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# Acute and long-term management of severe bronchiectasis with high-flow nasal therapy: A case report

**Pietro Impellizzeri[1*], Santi Nolasco[1*], Raffaele Campisi[2], Antonino Cipolla[1], Alba Borgese[1], Stefano Alia[2], Nunzio Crimi[1], Claudia Crimi[2]**

*[1]Department of Clinical and Experimental Medicine, University of Catania; [2]Respiratory Medicine Unit, Policlinico "G. Rodolico - San Marco" University Hospital, Catania, Italy*

**Co-first author; these authors contributed equally to this work.*

## Abstract

Bronchiectasis (BE) is a long-term, chronic lung condition featured by widened and scarred airways. These can alter the physiological mucociliary clearance, making it difficult to clear mucus and microorganisms, leading to frequent exacerbations. High-flow nasal therapy (HFNT) is a noninvasive respiratory support that delivers heated and humidified gas eventually enriched with oxygen, through a nasal cannula. Humidification is crucial for adequate airways mucociliary clearance, improving ciliary function and consequently reducing airways inflammation and recurrent infections. HFNT has been mostly used in patients with acute hypoxemic respiratory failure and in selected patients with chronic respiratory failure due to COPD. Still, evidence about its use in acute and long-term home setting in patients with clinically relevant BE are lacking. We report a case of severe widespread BE, already on top medical therapy and pulmonary rehabilitation, still suffering from difficult mucus expectoration and recurrent exacerbations, who has been additionally treated with HFNT, both in hospital and domiciliary, reporting significant improvements on relevant clinical and patient-centred outcomes. Thus, HFNT may confer additional benefits as an add-on treatment of patients with severe BE and respiratory failure.

Correspondence: Claudia Crimi, Respiratory Medicine Unit, A.O.U. Policlinico "G. Rodolico - San Marco", Catania, Italy.
Tel. +39.095.3781253.
E-mail: dott.claudiacrimi@gmail.com

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## Introduction

Bronchiectasis (BE) is a chronic airway disease characterized by irreversible bronchial dilatation and disruption of mucociliary clearance which can lead to infection and inflammation. Indeed, BE is a disabling and progressively worsening condition, responsible for high healthcare costs due to frequent exacerbations [1].

High-flow nasal therapy (HFNT) is a relatively recent type of noninvasive respiratory support, which provides heated and humidified gas eventually enriched with oxygen, through a nasal cannula. Humidification is crucial for adequate airways mucociliary clearance, and mucus hydration [2,3], improving ciliary function and consequently reducing airways inflammation and recurrent infections. Despite is well established that optimal cilia movements occur at core temperature and high humidity [2-4], data on HFNT effectiveness in patients with severe bronchiectasis management are still lacking. Few studies have shown that HFNT improves mobilization and fluidification of pulmonary secretions in patients with chronic muco-obstructive lung diseases [5-7].

Here, we present a case of a patient affected with severe non-cystic fibrosis BE, who had been admitted to the hospital for an acute exacerbation which had been managed with maximal pharmacological therapy and airway clearance techniques as suggested by guidelines [8] combined with HFNT. Later on, upon discharge, he had been prescribed long-term domiciliary HFNT with improvement in the ease of expectoration and reduction of airways mucus

accumulation, confirmed *via* high-resolution chest computed tomography scan at 6-month follow-up. To our knowledge this is the first study to describe a case of severe bronchiectasis treated with HFNT both in acute and chronic settings.

## Case Report

An 80-year-old male, former occasional smoker (<1 pack-years), with a medical history of osteoporosis, glaucoma and ulcerative colitis, has been regularly followed-up in our Respiratory Medicine outpatient Unit for his severe non-cystic fibrosis cylindrical BE since 2017. His usual therapeutic regimen over the years was umeclidinium bromide/vilanterol 55 mcg/22 mcg, one puff/day, with good inhaler adherence and technique, long-term azithromycin and airways clearance techniques, including postural drainage and respiratory physiotherapy in order to facilitate the excretion of his thick yellowish secretions. During the regular visits in our outpatient service, cystic fibrosis diagnosis, alfa-1 antitrypsin deficiency, and immune deficiency were excluded. Multiple sputum samples, collected a minimum of 3 months apart [9], were negative for acid-fast bacilli and non-tuberculous mycobacteria, but confirmed the presence of *Pseudomonas aeruginosa* chronic colonization, despite three attempts of eradication.

Notwithstanding this high-regimen therapy, he referred difficult expectoration, rated 8-9 using a 10-cm visual analog scale (VAS, 0 = extremely easy; 10 = extremely difficult) and persistent symptoms, in concordance with a Saint George Respiratory Questionnaire (SGRQ) [10] total score of 47. The patient complains nearly 5 exacerbations per year, with a hospitalization rate of 3 admissions per year. Indeed, his bronchiectasis severity Index was 16, suggesting severe BE.

In December 2020, he was admitted to the hospital due to worsening dyspnoea [modified Medical Research Council scale (mMRC)] [4], productive cough with increased sputum, which had changed from yellow to greenish, fatigue, fever (37.8°C), increased respiratory rate (26 breaths/minute) and low oxygen saturation at rest in room air ($SpO_2$ 84%). Auscultation of the chest revealed widespread rhonchi, wheezing and crackles. Arterial blood gas analysis (ABG) in room air revealed the presence of acute hypercapnic respiratory failure (pH 7.31, $PaCO_2$ 72.4 mmHg, $PaO_2$ 51.3 mmHg, $SaO_2$ 84.1 %). Laboratory tests showed high C-reactive protein (81 mg/dL), and neutrophilic leukocytosis (17.000 cells/µL). Protein Chain Reaction test for SARS-CoV2 was negative. Chest HRCT scan confirmed the presence of multiple varicose and cystic bronchiectasis, with an almost ubiquitous distribution, prevalent at the bases, with marked bronchial cuffing and mucoid content, especially in the right basal area with concomitant centrilobular involvement and "tree-in-bud" appearance (Figure 1).

Oxygen was administered via Venturi-mask ($FiO_2$ 31%), to maintain a $SpO_2$ ≥92%. Empiric antibiotic therapy with intravenous levofloxacin 500 mg once every 24 hours and Meropenem 1 g every 8 hours, in addition to methylprednisolone 1 mg/kg once a day, were initiated at hospital admission. On day 3, due to the persistence of productive cough with abundant purulent sputum and difficult expectoration despite pharmacological treatment and airway clearance techniques, and fatigue with high respiratory rate, HFNT (MyAirvo 2, Fisher & Paykel Healthcare) was started with a flow of 40 L/min, $FiO_2$ 28% and temperature of 37°C. The size of the high flow nasal cannula (Optiflow; Fisher & Paykel Healthcare) was selected to occlude a patient's nostril of about 2/3 of their size.

From day 4, the patient referred a substantial improvement in the ease of mucus expectoration and a slight decrease in dyspnoea (mMRC 2-3) and respiratory rate (14 breaths/min). On day 5, sputum cultures resulted positive for *Pseudomonas aeruginosa* and inhaled tobramycin (300 mg/ 5 ml) every 12 hours was added. The patient continued HFNT with adequate compliance for at least 18 hours a day. On day 12 sputum culture was negative and he referred a marked reduction in productive cough. His ABG in HFNT (flow: 40 L/min; $FiO_2$ 26%; temperature: 37°C) showed a resolution of his hypercapnic respiratory failure (pH 7.39, $PaCO_2$ 39.4 mmHg, $PaO_2$ 66.9 mmHg, $SaO_2$ 94.1%).

After 12 days of hospital stay, he was discharged home and long-term home HFNT was prescribed, with the indication to use the device for at least 8 hours each day. Follow-up visits were scheduled every 4 weeks for the next six months. The patient reported significant mucus reduction and improved ease on expectoration (VAS 6). Sputum cultures remained negative. Pulmonary function has improved from the last assessment at stable condition before hospital admission: FVC 78% of predicted value (2.7 L, +13 % compared to 7 months before), $FEV_1$ 71% of predicted value (1.9 L, + 11%),

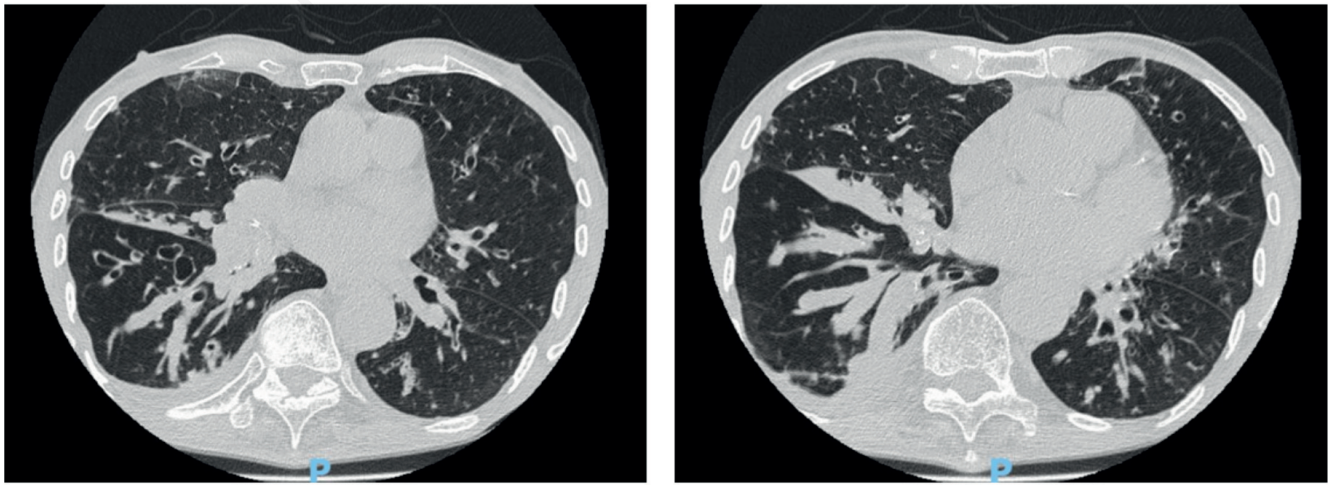

**Figure 1. Chest CT scan showing varicose and cystic bronchiectasis with abundant mucous content.**

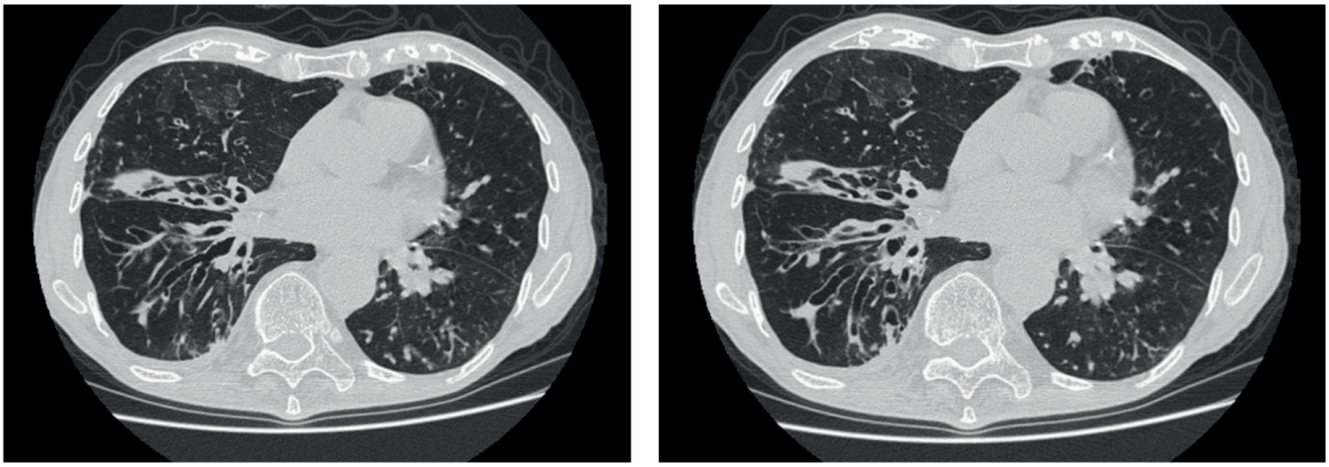

**Figure 2. Chest CT scan showing varicose and cystic bronchiectasis now cleared of mucous contents. Performed after 6 months of long-term home HFNT.**

$FEV_1$/FVC 70% (+10 %). The SGRQ total score reached 59 (+12 compared to 7 months before). At his six months follow-up the HRTC showed, reduction of intraluminal mucosal impacts in some bronchiectasis, especially in those located in the right lower lobe and in the middle lobe, in comparison to previous CT scan (Figure 2).

## Discussion

To the best of our knowledge, this is the first report documenting the successful management of severe non-cystic fibrosis BE using HFNT during both the exacerbation and stable phases of the disease, as an adjunct to maximal medical treatment and airway clearance regimen.

Mucus hypersecretion and its excessive accumulation resulting in plug formation and partial or complete airway obstruction is a hallmark of bronchiectasis and may contribute to serious consequences such as atelectasis and recurrent infections. In this context, muco-ciliary clearance is the first-line defense mechanism of the airways and depends on synchronous cilia movement and adequate water content in the mucus [11,12]. Williams *et al.* [13] showed that respiratory gases at body temperature and 100% relative humidity are optimal for mucociliary transport and even small changes to the temperature or humidity may have a negative impact on its efficiency. Thus, the delivery of essential humidity through HFNT can preserve the function of the mucociliary transport system [2-4], avoiding the inflammatory response caused by the dehydration of the mucosa [14] and preventing the bronchoconstriction triggered by dry air [15]. HFNT might serve as a muco-active agent facilitating patients' ability to effectively clear secretions, reducing mucus viscosity and increasing mucokinetics, promoting cough transportability in airway disease in which mucus hypersecretion is a pathophysiological and clinical issue. Moreover, HFNT creates a certain level of pulmonary distending pressure generating a positive airway pressure effect [16] providing alveolar recruitment, preventing atelectasis and indirectly improving oxygenation and patients'comfort [17].

There is growing evidence on the use of HFNT for the treatment of patients with COPD in both acute [18] and chronic settings [19] and a strong physiological rationale supporting its use, but only limited data are available for bronchiectasis. However, COPD and BE are both muco-obstructive lung diseases [20-22] characterized by similar physiopathological mechanisms such as chronic airway inflammation, mucus hypersecretion and retention and impaired mucociliary transport. Only one small feasibility study explored the use of HFNT in patients with acute exacerbations of COPD and coexisting bronchiectasis showing a significant improvement in mucus production (1.1±0.6 *vs* 2.4±0.7, p<0.001), dyspnea (Borg scale from 6.7±1.4 to 4.1±1.3, p<0.001) and respiratory rate (29.6±2.7 breaths/min *vs* 23.2±2.9 breaths/min (p<0.001) [5]. Similarly, in the chronic setting, Rea and coworkers in a randomized controlled trial showed that the long-term use of HFNT significantly reduce exacerbation frequency compared to usual care in 108 patients with either COPD or BE at 12-months [6]. A recent *post-hoc* analysis of Rea *et al*. clinical trial [6] focusing exclusively on the subgroup of the 45 BE patients, showed a significant reduction in the annual exacerbation rate with HFNT [2.39 per patient per year in the HFNT group vs 3.48 in the control group, corresponding to a 31.3% relative reduction with HFNT [rate ratio 0.69 (95% CI 0.49-0.97; p=0.03)] and improved quality of life compared with usual care [7].

Our case demonstrated that HFNT may be a valuable non-pharmacological add-on therapeutic option in patients with severe BE both during exacerbations and in the long-term, enhancing patient's ability to mobilize mucus and thereby improving therapeutic effectiveness. Considering the theoretical beneficial physiopathological effects of HFNT and the limited but growing positive results from the scientific literature, future high-quality research focusing on the role of HFNT in this specific patient population is highly needed.

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