraco-abdominal asynchrony in critically ill patients[45]. These effects collectively contribute to a reduction in dyspnea[46], and respiratory rate[47]. However, despite these advantages, robust evidence for CO_2 elimination using HFNC remains limited[48].

3. Delivery of warmed and humidified gas

The active heated humidifier in the HFNC system, along with the connected heated circuit, delivers warmed and humidified gas, offering multiple physiological benefits. Mucus secretion and mucociliary transport are vital to maintain respiratory defenses. The cilia lining the respiratory epithelium propel mucus, which traps particles and pathogens[49]. Since airway mucus is 97% water, adequate hydration is essential to effectively mobilize secretion. Dry gas inhalation can lead to epithelial desiccation, damage, and impaired mucosal function[50,51]. Proper humidification enhances mucociliary clearance, maintains mucosal function, and potentially reduces WOB[52]. Optimal alveolar temperature is 37°C with 100% relative humidity[53], and inhaling warmed air at this level further supports mucociliary clearance[51].

4. Increased positive airway pressure

Although HFNC is not a closed system and allows air leaks, increased flow rates induce expiratory resistance, thereby increasing nasopharyngeal airway pressure[54]. HFNC at a flow rate of 35 L/min with the mouth closed generates approximately 2.7 cmH_2O of airway pressure[54]. When the mouth is open, this pressure can decrease to 1.2 cmH_2O, but overall, mean airway pressure rises in proportion to increased flow rate[55-57]. Parke and McGuinness[57] demonstrated that HFNC could produce a positive end-expiratory pressure (PEEP) of 3–5 cmH_2O at flow rates of 30–50 L/min with the mouth closed. PEEP offers several benefits that include prevention of alveolar collapse, improved oxygenation, enhanced lung compliance, and reduced respiratory effort, ultimately decreasing WOB[54].

Home HFNC for Chronic Lung Diseases

1. COPD with hypercapnia

Recent studies have investigated the potential benefits of home HFNC in patients with chronic stable hypercapnic COPD (Table 1). Although data remain limited, evidence suggests that home HFNC may provide effects that are comparable to home NIV, including improved ventilation and symptom management. Moreover, compared to LTOT (defined as supplemental oxygen use for over 15 hours daily), home HFNC has shown promise in improving quality of life, lowering partial pressure of carbon dioxide ($PaCO_2$) levels, and reducing the frequency of moderate to severe exacerbations[10,16-20]. These findings highlight its potential role as an adjunct therapy to manage chronic hypercapnic COPD.

1) Physiologic study

A study involving 14 patients with stable hypercapnic COPD demonstrated that using HFNC at flow rates of 20–30 L/min reduced intrinsic PEEP, prolonged expiratory time, and decreased the trans-diaphragmatic pressure–time product[21]. These physiological changes improved lung mechanics, reduced diaphragm fatigue, and alleviated WOB, ultimately ameliorating hypercapnia. Notably, when patients kept their mouths closed, these effects were more pronounced, likely due to better pressure maintenance and reduced air leakage. Another study of 36 patients with stable hypercapnic COPD ($PaCO_2$ >45 mm Hg), using varying flow rates and degrees of air leakages, also showed significant reductions in hypercapnia across all participants[22]. However, those with higher flow rates (40 L/min) and higher air leakage (i.e., two prongs with one outside the nostril) experienced the greatest reductions in $PaCO_2$, particularly those with baseline $PaCO_2$ >55 mm Hg. This indicates airway washout and reduction of functional dead space, rather than increased mean airway pressure, as important mechanisms of HFNC therapy in this patient group.

2) Randomized controlled trials

Braunlich et al.[23] compared HFNC and NIV in COPD patients with baseline $PaCO_2$ levels of 50 mm Hg or higher. In this study, 94 patients alternated between HFNC and NIV treatments every 6 weeks. Although the NIV group showed a slightly greater reduction in $PaCO_2$ (−7.1% vs. −4.7% for HFNC), the difference was not statistically significant. These findings suggest that HFNC may offer comparable CO_2 reduction, with potentially greater comfort and ease of use.

A crossover RCT by Nagata et al.[16] studied COPD patients at Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages 2–4 with hypercapnia. Participants alternated between two 6-week periods: HFNC/LTOT (HFNC at night, and LTOT during waking hours), and LTOT alone. During the HFNC/LTOT phase,

patients used HFNC at 30–40 L/min for at least 4 hours during sleep. The results showed significant improvements in St. George's Respiratory Questionnaire (SGRQ) scores, $PaCO_2$ levels, nocturnal transcutaneous pCO_2, and exacerbation rates (0% vs. 19% for HFNC/LTOT vs. LTOT alone). A follow-up RCT also demonstrated that adding HFNC to LTOT reduced moderate to severe exacerbation rates, compared to LTOT alone over 52 weeks, with an adjusted exacerbation ratio of 2.85 (95% confidence interval, 1.48 to 5.47)[17]. Although most benefits were observed in moderate exacerbations, limiting conclusions about severe exacerbations or mortality, this marked the first RCT to demonstrate that home HFNC reduces exacerbations.

3) Non-randomized controlled trials

Studies that focus exclusively on hypercapnic COPD patients are limited. In 2015, Braunlich et al.[24] reported the results of a crossover study, which served as a precursor to their multicenter crossover RCT[23]. This earlier study involved stable hypercapnic COPD patients with $PaCO_2$ ≥50 mm Hg, who alternated between HFNC and NIV for at least 5 hours per day over a 6-week period. At the end of each intervention, no statistically significant differences between the two groups were found in the changes in $PaCO_2$. Although the NIV settings in this study were not explicitly described, HFNC was administered at a maximum flow rate of 20 L/min. Subsequent research by the same group included a *post hoc* analysis from an RCT originally conducted on COPD patients with chronic hypoxemic respiratory failure, focusing on those with hypercapnic respiratory failure[19]. This analysis demonstrated that over a 12-month period, patients receiving HFNC with LTOT showed reductions in $PaCO_2$ levels, exacerbation rates, and hospital admissions, compared to the LTOT-only group. A more recent retrospective study by Weinreich and Storgaard[25] compared long-term HFNC and long-term NIV as secondary add-on therapies for patients already on LTOT. Both groups showed reduced hospitalization rates over 12 months (HFNC: from 2.5 to 1.5 admissions, p=0.022; NIV: from 2.9 to 1.6 admissions, p=0.014).

2. COPD with hypoxemia

LTOT is known to prolong survival in COPD patients with severe resting hypoxemia[58-60]. Additionally, LTOT improves exercise capacity[61], neuropsychiatric function[62], health-related quality of life[63], and pulmonary hemodynamics[64]. HFNC therapy, which was originally designed for hospital use, is also gradually being introduced as a home-based treatment for patients with chronic respiratory diseases[26,44,65]. Short-term studies of patients with stable, advanced COPD and chronic hypoxemic respiratory failure showed HFNC therapy to be associated with reductions in respiratory rate and $PaCO_2$, as well as improved exercise performance[26,44,65].

Table 1 includes clinical studies of patients with COPD and chronic hypoxemic respiratory failure. In an RCT by Storgaard et al.[18] (the Aalborg study), 200 patients with COPD and chronic hypoxemic respiratory failure were randomized to receive usual care with or without HFNC. The HFNC group, who used the device for an average of 6 hours daily, demonstrated significantly fewer acute exacerbations (3.12/patient/year vs. 4.95/patient/year, p=0.001) and hospital admissions, along with improvements in modified Medical Research Council and SGRQ scores[18]. However, no significant difference between the two groups in all-cause mortality was observed. *Post hoc* analysis revealed that HFNC showed the greatest benefit in patients with two or more exacerbations in the year prior to the study, significantly reducing both exacerbation rates and hospitalization days[27]. Similarly, an RCT by Rea et al.[10] studied 108 patients with COPD or bronchiectasis who in the previous 12 months had experienced at least two exacerbations. Compared to the usual care, patients using humidification therapy over 12 months experienced fewer exacerbation days (18.2 days vs. 33.5 days, p=0.045), longer time to first exacerbation (52 days vs. 27 days, p=0.049), and improvements in quality of life and lung function[10]. However, the Aalborg study interestingly observed a significant reduction in exacerbation rates with a longer duration of HFNC use, i.e., 6–7 hr/day, which underscores the importance of consistent usage[18].

HFNC appears to be more effective than usual care or other home respiratory therapies as a long-term strategy to reduce exacerbations and enhance quality of life in patients with stable COPD. However, it does not improve all-cause mortality. Further real-world studies are required to clarify its effectiveness, and to determine optimal settings and usage durations, especially during sleep, to maximize its benefits.

3. Bronchiectasis

Bronchiectasis is a chronic condition that is characterized by persistent airway inflammation, leading to excessive production of purulent secretions and impaired secretion clearance due to reduced mucociliary function[66]. The accumulation of secretions can provide a nutrient-rich environment for bacterial overgrowth and obstruct the bronchial airways, which potentially results in respiratory failure[67]. HFNC delivers warm,

humidified gas that enhances mucociliary function and facilitates secretion clearance through sufficient liquefaction. This therapy improves gas exchange by reducing airway resistance, while also decreasing the risk of pneumonia[68]. Despite these potential benefits, research on the long-term use of HFNC in bronchiectasis remains limited. A *post hoc* analysis of the study by Rea et al.[10] and Good et al.[28] followed patients with bronchiectasis over 12 months, comparing outcomes between those treated with HFNC (humidified air at 37°C, 20–25 L/min for at least 2 hr/day), and those receiving usual care. Among 45 patients, the 26 who adhered to HFNC therapy experienced a significant reduction in acute exacerbation rates (2.39 exacerbations/patient/year vs. 3.48 exacerbations/patient/year) in the usual care group, and demonstrated notable improvements in lung function and SGRQ scores at 12 months[28]. Similarly, a retrospective case-control study involving 40 patients with bronchiectasis reported that when HFNC was used over a 12-month period for more than 6 hours daily, significant reductions in acute exacerbations and hospitalizations occurred, along with improved lung function[29]. Given the physiological benefits of HFNC and the encouraging findings from small clinical studies, long-term home HFNC therapy appears to offer promise for patients with bronchiectasis.

4. Interstitial lung diseases

In patients with interstitial lung disease (ILD), tidal volume decreases when increased lung elasticity cannot be adequately compensated by the strength of the respiratory muscles[69]. This reduction in tidal volume often results in progressive dyspnea, which worsens during exercise, and is frequently accompanied by hypoxemia and hypercapnia[70]. As a modality for respiratory support, HFNC can alleviate dyspnea in patients with ILD by increasing airway pressure and reducing functional dead space, thereby decreasing the WOB[52].

In a crossover retrospective study, 10 patients with ILD underwent alternating 6-week periods of home HFNC therapy (flow rate of 30 L/min, average usage of 6.5 hr/day) and standard oxygen therapy. While no significant improvements were observed in SGRQ scores or sleep quality, home HFNC therapy resulted in reduced dyspnea severity and improved exercise capacity[30]. Another recent study evaluated 25 patients with ILD using a 6 minutes walk test under three different conditions in a crossover design: room air (flow 0 L/min, FiO_2 0.21), HFNC (flow 40 L/min, FiO_2 0.21), and HFNC with oxygen supplementation (flow 40 L/min, FiO_2 0.6). Compared to the other two modalities, HFNC therapy with oxygen supplementation significantly improved exercise duration and resting saturation of partial pressure oxygen (SpO_2)[31]. Currently, data on the long-term use of home HFNC in ILD patients remains scarce. The benefits of HFNC in improving exercise capacity may depend on the severity of ILD. Future studies should investigate the potential role of home HFNC to enhance quality of life and prevent acute exacerbations in this patient population.

Cost-Effectiveness of Home HFNC

Three clinical studies have assessed the cost-effectiveness of long-term home HFNC therapy, particularly in patients with severe COPD. A New Zealand study demonstrated significant healthcare cost savings in patients receiving home HFNC, compared to those on LTOT alone[32]. Similarly, a Danish RCT found that adding HFNC to usual care was highly cost-effective, with an incremental cost-effectiveness ratio of £3,605 per quality-adjusted life-year (QALY) gained[11]. An American study reported that incorporating HFNC into standard treatment for severe COPD patients on LTOT resulted in both health benefits (incremental QALYs of 0.058) and cost savings (incremental total costs of −$3,939). These cost savings were attributed to reductions in exacerbation rates, which more than offset the higher device costs[33].

Safety Issues for Home HFNC

To date, RCTs have not identified significant safety concerns associated with the use of HFNC. Nagata et al.[16] in 2018 found the most common HFNC-related adverse event to be nighttime sweating, reported in six of 32 patients in the HFNC group, and one patient in the LTOT group; this was classified as a mild adverse event, and no cases resulted in the discontinuation of HFNC therapy. Similarly, an RCT by Nagata et al.[17] in 2022 found no HFNC-related safety issues. Braunlich et al.[23] in 2019 compared HFNC with NIV, observing non-lethal serious adverse events to be more frequent in the NIV group. While panic attacks were more commonly associated with NIV, HFNC was linked to a higher incidence of epistaxis, nasal dryness, and nasal irritation. Although rare, a case report described HFNC-induced tension pneumocephalus in a patient with head trauma, highlighting the need for caution when applying HFNC to individuals with suspected skull base or paranasal sinus fractures, particularly at higher flow rates[71].

Discussion

Long-term HFNC therapy has been increasingly adopted recently as a home-based respiratory treatment for various chronic lung diseases. Compared to traditional home oxygen therapy, HFNC provides superior humidification, which supports mucociliary clearance[72,73], while offering physiological benefits[41,74], with added convenience and minimal side effects[12,75,76]. While the clinical efficacy of HFNC in hospital settings is well-documented, research on its long-term use at home for patients with chronic lung diseases remains limited. Nevertheless, home HFNC therapy has attracted growing attention from clinicians, with the publication of the first guidelines on long-term HFNC therapy by the Danish Respiratory Society[77].

Most studies on home HFNC therapy have focused on patients with COPD, with limited research on other chronic lung diseases, such as bronchiectasis and ILD. Much of the evidence among COPD patients pertains to those with persistent hypoxemic failure, where when added to LTOT, home HFNC therapy has been associated with significant reductions in exacerbation and hospitalization rates, as well as improvements in quality of life and exercise tolerance[16,18,46,78,79]. While data on stable hypercapnic COPD are more limited, home HFNC therapy has demonstrated benefits in these patients in reducing $PaCO_2$ levels and exacerbation rates[17,20,23,29,46]. Recent meta-analysis also reported a reduction in exacerbation rates and improved quality of life among COPD patients with chronic hypercapnia, compared to those who received COT[15,48].

NIV is well-established in reducing $PaCO_2$ levels in hypercapnic COPD patients, and is indicated for those with persistent hypercapnia following acute exacerbation of COPD[8], though discomfort and intolerance to NIV often hinder its long-term use at home. In contrast, HFNC is simpler, more comfortable, and hence a viable alternative for long-term therapy. Studies have shown no significant differences in reducing $PaCO_2$ or hospitalization rates between home HFNC and NIV[23-25]. In cases where home NIV is not tolerated or indicated, home HFNC may thus serve as an alternative for COPD patients with mild to moderate hypercapnia. However, clinicians need to be aware that as flow rates increase, adherence to HFNC therapy may decline[80], while in some patients with chronic hypercapnia, higher FiO_2 levels could exacerbate hypercapnia[9,81].

In this review, we provide suggestions for the clinical use of home (long-term) HFNC (Table 3). While data remain insufficient, we believe offering preliminary guidance for healthcare providers is necessary. First, we outline potential indications for home HFNC based on previous study populations, including stable COPD with hypoxemic or hypercapnic respiratory failure, bronchiectasis with exacerbations in the previous year, and ILD with persistent hypoxemia. We further propose optimal HFNC settings derived primarily from expert opinions and manufacturers' instructions, rather than clinical trials, in the hope that these suggestions will assist clinicians in prescribing home HFNC, and support medical staff in managing these patients.

However, this review has several limitations that need to be acknowledged. First, the referenced studies used diverse designs and HFNC settings, which might affect the generalizability of their findings; also, both trials and participants included were relatively small in number, with significant variability in follow-up durations across studies. Second, most studies focused on stable patients, leaving uncertainty about whether patients with more severe conditions would experience similar benefits. Third, this review does not comprehensively address the potential limitations of home HFNC. Notably, the cost of home HFNC devices and their operation is higher than that of LTOT; this may pose a barrier to widespread long-term use. Also, current HFNC systems are less portable than LTOT, potentially restricting patient mobility and affecting quality of life. Hence, given the limited evidence that is available, home HFNC should be considered only for selected patient populations. Finally, a significant gap in the literature exists regarding data from Korea, while the absence of insurance coverage for home HFNC poses a substantial barrier to its broader application. Addressing these challenges will require strategies such as the development of more cost-effective HFNC devices, the conducting of cost-effectiveness and long-term effectiveness studies to inform policy decisions, and advocacy for insurance reimbursement policies.

In conclusion, the efficacy of home HFNC therapy has been demonstrated in managing chronic lung diseases, such as COPD, ILD, and bronchiectasis, with the potential for broader clinical adoption. Further large-scale studies are needed to identify target populations, refine application methods, and establish comprehensive management strategies. In particular, comparative studies between home HFNC and COTs, as well as subgroup analyses for specific patient populations—such as those with severe chronic respiratory failure—are essential to better define its role in clinical practice. These efforts will provide the evidence required for the development of definitive practice guidelines and supportive insurance policies.

Authors' Contributions

Conceptualization: Chang Y, Kim JW, Cho JH, Park S. Methodology: Chang Y, Baek MS, Kim SW, Lee SH, Kim JS, Park SY, Park S. Formal analysis: Chang Y, Park S. Data curation: Chang Y, Baek MS, Kim SW, Lee SH, Kim JS, Park SY, Park S. Project administration: Chang Y, Park S. Visualization: Chang Y, Park S. Software: Chang Y, Park S. Validation: Kim JW, Cho JH, Park S. Investigation: Chang Y, Baek MS, Kim SW, Lee SH, Kim JS, Park SY, Park S. Writing - original draft preparation: Chang Y, Baek MS, Kim SW, Lee SH, Kim JS, Park SY, Park S. Writing - review and editing: Chang Y, Park S. Approval of final manuscript: all authors.

Conflicts of Interest

Jae Hwa Cho is a deputy editor of the journal, but he was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

Acknowledgments

We wish to thank Tai Sun Park (Hanyang University Guri Hospital), Ae-Rin Baek (Soonchunhyang University Bucheon Hospital), Jick Hwan Ha (Incheon St. Mary's Hospital), and Hyonsoo Joo (Uijeongbu St. Mary's Hospital) for their assistance in data collection and interpretation.

Funding

No funding to declare.

References

1. Choudhury R. Hypoxia and hyperbaric oxygen therapy: a review. Int J Gen Med 2018;11:431-42.
2. O'Driscoll BR, Howard LS, Earis J, Mak V. British Thoracic Society guideline for oxygen use in adults in healthcare and emergency settings. BMJ Open Respir Res 2017;4:e000170.
3. Spicuzza L, Schisano M. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. Ther Adv Chronic Dis 2020;11:2040622320920106.
4. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 2015;372:2185-96.
5. Jacome C, Jacome M, Correia S, Flores I, Farinha P, Duarte M, et al. Effectiveness, adherence and safety of home high flow nasal cannula in chronic respiratory disease and respiratory insufficiency: a systematic review. Arch Bronconeumol 2024;60:490-502.
6. Oczkowski S, Ergan B, Bos L, Chatwin M, Ferrer M, Gregoretti C, et al. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. Eur Respir J 2022;59:2101574.
7. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, et al. The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med 2020;46:2226-37.
8. Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017;50:1602426.
9. Jacobs SS, Krishnan JA, Lederer DJ, Ghazipura M, Hossain T, Tan AM, et al. Home oxygen therapy for adults with chronic lung disease: an official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med 2020;202:e121-41.
10. Rea H, McAuley S, Jayaram L, Garrett J, Hockey H, Storey L, et al. The clinical utility of long-term humidification therapy in chronic airway disease. Respir Med 2010;104:525-33.
11. Sorensen SS, Storgaard LH, Weinreich UM. Cost-effectiveness of domiciliary high flow nasal cannula treatment in COPD patients with chronic respiratory failure. Clinicoecon Outcomes Res 2021;13:553-64.
12. Maggiore SM, Jaber S, Grieco DL, Mancebo J, Zakynthinos S, Demoule A, et al. High-flow versus venturimask oxygen therapy to prevent reintubation in hypoxemic patients after extubation: a multicenter randomized clinical trial. Am J Respir Crit Care Med 2022;206:1452-62.
13. Bonnevie T, Elkins M, Paumier C, Medrinal C, Combret Y, Patout M, et al. Nasal high flow for stable patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. COPD 2019;16:368-77.
14. Duan L, Xie C, Zhao N. Effect of high-flow nasal cannula oxygen therapy in patients with chronic obstructive pulmonary disease: a meta-analysis. J Clin Nurs 2022;31:87-98.
15. Yang H, Huang D, Luo J, Liang Z, Li J. The use of high-flow nasal cannula in patients with chronic obstructive pulmonary disease under exacerbation and stable phases: a systematic review and meta-analysis. Heart Lung 2023;60:116-26.
16. Nagata K, Kikuchi T, Horie T, Shiraki A, Kitajima T, Kadowaki T, et al. Domiciliary high-flow nasal cannula oxygen therapy for patients with stable hypercapnic chronic obstructive pulmonary disease: a multicenter random-

ized crossover trial. Ann Am Thorac Soc 2018;15:432-9.
17. Nagata K, Horie T, Chohnabayashi N, Jinta T, Tsugitomi R, Shiraki A, et al. Home high-flow nasal cannula oxygen therapy for stable hypercapnic COPD: a randomized clinical trial. Am J Respir Crit Care Med 2022;206:1326-35.
18. Storgaard LH, Hockey HU, Laursen BS, Weinreich UM. Long-term effects of oxygen-enriched high-flow nasal cannula treatment in COPD patients with chronic hypoxemic respiratory failure. Int J Chron Obstruct Pulmon Dis 2018;13:1195-205.
19. Storgaard LH, Hockey HU, Weinreich UM. Development in PaCO2 over 12 months in patients with COPD with persistent hypercapnic respiratory failure treated with high-flow nasal cannula-post-hoc analysis from a randomized controlled trial. BMJ Open Respir Res 2020;7:e000712.
20. Pisani L, Betti S, Biglia C, Fasano L, Catalanotti V, Prediletto I, et al. Effects of high-flow nasal cannula in patients with persistent hypercapnia after an acute COPD exacerbation: a prospective pilot study. BMC Pulm Med 2020;20:12.
21. Pisani L, Fasano L, Corcione N, Comellini V, Musti MA, Brandao M, et al. Change in pulmonary mechanics and the effect on breathing pattern of high flow oxygen therapy in stable hypercapnic COPD. Thorax 2017;72:373-5.
22. Braunlich J, Mauersberger F, Wirtz H. Effectiveness of nasal highflow in hypercapnic COPD patients is flow and leakage dependent. BMC Pulm Med 2018;18:14.
23. Braunlich J, Dellweg D, Bastian A, Budweiser S, Randerath W, Triche D, et al. Nasal high-flow versus noninvasive ventilation in patients with chronic hypercapnic COPD. Int J Chron Obstruct Pulmon Dis 2019;14:1411-21.
24. Braunlich J, Seyfarth HJ, Wirtz H. Nasal high-flow versus non-invasive ventilation in stable hypercapnic COPD: a preliminary report. Multidiscip Respir Med 2015;10:27.
25. Weinreich UM, Storgaard LH. A real-life study of combined treatment with long-term non-invasive ventilation and high flow nasal cannula in patients with end-stage chronic obstructive lung disease. J Clin Med 2023;12:4485.
26. Fraser JF, Spooner AJ, Dunster KR, Anstey CM, Corley A. Nasal high flow oxygen therapy in patients with COPD reduces respiratory rate and tissue carbon dioxide while increasing tidal and end-expiratory lung volumes: a randomized crossover trial. Thorax 2016;71:759-61.
27. Weinreich UM. Domiciliary high-flow treatment in patients with COPD and chronic hypoxic failure: in whom can we reduce exacerbations and hospitalizations? PLoS One 2019;14:e0227221.
28. Good WR, Garrett J, Hockey HU, Jayaram L, Wong C, Rea H. The role of high-flow nasal therapy in bronchiectasis: a post hoc analysis. ERJ Open Res 2021;7:00711-2020.
29. Crimi C, Nolasco S, Campisi R, Nigro M, Impellizzeri P, Cortegiani A, et al. Long-term domiciliary high-flow nasal therapy in patients with bronchiectasis: a preliminary retrospective observational case-control study. J Clin Med 2022;11:7323.
30. Weinreich UM, Burchardt C, Huremovic J. The effect of domiciliary high flow nasal cannula treatment on dyspnea and walking distance in patients with interstitial lung disease: a pilot study. Chron Respir Dis 2022;19:14799731221137085.
31. Yanagita Y, Arizono S, Yokomura K, Ito K, Machiguchi H, Tawara Y, et al. Enhancing exercise tolerance in interstitial lung disease with high-flow nasal cannula oxygen therapy: a randomized crossover trial. Respirology 2024;29:497-504.
32. Milne RJ, Hockey HU, Garrett J. Hospital cost savings for sequential COPD patients receiving domiciliary nasal high flow therapy. Int J Chron Obstruct Pulmon Dis 2022;17:1311-22.
33. Groessl EJ, Tally SR, Hillery N. Cost-effectiveness of humidified high-flow therapy (HHFT) for COPD patients on long-term oxygen therapy. Clinicoecon Outcomes Res 2023;15:239-50.
34. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis 2008;5:81-6.
35. Hui D, Mahler DA, Larsson L, Wu J, Thomas S, Harrison CA, et al. High-flow nasal cannula therapy for exertional dyspnea in patients with cancer: a pilot randomized clinical trial. Oncologist 2021;26:e1470-9.
36. Harada J, Nagata K, Morimoto T, Iwata K, Matsunashi A, Sato Y, et al. Effect of high-flow nasal cannula oxygen therapy on exercise tolerance in patients with idiopathic pulmonary fibrosis: a randomized crossover trial. Respirology 2022;27:144-51.
37. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2024 report) [Internet]. Deer Park: GOLD; 2024 [cited 2025 Mar 5]. Available from: https://goldcopd.org/2024-gold-report.
38. Nishimura M. High-flow nasal cannula oxygen therapy devices. Respir Care 2019;64:735-42.
39. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults: mechanisms of action and clinical implications. Chest 2015;148:253-61.
40. D'Cruz RF, Hart N, Kaltsakas G. High-flow therapy: physiological effects and clinical applications. Breathe (Sheff) 2020;16:200224.
41. Moller W, Feng S, Domanski U, Franke KJ, Celik G, Bartenstein P, et al. Nasal high flow reduces dead space. J

Appl Physiol (1985) 2017;122:191-7.
42. Bazuaye EA, Stone TN, Corris PA, Gibson GJ. Variability of inspired oxygen concentration with nasal cannulas. Thorax 1992;47:609-11.
43. Puddy A, Younes M. Effect of inspiratory flow rate on respiratory output in normal subjects. Am Rev Respir Dis 1992;146:787-9.
44. Chatila W, Nugent T, Vance G, Gaughan J, Criner GJ. The effects of high-flow vs low-flow oxygen on exercise in advanced obstructive airways disease. Chest 2004;126:1108-15.
45. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med 2011;37:1780-6.
46. Cirio S, Piran M, Vitacca M, Piaggi G, Ceriana P, Prazzoli M, et al. Effects of heated and humidified high flow gases during high-intensity constant-load exercise on severe COPD patients with ventilatory limitation. Respir Med 2016;118:128-32.
47. Mundel T, Feng S, Tatkov S, Schneider H. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. J Appl Physiol (1985) 2013;114:1058-65.
48. Zhang L, Wang Y, Ye Y, Gao J, Zhu F, Min L. Comparison of high-flow nasal cannula with conventional oxygen therapy in patients with hypercapnic chronic obstructive pulmonary disease: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2023;18:895-906.
49. Wanner A, Salathe M, O'Riordan TG. Mucociliary clearance in the airways. Am J Respir Crit Care Med 1996; 154(6 Pt 1):1868-902.
50. Fahy JV, Dickey BF. Airway mucus function and dysfunction. N Engl J Med 2010;363:2233-47.
51. Williams R, Rankin N, Smith T, Galler D, Seakins P. Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. Crit Care Med 1996;24:1920-9.
52. Park S. High-flow nasal cannula for respiratory failure in adult patients. Acute Crit Care 2021;36:275-85.
53. Dery R. Humidity in anaesthesiology: IV. determination of the alveolar humidity and temperature in the dog. Can Anaesth Soc J 1971;18:145-51.
54. Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med 2017;195:1207-15.
55. Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. Aust Crit Care 2007;20:126-31.
56. Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. Br J Anaesth 2009;103:886-90.
57. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. Respir Care 2013;58:1621-4.
58. Kent BD, Mitchell PD, McNicholas WT. Hypoxemia in patients with COPD: cause, effects, and disease progression. Int J Chron Obstruct Pulmon Dis 2011;6:199-208.
59. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial: nocturnal oxygen therapy trial group. Ann Intern Med 1980;93: 391-8.
60. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema: report of the medical research council working party. Lancet 1981;1:681-6.
61. Morrison DA, Stovall JR. Increased exercise capacity in hypoxemic patients after long-term oxygen therapy. Chest 1992;102:542-50.
62. Wedzicha JA. Effects of long-term oxygen therapy on neuropsychiatric function and quality of life. Respir Care 2000;45:119-26.
63. Eaton T, Lewis C, Young P, Kennedy Y, Garrett JE, Kolbe J. Long-term oxygen therapy improves health-related quality of life. Respir Med 2004;98:285-93.
64. Zielinski J, Tobiasz M, Hawrylkiewicz I, Sliwinski P, Pałasiewicz G. Effects of long-term oxygen therapy on pulmonary hemodynamics in COPD patients: a 6-year prospective study. Chest 1998;113:65-70.
65. Nilius G, Franke KJ, Domanski U, Ruhle KH, Kirkness JP, Schneider H. Effects of nasal insufflation on arterial gas exchange and breathing pattern in patients with chronic obstructive pulmonary disease and hypercapnic respiratory failure. Adv Exp Med Biol 2013;755:27-34.
66. Murray MP, Turnbull K, MacQuarrie S, Pentland JL, Hill AT. Validation of the Leicester cough questionnaire in non-cystic fibrosis bronchiectasis. Eur Respir J 2009;34: 125-31.
67. Chalmers JD, Smith MP, McHugh BJ, Doherty C, Govan JR, Hill AT. Short- and long-term antibiotic treatment reduces airway and systemic inflammation in non-cystic fibrosis bronchiectasis. Am J Respir Crit Care Med 2012; 186:657-65.
68. Sotello D, Rivas M, Mulkey Z, Nugent K. High-flow nasal cannula oxygen in adult patients: a narrative review. Am J Med Sci 2015;349:179-85.
69. Braunlich J, Kohler M, Wirtz H. Nasal high-flow (NHF) improves ventilation in patients with interstitial lung disease (ILD): a physiological study. J Clin Med 2023;12:5853.
70. Faverio P, De Giacomi F, Bonaiti G, Stainer A, Sardella L, Pellegrino G, et al. Management of chronic respiratory failure in interstitial lung diseases: overview and clinical insights. Int J Med Sci 2019;16:967-80.
71. Chang Y, Kim TG, Chung SY. High-flow nasal cannula-in-

duced tension pneumocephalus. Indian J Crit Care Med 2020;24:592-5.
72. Chikata Y, Izawa M, Okuda N, Itagaki T, Nakataki E, Onodera M, et al. Humidification performance of two high-flow nasal cannula devices: a bench study. Respir Care 2014;59:1186-90.
73. Chikata Y, Morinishi K, Nishimura M. Humidification in very-high-flow nasal-cannula therapy in an adult lung model. Respir Care 2019;64:809-17.
74. Pisani L, Vega ML. Use of nasal high flow in stable COPD: rationale and physiology. COPD 2017;14:346-50.
75. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation: effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med 2014;190:282-8.
76. Nishimura M. High-flow nasal cannula oxygen therapy in adults. J Intensive Care 2015;3:15.
77. Weinreich UM, Juhl KS, Soby Christophersen M, Gundestrup S, Hanifa MA, Jensen K, et al. The Danish Respiratory Society guideline for long-term high flow nasal cannula treatment, with or without supplementary oxygen. Eur Clin Respir J.2023;10:2178600.
78. Storgaard LH, Weinreich UM, Laursen BS. COPD patients' experience of long-term domestic oxygen-enriched nasal high flow treatment: a qualitative study. COPD 2020;17:175-83.
79. Criner GJ, Criner LH, George SA, Thomas JK, Jacobs MR. Feasibility of using daily home high-flow nasal therapy in COPD patients following a recent COPD hospitalization. Chronic Obstr Pulm Dis 2022;9:4-14.
80. Elshof J, Duiverman ML. Clinical evidence of nasal high-flow therapy in chronic obstructive pulmonary disease patients. Respiration 2020;99:140-53.
81. Park YB, Rhee CK, Yoon HK, Oh YM, Lim SY, Lee JH, et al. Revised (2018) COPD clinical practice guideline of the Korean Academy of Tuberculosis and Respiratory Disease: a summary. Tuberc Respir Dis (Seoul) 2018;81:261-73.