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ORIGINAL RESEARCH

Microbial Colonization and Potential Bacterial Translocation of High-Flow Nasal Cannula Circuits During Prolonged Use in Elderly Hospitalized Patients: A Prospective Observational Study

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Background: High-flow nasal cannula (HFNC) oxygen therapy provides effective respiratory support with enhanced comfort and airway humidification. Long-term use of HFNC is increasingly adopted in respiratory oxygen therapy for elderly patients, yet Catheter-related bacterial translocation and colonization risks remain unstudied.

Methods: This prospective study enrolled 102 elderly hospitalized patients (mean age: 94.2 ± 5.1 years old) receiving HFNC therapy. Microbial samples were collected from the HFNC circuits and analyzed to assess respiratory circuit colonization. The optimal tubing replacement interval was determined through ROC curve analysis. Additionally, for one patient who developed pulmonary infection after receiving HFNC, microbial homology was evaluated between microorganisms cultured isolates from the lower respiratory tract and those from the HFNC tubing using whole-genome sequencing and antibiotic resistance gene profiling.

Results: Microbial colonization of HFNC tubing was detected in 56.9% (58/102) of patients, with prevalent pathogens including *Filamentous fungi* (25.9%), *Methicillin-resistant Staphylococcus aureus* (20.7%), and *Streptococcus spp*. (13.8%). The median time to tubing colonization was 136.2 ± 58.2 days. Pulmonary infections occurred significantly more frequently in the culture-positive group (37/58=63.8%) compared to the culture-negative group (17/44=38.6%; $P = 0.016$). ROC analysis identified 90.5 days as the study-specific optimal cutoff associated with tubing contamination. In the case study, *Pseudomonas aeruginosa* was isolated from both the patient's lower respiratory tract and HFNC tubing. Homology analysis confirmed the strains were identical (*ST2069, O6 serotype*) and harbored six shared resistance genes (aph(3′)-IIb, crpP, catB7, blaPAO, blaOXA-488, fosA).

Conclusion: Prolonged HFNC use was associated with substantial microbial colonization of the circuit in elderly hospitalized patients. Replacing HFNC tubing at approximately 90-day intervals may reduce microbial colonization and pneumonia risk in elderly patients during HFNC therapy. The HFNC tube circuit serves as a potential reservoir for pathogenic translocation, highlighting the importance of timely tubing replacement and microbial monitoring of the tube in infection prevention protocols.

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Keywords: high-flow nasal cannula, HFNC, elderly hospitalized patients, microbial colonization, tubing replacement, ROC curve analysis, prospective observational study

Introduction

High-Flow Nasal Cannula(HFNC) oxygen therapy is a respiratory support treatment method that continuously delivers regulated and relatively constant oxygen concentrations, temperatures, and humidity, with high flow rates (8 to 80 L/min) of inhaled gas.[1] Compared with traditional oxygen therapy and Noninvasive Positive Pressure Ventilation (NPPV), HFNC offers improved comfort and airway humidification, making it the optimal respiratory support choice for awake elderly patients with secretion clearance impairments.[2,3] Consequently, long-term use of HFNC is increasingly common in oxygen therapy for geriatric respiratory care.[4] In current clinical practice, HFNC has become a frequently used noninvasive respiratory support modality and is often positioned between conventional oxygen therapy and noninvasive ventilation(NIV). One study including patients aged over 75 years specifically used HFNC in elderly patients with acute respiratory failure who had a poor response to conventional oxygen therapy or were intolerant to NIV.[4] However, evidence from mechanical ventilation circuits, oxygen humidifiers, and other respiratory care devices suggests that moisture-containing respiratory equipment may act as a reservoir for microbial persistence and cross-contamination.[5,6] Thus, prolonged HFNC therapy in elderly patients carries an elevated risk of device-related respiratory infections, particularly due to tubing contamination.[7] Currently, there is limited research on HFNC tubing circuit microbial colonization or translocation and infection risks, and no established guidelines exist for optimal tubing replacement intervals.

To address this gap, this study aims to investigate microbial colonization patterns in HFNC circuits used by elderly patients and assess the associated risk of respiratory infections. Also determine the time threshold for significant tubing contamination using microbial monitoring and ROC curve analysis thus establish evidence-based recommendations for the optimal tubing replacement schedule. The findings will provide clinical data to support standardized HFNC management, helping to minimize infection risks and improve patient outcomes in long-term use of HFNC respiratory support.

Methods

Study Design and Patients' Enrollment

This prospective observational study enrolled 113 elderly hospitalized patients receiving HFNC therapy at a medical center of the Chinese PLA General Hospital between June 1, 2022, and July 28, 2023. Eligibility criteria for inclusion were as follows: (1) Age >65 years; (2) Daily HFNC use ≥18 hours; (3) Ability to provide lower respiratory tract samples; (4) Availability of complete medical records. The exclusion criteria were as follows: (1) Incomplete medical records; (2) Change in HFNC tubing or ventilation method during follow-up; (3) Confirmed pulmonary infection at enrollment; (4) Inability to cooperate with follow-up; (5) Death during the study period. This study was designed as a prospective single-arm descriptive study, with the primary outcome being the positivity rate of microbial cultures from HFNC tubing samples. Based on pilot observations, the expected positivity rate was estimated to be approximately 50%. Using a two-sided α of 0.05 and an allowable error (δ) of 0.10, the required effective sample size was calculated to be 97 patients according to the formula for estimating a single proportion. To ensure adequate study precision and to account for an anticipated 15% loss to follow-up or missing data, we planned to enroll 118 elderly patients receiving HFNC therapy. During the study period, a total of 113 patients met the inclusion and exclusion criteria. The study protocol was approved by the Ethics Committee of the Chinese PLA General Hospital (Approval No. S2020-25601). This study adheres to the Declaration of Helsinki, and all participants signed informed consent forms before being enrolled in the study.

Clinical Data Collection, Microbial Sampling and Analysis

Demographic and clinical data were collected from enrolled patients, including gender, age, smoking history, comorbidities, complete blood count and biochemistry results. HFNC tubing samples were collected weekly from all participants.

Microbiological specimens were collected from three sites of the HFNC circuit system: the humidification chamber, the heated breathing circuit at 6–8 cm distal to the humidification chamber (distal tubing), and the heated breathing circuit at 6–8 cm proximal to the nasal cannula (proximal tubing). For sampling of the humidification chamber, a sterile cotton swab was used to collect liquid from the chamber. For sampling of the breathing circuit, a sterile swab moistened with sterile normal saline was inserted into the inner lumen and rotated along the inner wall for five full turns over a depth of 6–8 cm. The collected specimens were inoculated onto blood agar plates and China blue agar plates, and incubated at 37°C for 48 h for microbiological culture and surveillance analysis. Routine clinical microbiological cultures were performed mainly to detect common hospital-acquired pathogens. Specifically, HFNC tubing samples were cultured for common aerobic bacteria and fungi recoverable under standard laboratory conditions, including yeasts and molds. These cultures were used to evaluate the microbial colonization rate and the spectrum of clinically relevant organisms in the HFNC tubing. Systematic screening for viruses, anaerobic bacteria, mycobacteria, or other atypical pathogens was not performed.

Monitoring of Pulmonary Infections and Microbial Homology Analysis

Pulmonary infection during the follow-up period was considered a secondary outcome, and the incidence of pulmonary infections was analyzed. The diagnosis of pulmonary infection was made with reference to the Chinese expert consensus on the diagnosis and treatment of pneumonia in the elderly (2024 Edition).[8] Specifically, pulmonary infection was recognized based on a combination of new or worsening respiratory symptoms/signs, new radiographic infiltrates, and supportive laboratory or microbiological evidence.

For patients who developed pulmonary infections, microbial homology analysis was conducted between pathogens isolated from lower respiratory tract specimens (sputum) and those from HFNC tubing cultures. Genomic DNA was extracted from two *Pseudomonas aeruginosa* clinical isolates and subjected to whole-genome sequencing (WGS) on the Illumina NovaSeq platform with 150 bp paired-end reads. Raw sequencing reads were quality-filtered to remove low-quality bases, adapter sequences, and ambiguous nucleotides prior to assembly. De novo genome assembly was performed using SPAdes (v3.15.5). Multilocus sequence typing (MLST), O-antigen serotyping, and antimicrobial resistance gene profiling were subsequently performed using web-based tools available on the Center for Genomic Epidemiology (CGE) platform (http://www.genomicepidemiology.org/services/). Specifically, sequence types were assigned using the CGE MLST 2.0 tool with the *Pseudomonas aeruginosa*-specific MLST scheme; O-serogroup prediction was performed using PAst 1.0, which classifies isolates based on a BLAST analysis of the O-specific antigen (OSA) gene cluster; and acquired antimicrobial resistance genes were identified using ResFinder 4.6.0, with a minimum nucleotide identity threshold of 90% and a minimum gene length coverage of 60%. For SNP-based clonal relatedness analysis, quality-filtered paired-end reads were mapped to the complete reference genome of *P. aeruginosa* PAO1 (NCBI RefSeq accession NC_002516.2) using the Snippy pipeline (v4.6.0). A core genome SNP alignment was constructed using snippy-core across all isolates. To minimize false-positive SNP calls attributable to horizontal gene transfer, recombination regions were identified and masked using Gubbins (v3.3.1), with FastTree employed as the phylogenetic tree builder. Pairwise core genome SNP distances were subsequently calculated from the recombination-filtered alignment using snp-dists. In accordance with validated genomic thresholds established for nosocomial *P. aeruginosa* outbreak investigations, isolates differing by ≤ 25 recombination-filtered core genome SNPs were classified as clonally related, whereas those exceeding this threshold were considered genetically distinct.[9,10]

ROC Curve Analysis

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal timing for tubing replacement based on the occurrence of microbial contamination during treatment. The presence or absence of microbial growth in tubing cultures served as the classification criterion. For each candidate cutoff value of tubing-use duration, sensitivity was calculated as the proportion of culture-positive patients correctly identified, and specificity was calculated as the proportion of culture-negative patients correctly identified. Sensitivity, specificity, and the area under the curve (AUC) were calculated to identify the most predictive time threshold for tubing contamination.

Statistical Analysis

Baseline characteristics of the study population, including demographic and clinical data, were summarized using descriptive statistics. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), whereas non-normally distributed variables are presented as median (interquartile range, IQR). Categorical variables were expressed as frequencies and percentages. ROC curve analysis was employed to evaluate the optimal timing for tubing replacement using microbial positivity in HFNC tubing samples as the classification criterion. The analysis included calculation of sensitivity, specificity, and area under the curve (AUC) to establish the contamination time threshold. The optimal cutoff point for tubing replacement was determined by maximizing Youden's index from the ROC curve. All analyses were conducted using SAS (version 9.4) and R (version 3.6.3) statistical software. A two-tailed p-value <0.05 was considered statistically significant.

Results

Patient Demographic and Clinical Characteristics

Of the initial 113 enrolled patients, 11 were excluded from the final analysis, including 1 due to incomplete medical records, 4 due to change in HFNC tubing or ventilation modality during follow-up, 2 due to confirmed pulmonary infection at enrollment, 2 due to inability to complete follow-up, and 2 due to death during the study period. In this study, most participants were very elderly bedridden patients who required long-term oxygen therapy, improvement of airway mucus clearance, and optimization of pulmonary mechanics. All included patients were conscious and able to cooperate with HFNC treatment, and prolonged HFNC use was determined by the treating physicians based on clinical evaluation. The mean age was 94.2 ± 5.1 years. The median follow-up time of this cohort was 67 days. There were 58 patients (58/102=56.9%) in the microbial culture positive group and 44 patients (44/102=43.1%) in the culture negative group. Demographic and clinical characteristics of enrolled patients are presented in Tables 1–4 separately. The study flow is shown in Figure 1.

Microbial Contamination Patterns

As Figure 2 and Table 3 shown: Microbial colonization was detected in 56.9% (58/102) of HFNC tubing samples. The pathogens identified were: *Molds/Filamentous fungi* (25.9%, median days: 88.9±50.2), *Methicillin-resistant Staphylococcus aureus* (MRSA) (20.7%, median days: 109.22±60.8), *Streptococcus spp*. (13.8%, median days: 55.1 ±28.2), *Bacillus* (10.3%, median days: 116.3±39.1), *Staphylococcus* (6.9%, median days: 70.5±22.3), *Sphingomonas paucimobilis* (8.6%, median days: 84.6±25.4), *Candida parapsilosis* (5.2%, median days: 81.3±72.7), *Pseudomonas putida* (1.7%, median days: 98.0), *Acinetobacter baumannii* (1.7%, median days: 100.0), *Ralstonia mannitolilytica* (1.7%, median days: 56.0), *Comamonasacidovorans* (1.7%, median days: 69.0), *Micrococcus luteus* (1.7%, median days: 36.0). The mean time to microbial detection in HFNC tubing was 136.2 ±58.2 days (Table 4).

Analysis of Laboratory Test Results Between Microbial Culture Positive and Negative Groups

There was no statistically significant difference in the blood test results between the microbial culture positive and negative groups ($P > 0.05$) (Figure 3). Specifically, there were no differences observed in the following parameters: Hemoglobin, Red cell count, White cell count, Neutrophils percentage, Lymphocytes percentage, Monocytes percentage, Eosinophils percentage, Basophils percentage, Platelet Count, CRP (C-reactive protein), Serum albumin, NPAR (Neutrophil percentage-to-albumin ratio), NLR (Neutrophil-to-lymphocyte ratio), PLR (Platelet-to-lymphocyte ratio), and MLR (Monocyte-to-lymphocyte ratio).

Optimal Tubing Replacement Timing Analysis

ROC curve analysis identified day 90.5 as the study-specific optimal cutoff associated with tubing contamination (AUC=0.767, 95% CI: 0.669–0.864) (Figure 4). This timepoint demonstrated balanced sensitivity and specificity for predicting microbial contamination while effectively minimizing infection risk.

Table 1 Baseline Demographic Characteristics of the Enrolled Patients

Characteristic	All Patients (n = 102)	Microbial Culture-Positive Group (n = 58)	Microbial Culture-Negative Group (n = 44)	*P*- value
Age, year (mean±SD)	94.2±5.1	93.7±5.2	94.5±5.1	0.464
Gender, n (%)				
Female	8 (7.8)	4 (6.9)	4 (9.1)	0.723
Male	94 (92.12)	54 (93.1)	40 (90.9)	
Department, n (%)				
Respiratory	45 (44.1)	25 (43.1)	20 (31.8)	0.688
Non-respiratory	57 (55.9)	33 (56.9)	22 (68.2)	
Smoking, n (%)				
No	58 (56.9)	36 (62.1)	22 (50.0)	0.234
Yes	44 (43.1)	22 (37.9)	22 (50.0)	
Chronic obstructive pulmonary disease, n (%)				
No	57 (55.9)	32 (55.2)	25 (56.8)	1
Yes	45 (44.1)	26 (44.8)	19 (43.2)	
Hypertension, n (%)				
No	24 (23.5)	11 (19.0)	13 (29.6)	0.244
Yes	78 (76.5)	47 (81.0)	31 (70.4)	
Coronary disease, n (%)				
No	38 (37.2)	17 (29.3)	21 (47.7)	0.066
Yes	64 (62.8)	41 (70.7)	23 (52.3)	
Use of antibiotics	92 (90.2)	52 (89.7)	40 (90.9)	1

Incidence of Pulmonary Infections and Microbial Homology Analysis

The incidence of pulmonary infections among HFNC patients was 52.9% (54/102) (Table 4). In one 92-year-old male patient with pneumonia (Figure 5 demonstrates the patient's chest CT findings), we identified genetically homologous

Table 2 Laboratory Characteristics of the Enrolled Patients

Characteristic	All Patients (n = 102)	Microbial Culture-Negative Group (n = 44)	Microbial Culture-Positive Group (n = 58)	*P* -value
Hemoglobin (g/L)	112.0 (100.0, 126.0)	112.0 (102.0, 124.0)	111.0 (100.0, 127.0)	0.981
Red cell count (10^{12}/L)	3.7 (3.2, 4.1)	3.7 (3.3, 4.0)	3.7 (3.1, 4.1)	0.889
White cell count (10^{9}/L)	6.7 (5.2, 8.8)	6.5 (5.2, 8.4)	7.0 (5.2, 9.4)	0.388
Neutrophils (%)	0.7 (0.6, 0.7)	0.7 (0.6, 0.8)	0.7 (0.6, 0.7)	0.736
Lymphocytes (%)	0.2 (0.1, 0.3)	0.2 (0.1, 0.3)	0.2 (0.2, 0.3)	0.975
Monocytes (%)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.818
Eosinophils (%)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.309
Basophils (%)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.472
Platelet Count (10^{9}/L)	157.0 (115.0, 214.0)	166.0 (126.5, 211.0)	149.0 (115.0, 216.2)	0.77
*CRP (mg/L)	1.1 (0.3, 3.3)	1.1 (0.3, 3.7)	1.1 (0.3, 2.6)	0.973
Serum albumin (g/L)	34.1 (31.4, 37.3)	34.1 (30.6, 37.5)	33.9 (31.6, 36.9)	0.91

Abbreviation: *CRP, C-reactive protein.

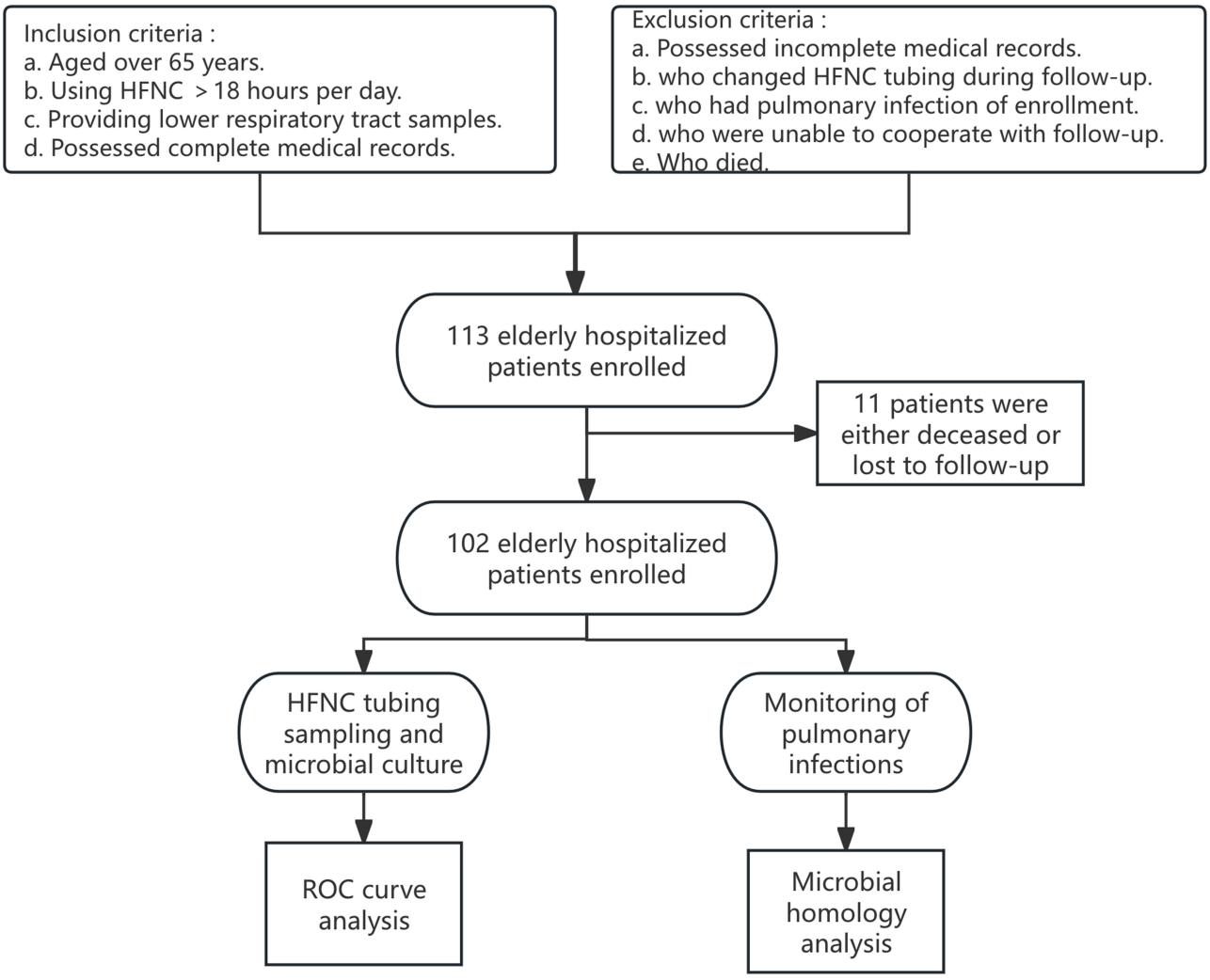

Figure 1 The flowchart of study.

Pseudomonas aeruginosa strains in both sputum and HFNC tubing samples. BLAST analysis confirmed that both strains were *Pseudomonas aeruginosa ST2069, O6 serotype*, carrying six shared resistance genes: aph(3′)-IIb, crpP, catB7, blaPAO, blaOXA-488, and fosA (Figures 6 and 7). Using the *Pseudomonas aeruginosa* PAO1 reference genome as the reference strain for SNP-based phylogenetic analysis, a total of 20,535 SNP sites were identified. Compared with the reference genome, the two strains differed by 20,534 and 20,530 SNP sites, respectively, while only six SNP site differences were found between the two strains. Therefore, the two strains were preliminarily determined to be homologous.

Discussion

This prospective study systematically evaluates microbial colonization patterns in elderly patients receiving HFNC therapy. By integrating microbial surveillance data with ROC curve analysis, we aim to establish evidence-based tubing replacement protocols. Furthermore, microbial homology analysis of paired lower respiratory tract and tubing samples from pneumonia cases will elucidate potential transmission pathways. These findings will inform optimized infection-control strategies for HFNC use in geriatric populations.

The concept of HFNC was first introduced in the 1990s, when researchers began exploring the potential of delivering high-flow oxygen via nasal cannula.[11] Early studies primarily focused on the effects of HFNC in patients with acute respiratory failure, demonstrating its ability to significantly improve oxygenation and respiratory efficiency.[12] As

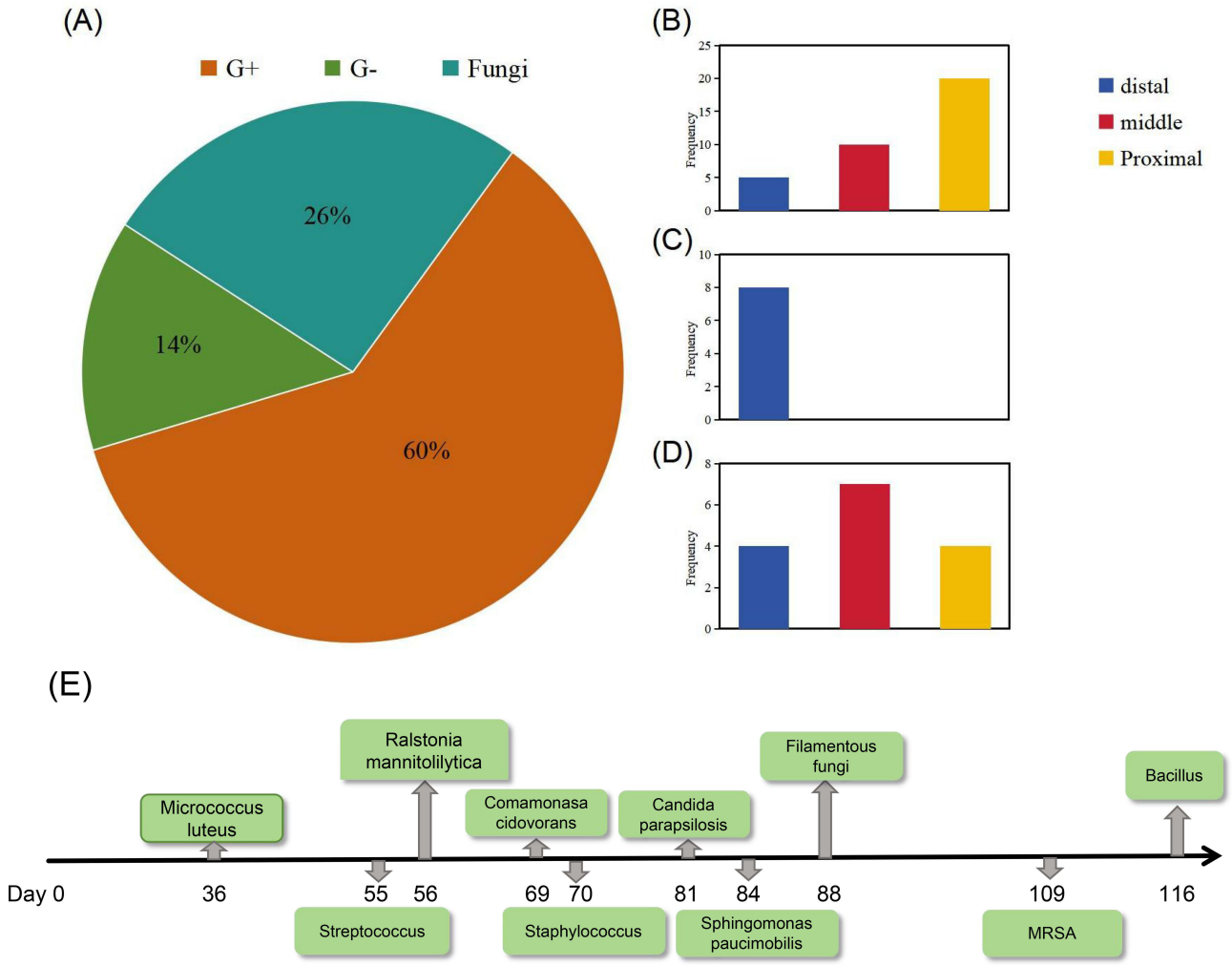

Figure 2 Microbial surveillance status and microbial species. (**A**) Pie chart of microbial species in culture-positive samples. (**B**) Detection of Gram-positive bacteria at different positions of the HFNC circuit. (**C**) Detection of Gram-negative bacteria at different positions of the HFNC circuit. (**D**) Detection of fungi at different positions of the HFNC circuit. (**E**) Microbial timeline of the positive microbial culture group.

respiratory therapy technologies advanced, the design and functionality of HFNC devices have undergone continuous refinement, particularly in terms of flow control, humidification, and heating.[13,14] Studies have shown that HFNC yields significant benefits in conditions such as acute respiratory distress syndrome (ARDS) and acute exacerbations of chronic obstructive pulmonary disease (COPD).[15] In the 2010s, the clinical application of HFNC gradually expanded to the neonatal and pediatric populations, particularly in the treatment of neonatal respiratory distress syndrome.[16] During the COVID-19 pandemic, HFNC received widespread attention, with many hospitals adopting it as a crucial respiratory support method to reduce the need for intubation in critically ill patients.[17] Today, HFNC represents a standard respiratory intervention, with ongoing innovations refining its clinical implementation. Although HFNC tubing is generally designated by manufacturers as a single-use disposable component, and prolonged use or reuse after cleaning is usually not recommended, prolonged HFNC support may still be encountered in real-world geriatric practice, particularly among very elderly bedridden patients with chronic respiratory support needs. In this setting, clinicians face a practical gap between manufacturer recommendations and long-term care demands. At present, there is no clear evidence-based consensus regarding the optimal replacement interval for HFNC tubing during prolonged use in elderly hospitalized patients.

Multiple studies have demonstrated comparable efficacy between High-Flow Nasal Cannula HFNC and Non-Invasive Ventilation (NIV) in preventing post-extubation respiratory failure and reintubation among patients with both hypoxemic

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Table 3 Types of Cultured Microorganisms and Duration of Positive Cultures

Category	All Patients (n = 102)	Microbial Culture-Positive Group (n = 58)	Microbial Culture-Positive Median Days
Microbial species, n (%)			
Molds/Filamentous fungi	15 (14.7)	15 (25.9)	88.9±50.2
*MRSA	12 (11.8)	12 (20.7)	109.2±60.8
Streptococcus spp.	8 (7.8)	8 (13.8)	55.1±28.2
Bacillus	6 (5.9)	6 (10.3)	116.3±39.1
Staphylococcus	4 (3.9)	4 (6.9)	70.5±22.3
Sphingomonas paucimobilis	5 (4.9)	5 (8.6)	84.6±25.4
Candida parapsilosis	3 (2.9)	3 (5.2)	81.3±72.7
Pseudomonas putida	1 (1.0)	1 (1.7)	98
Acinetobacter baumannii	1 (1.0)	1 (1.7)	100
Ralstonia mannitolilytica	1 (1.0)	1 (1.7)	56
Comamonasacidovorans	1 (1.0)	1 (1.7)	69
Micrococcus luteus	1 (1.0)	1 (1.7)	36

Abbreviation: *MRSA: Methicillin-resistant Staphylococcus aureus.

Table 4 Microbial Surveillance of HFNC Tubing and Incidence of Pulmonary Infections

Category	All Patients (n = 102)	Microbial Culture-Positive Group (n = 58)	Microbial Culture-Negative Group (n = 44)	*P*- value
Microbial monitoring, n (%)				
Number of positive Microbial cultures	58 (56.9)	58 (100.00)	–	
Days of positive Microbial cultures (mean±SD)	–	136.2±58.2	–	
Pulmonary infections, n (%)	54 (52.9)	37 (63.8)	17 (38.6)	0.016

and hypercapnic respiratory failure.[18] As a non-invasive alternative to invasive mechanical ventilation, HFNC significantly reduces risks associated with intubation and ventilator-associated complications.[19] However, the extended exposure of HFNC circuits to environmental pathogens raises concerns about microbial colonization risks, particularly when improper circuit maintenance or connection contamination occurs.

Our investigation revealed a 56.9% microbial culture positivity rate in HFNC circuits, with predominant isolates including *Filamentous fungi, methicillin-resistant Staphylococcus aureus*, and *Streptococcus spp*. This contamination rate may be related to several factors in our study population: 1) the inclusion of elderly patients with diminished self-care capacity, predisposing them to frequent nasal cannula dislodgement and subsequent environmental pathogen exposure; and 2) prolonged HFNC utilization durations. Notably, the identified microorganisms correspond with typical nosocomial pathogens,[20] mirroring ventilator-associated pneumonia (VAP) microbiology profiles where Gram-negative pathogens (Pseudomonas aeruginosa and Acinetobacter spp.) predominate, alongside Gram-positive organisms like Staphylococcus aureus.[21]

Current evidence indicates that extended application of HFNC therapy may increase susceptibility to secondary pulmonary infections.[22,23] Notably, a critical knowledge gap persists regarding the relationship between microbial colonization in HFNC circuits and subsequent respiratory infections in clinical populations. Our findings demonstrate a significantly elevated incidence of pulmonary infections in patients with positive microbial cultures compared to those

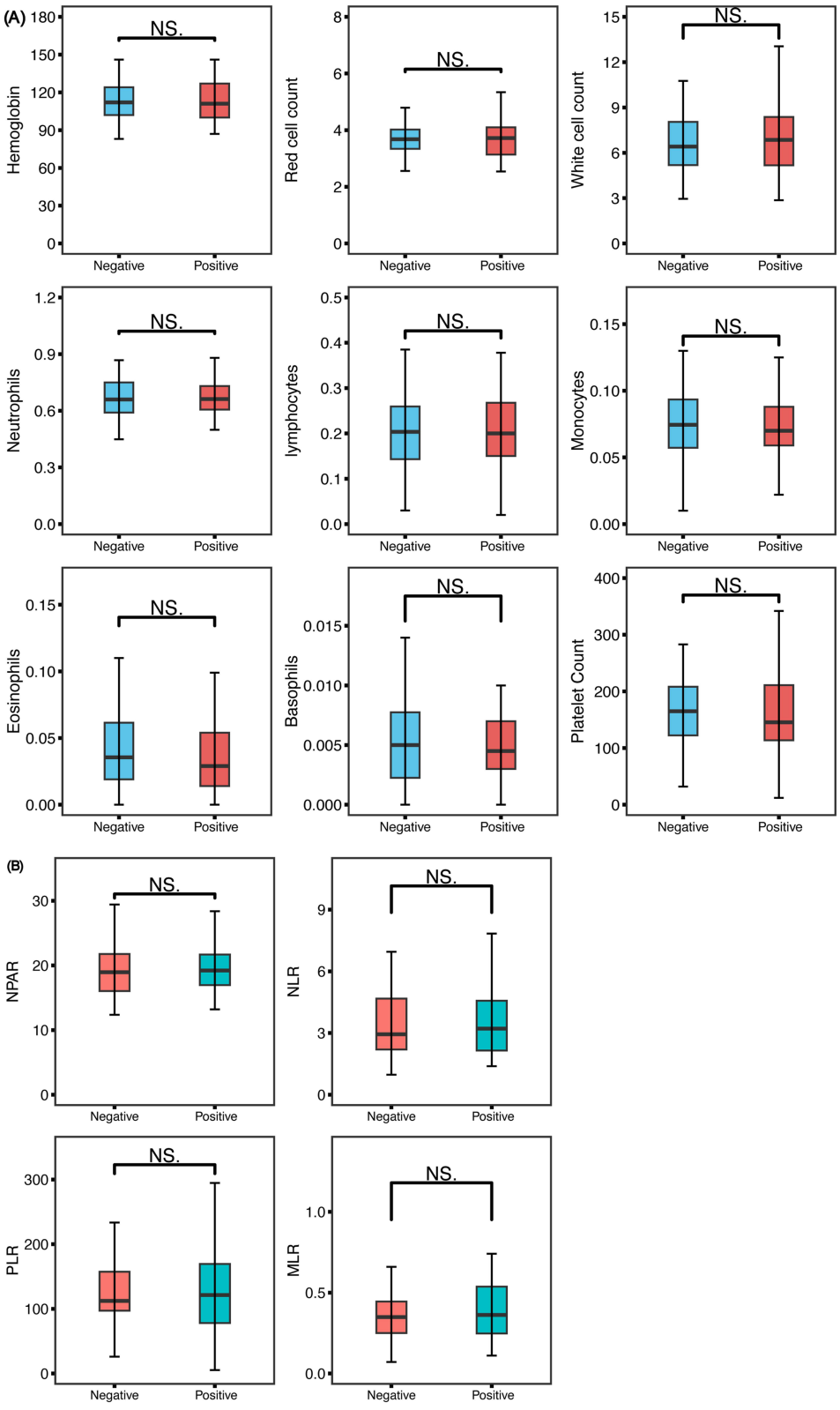

Figure 3 Laboratory parameter analysis of patients in the positive and negative microbial culture groups. (**A**) Boxplot of blood test parameters and microbial culture results. (**B**) Boxplot of blood test parameters ratios and microbial culture results. (*P*>0.05.).

Abbreviations: NS, Not significant; NPAR, Neutrophil percentage-to-albumin ratio; NLR, Neutrophil-to-lymphocyte ratio; PLR, Platelet-to-lymphocyte ratio; MLR, Monocyte-to-lymphocyte ratio.

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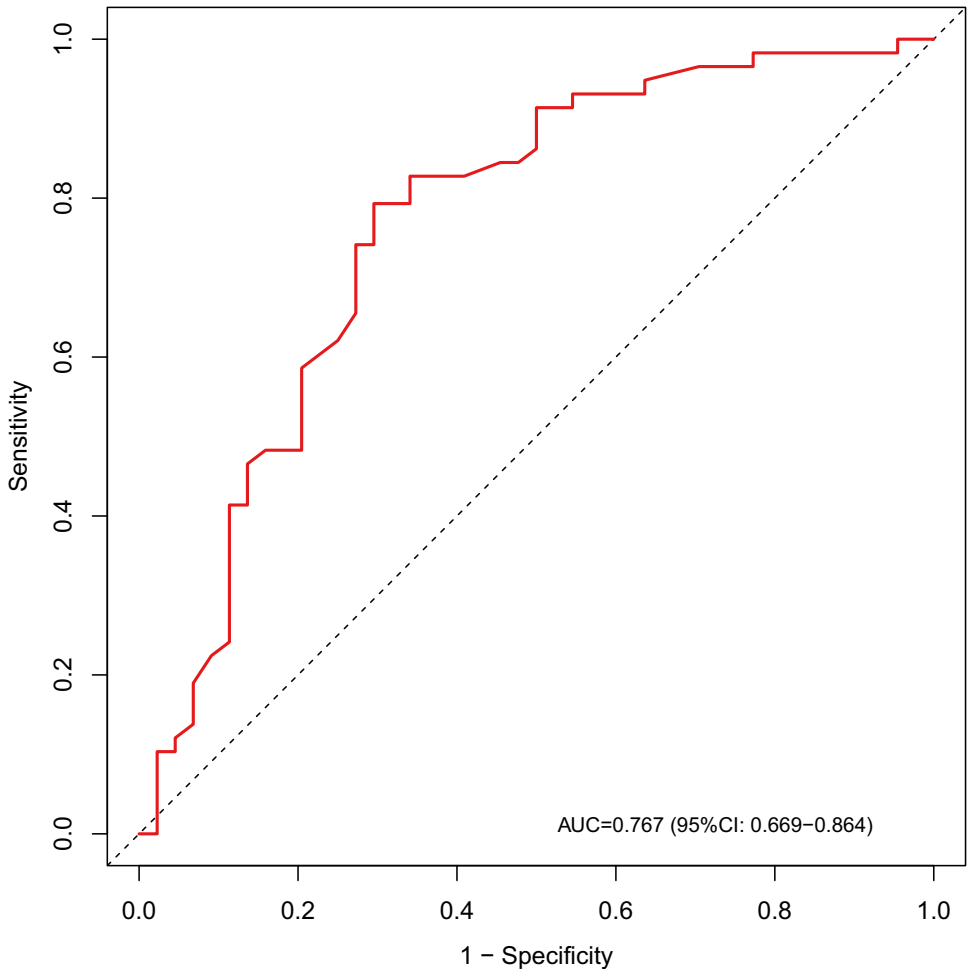

Figure 4 ROC Curve analysis. (Using the positivity of tubing system cultures as the classification criterion, the time threshold for tubing contamination was determined to be 90.5 days.) (AUC= 0.767; 95% CI: 0.669–0.864).

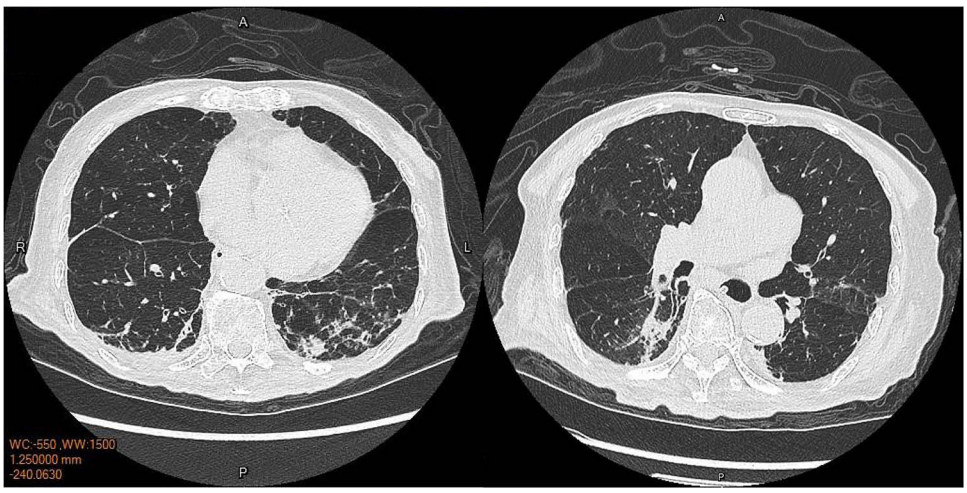

Figure 5 Chest CT of a pneumonia patient after HFNC application. (A: Anterior, P: Posterior, R: Right, L: Left).

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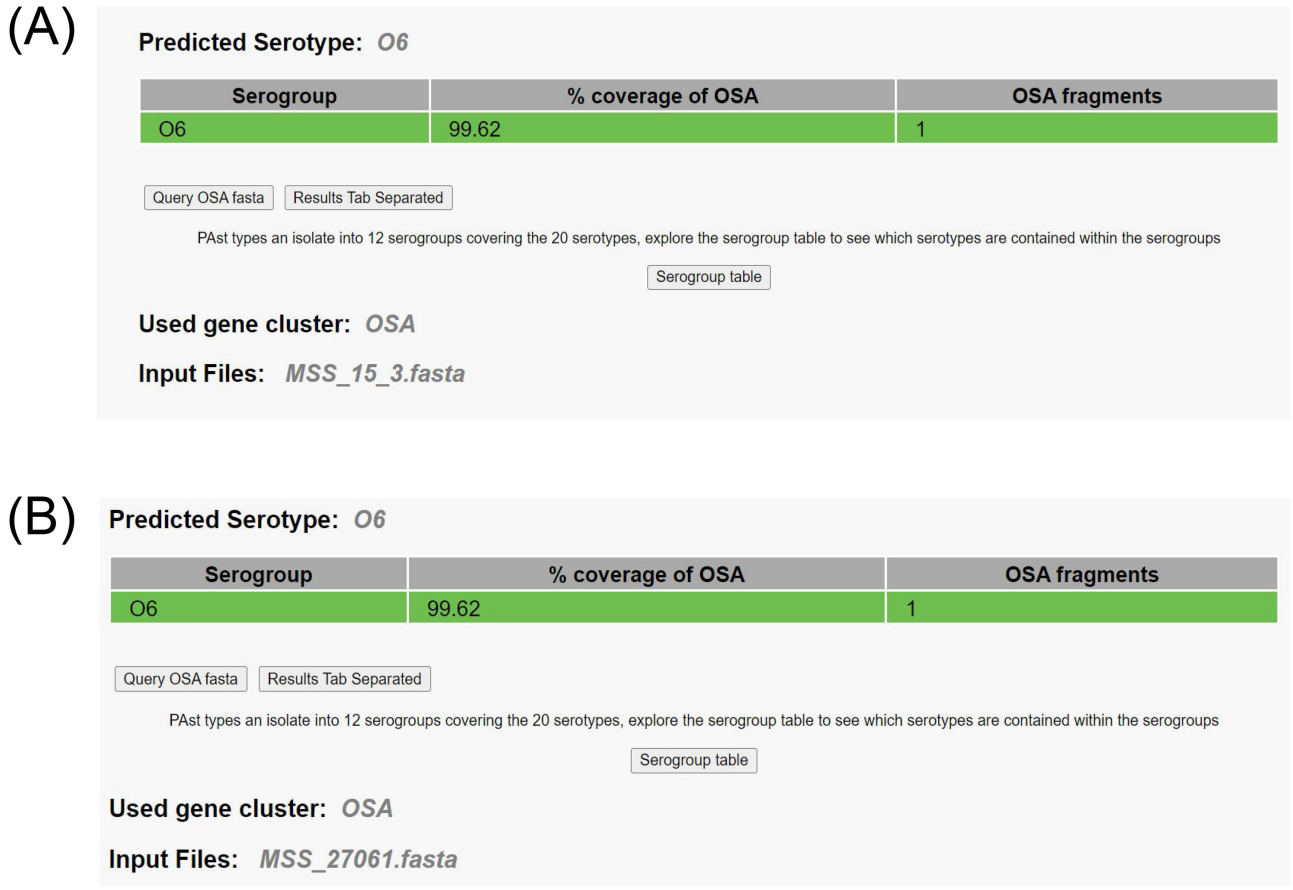

Figure 6 The sequence-based serotyping of Pseudomonas aeruginosa isolated from the patient's lower respiratory tract samples (**A**) and the ventilator tubing (**B**) (Both isolates (MSS_15_3 and MSS_27061) were predicted as serogroup O6, with 99.62% coverage of the O-specific antigen (OSA) locus, based on the OSA gene cluster).

with negative cultures. This statistically significant difference underscores the clinical relevance of circuit contamination, particularly in elderly patients requiring prolonged HFNC therapy where age-related immunosenescence may amplify infection risks.[24] To substantiate this observation, we conducted microbial homology analysis in a representative case involving a 92-year-old male pneumonia patient. Comparative BLAST analysis revealed genetic homology between *Pseudomonas aeruginosa* strains isolated from both the patient's sputum and the HFNC circuit. The observed homology between *Pseudomonas aeruginosa* isolated from the lower respiratory tract and HFNC tubing demonstrates strain identity, but does not establish the exact direction of transmission. The contamination may have been: ① from the HFNC circuit to the patient, ② from the patient to the HFNC circuit, ③ related to shared environmental or healthcare-associated contamination. This microbiological evidence supports the hypothesis that colonized circuits can serve as reservoirs for pathogenic microorganisms to translocation, potentially initiating lower respiratory tract infections.[20]

Current infection control protocols classify the HFNC system (comprising nasal cannula, heated humidification chamber, and connecting tubing) as single-use disposable medical devices intended for short-term applications.[25,26] However, critical gaps persist in clinical guidance regarding system replacement frequency during extended therapeutic use. Neither international guidelines nor expert consensus documents provide evidence-based recommendations for maintenance protocols in prolonged HFNC therapy scenarios. Our ROC curve analysis identified 90.5 days as the study-specific optimal cutoff associated with tubing contamination. From a clinical perspective, this finding may be more appropriately interpreted as suggesting a replacement interval of approximately 90 days, pending validation in larger prospective studies. These data provide preliminary evidence to inform standardized management protocols, potentially mitigating infection risks associated with circuit colonization.

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(A)

Resistance results:

Template	Score	Expected	template length	q_value	p_value	template_id	template_coverage	query_id	query_coverage	depth	depth_corr
NZ_CP008872.2 Pseudomonas aeruginosa strain X78812, complete genome	132411	8	144194	132386.01	1.0e-26	92.34	92.34	80.99	80.99	0.92	0.6321
aph(3')-IIb_2_CP006832	795	0	807	792.36	1.0e-26	99.38	100.00	99.38	100.00	1.00	0.6628
blaOXA-488_1_CP017969	777	0	789	774.41	1.0e-26	99.37	100.00	99.37	100.00	1.00	0.6628
blaPAO_4_AY083592	1179	1	1194	1175.57	1.0e-26	99.50	100.00	99.50	100.00	1.00	0.6628
fosA_4_ACWU01000146	402	0	408	400.50	1.0e-26	99.26	100.00	99.26	100.00	1.00	0.6628
catB7_1_AF036933	633	0	639	630.81	1.0e-26	99.53	100.00	99.53	100.00	1.00	0.6628
crpP_1_HM560971	180	0	198	179.23	1.0e-26	96.46	100.00	96.46	100.00	1.00	0.6628

Input Files: *MSS_15_3.fasta*

(B)

Resistance results:

Template	Score	Expected	template length	q_value	p_value	template_id	template_coverage	query_id	query_coverage	depth	depth_corr
NZ_CP008872.2 Pseudomonas aeruginosa strain X78812, complete genome	132423	8	144194	132398.00	1.0e-26	92.35	92.35	80.98	80.98	0.92	0.6321
aph(3')-IIb_2_CP006832	795	0	807	792.36	1.0e-26	99.38	100.00	99.38	100.00	1.00	0.6628
blaOXA-488_1_CP017969	777	0	789	774.41	1.0e-26	99.37	100.00	99.37	100.00	1.00	0.6628
blaPAO_4_AY083592	1179	1	1194	1175.57	1.0e-26	99.50	100.00	99.50	100.00	1.00	0.6628
fosA_4_ACWU01000146	402	0	408	400.50	1.0e-26	99.26	100.00	99.26	100.00	1.00	0.6628
catB7_1_AF036933	633	0	639	630.81	1.0e-26	99.53	100.00	99.53	100.00	1.00	0.6628
crpP_1_HM560971	180	0	198	179.23	1.0e-26	96.46	100.00	96.46	100.00	1.00	0.6628

Input Files: *MSS_27061.fasta*

Resistance results | Species results | Full resistance results | Resistance alignment results | Resistance consensus results | Not-sam file | Log file

Figure 7 Antimicrobial resistance gene profiling of Pseudomonas aeruginosa isolated from the patient's lower respiratory tract samples (**A**) and the ventilator tubing (**B**) (Both isolates (MSS_15_3 and MSS_27061) harbored an identical set of six resistance genes: aph(3′)-IIb, blaOXA-488, blaPAO, fosA, catB7, and crpP).

Limitation

There are three principal limitations warrant consideration: 1) The modest sample size from a single-center cohort necessitates validation through large-scale multicenter trials. 2) Conducted within a geriatric healthcare setting (mean age 94.2 ± 5.1 years old), findings may not extrapolate to younger populations due to age-related immunological differences. 3) Preliminary homology analysis (n=1 pneumonia case) between *Pseudomonas aeruginosa* isolates from sputum and circuitry requires confirmation through expanded microbial sampling. Future prospective studies with larger sample sizes are needed to validate these results, for example: Establish causal relationships through longitudinal microbial surveillance; Validate replacement intervals across diverse clinical populations; Investigate cost-benefit ratios of replacement protocols.

Conclusion

Prolonged HFNC use was associated with substantial microbial colonization of the circuit in elderly hospitalized patients. Our findings suggest that HFNC tubing replacement at approximately 90-days intervals may be considered as a preliminary strategy for prolonged use in elder hospitalized patients. Although this threshold still requires validation in larger further prospective investigations. The HFNC circuit serves as a potential site of translocation for pathogenic colonization in elderly patients, particularly those with immunosenescence, necessitating stringent microbial surveillance and protocolized tubing replacement as critical components of infection control strategies.

Data Sharing Statement

The data are available from the corresponding author on reasonable request (Guogang Xu: gxu@301hospital.org).

Ethical Approval and Consent to Participate

This research was approved and waived the consent by the Ethics Committee of Chinese PLA General Hospital (NO. S2020-25601). All participants signed informed consent forms before being enrolled in the study. All authors confirm this study adheres to the Declaration of Helsinki. Clinical trial number: not applicable.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors in this study declare no competing conflicts.

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