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Clinical Outcomes of Short- Versus Long-Course Antibiotic Therapy in Pseudomonas aeruginosa-Positive Mild-to-Moderate Bronchiectasis Stratified by Day-7 Sputum Bacterial Load

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Abstract

Objective

The optimal antibiotic duration for acute exacerbations of *Pseudomonas aeruginosa* (*P. aeruginosa*)-positive mild-to-moderate bronchiectasis remains undefined. This retrospective cohort study examined whether day-7 quantitative sputum bacterial load could identify patients suitable for early discontinuation, and whether antibiotic duration was associated with 12-month outcomes—including inflammation control, hospitalization for exacerbations, and antibiotic-free intervals.

Methods

We retrospectively reviewed 102 patients with mild-to-moderate bronchiectasis and microbiologically confirmed *P. aeruginosa*, grouped by actual treatment duration into a short-course arm (≤ 7 days, n = 42) or a long-course arm (> 7 days, n = 60). Clinical, laboratory, spirometric, and St. George's Respiratory Questionnaire (SGRQ) data were collected at baseline, 1 month, and 12 months post-discharge.

Results

At baseline, the long-course group had higher leukocyte, neutrophil, and C-reactive protein (CRP) concentrations. At 12 months, this group showed significantly lower FEV_1, FEV_1/forced vital capacity (FVC) ratio, and higher SGRQ activity and impact scores (all $P < 0.05$); these differences persisted after ANCOVA adjustment for baseline values (all adjusted $P < 0.05$). Severe exacerbations clustered among high-burden patients at readmission ($P < 0.05$). Among the least-confounded subset—low-burden patients in either arm—readmission rates and retreatment frequency within 6 months were similar ($P > 0.05$).

Conclusion

In this exploratory cohort, low day-7 *P. aeruginosa* load (≤ 10^6 CFU/mL) identified a subgroup in whom short-course (≤ 7-day) therapy yielded comparable rehospitalization rates and antibiotic-free intervals to longer courses, and was additionally associated with better pulmonary function and HRQoL outcomes that remained significant after adjusting for baseline imbalances. These findings support day-7 bacterial load as a potential stratification tool for individualizing antibiotic duration and provide a rationale for prospective randomized validation.

Introduction

Bronchiectasis is a chronic airway disorder characterized clinically by persistent cough, frequent production of purulent sputum, and occasionally hemoptysis [1]. The underlying pathophysiology

involves recurrent infectious insults from various etiologies, which cause progressive bronchial damage and obstruction, ultimately resulting in irreversible airway dilatation and structural distortion [2]. Although the global prevalence of bronchiectasis is substantial and continues to rise, the condition has received disproportionately less research attention and clinical focus than chronic obstructive pulmonary disease or bronchial asthma [3].

Acute exacerbation of bronchiectasis is the main adverse event in the natural process of the disease. Frequent acute exacerbations of bronchiectasis lead to significantly increased airway and systemic inflammation in patients, accompanied by an acceleration in the decline in pulmonary function, progressive pulmonary injury, and increased mortality [4]. Therefore, timely and effective treatment of acute exacerbations of bronchiectasis is very important for improving the outcomes and mitigating the financial burdens of patients with bronchiectasis. Colonization and infection by pathogens such as bacteria and fungi are the main factors that induce acute exacerbation of bronchiectasis. Among the diverse pathogens implicated in bronchiectasis, *P. aeruginosa* is particularly consequential: its colonization is disproportionately prevalent in patients with more severe disease and is independently associated with accelerated lung function decline, increased exacerbation frequency, and higher mortality [5, 6]. There is currently no uniform consensus regarding the optimal duration of antibiotic therapy for *P. aeruginosa*-infected bronchiectasis patients. Therefore, clinical practice relies more on empirical treatment.

The widespread use of broad-spectrum antibiotics, coupled with ongoing bacterial adaptation, has led to a marked increase in multidrug resistance among *P. aeruginosa* isolates, including resistance to β-lactams, fluoroquinolones, and aminoglycosides. This trend makes the rational deployment of antibiotics paramount for controlling bronchiectasis exacerbations. Concurrently, China has witnessed a heightened focus on establishing standardized protocols for the diagnosis, treatment, and holistic management of bronchiectasis, thereby addressing this pressing clinical challenge. Current ERS guidelines recommend 14 days of antibiotic treatment for acute exacerbations of bronchiectasis [8], though shorter courses may be appropriate for selected patients; the criteria for identifying such patients remain poorly defined [7]. While current guidelines and prior investigations have predominantly focused on moderate-to-severe bronchiectasis, evidence-based antibiotic duration strategies for mild acute exacerbations remain undefined. This gap carries practical consequences: prolonged empirical courses carry well-documented risks of resistance emergence and microbiome disruption, whereas premature discontinuation may result in incomplete infection control. A rational solution would be to identify an objective, measurable criterion that distinguishes patients who have responded sufficiently by a fixed early timepoint from those who require continued treatment. Day 7 represents a clinically logical decision point: it coincides with the period by which most patients with *P. aeruginosa*infection show initial microbiological and symptomatic response, and quantitative sputum culture at this timepoint provides a direct measure of residual bacterial burden.One proof-of-concept randomized trial has suggested that bacterial load-guided shortening of intravenous antibiotic courses in bronchiectasis is feasible [16], yet no observational evidence from routine clinical practice has examined whether day-7 quantitative load thresholds correlate with outcomes across a full year of follow-up. We therefore posited that a day-7

sputum *P. aeruginosa* burden of ≤10^6 CFU/mL may help identify patients who could safely discontinue antibiotic therapy early, and that treatment duration guided by this threshold could represent a more individualized alternative to fixed-duration regimens.

This study aimed to compare one-year clinical outcomes—including systemic inflammation, pulmonary function, exacerbation-related rehospitalization, and antibiotic-free intervals—between short-course (≤7 days) and long-course (>7 days) antibiotic therapy in patients with *P. aeruginosa*-positive mild-to-moderate bronchiectasis, stratified by day-7 quantitative sputum bacterial load. Unlike prior studies that compared fixed antibiotic durations without accounting for microbiological treatment response, this study specifically examines whether a quantitative day-7 bacterial load threshold can identify a subgroup of patients for whom shorter therapy is sufficient—a hypothesis intended to generate the biological and clinical rationale for a future randomized controlled trial.

Patients and Methods

1. Study patients

We reviewed all eligible patients with bronchiectasis who were consecutively hospitalized at the Respiratory Department of the Second Affiliated Hospital of Jiaxing University between January and December 2022 and met the eligibility criteria. Eligibility required: (a) acute exacerbation at admission with no antibiotics in the preceding 14 days; (b) a Bronchiectasis Severity Index (BSI) score ≤8 [9], indicating mild-to-moderate disease; (c) sputum culture positive for *P. aeruginosa* and negative for other organisms; and (d) complete data available at baseline and at 1- and 12-month follow-up. Exclusion criteria were: (a) BSI ≥9 (severe disease); (b) no P. aeruginosa on culture; (c) incomplete follow-up; or (d) coexisting malignancy, respiratory failure, or advanced heart disease.

Treatment course: On the basis of the sputum culture results, conventional antipseudomonal treatment and other symptomatic treatments, such as expectorant and oxygen inhalation, were performed. On day 7 of antipseudomonal therapy, the sputum bacterial load was assessed. Subsequent treatment decisions—whether to discontinue antibiotics or to complete the full 14-day course—were then made by the treating clinician based on the patient's clinical symptoms. Treatment duration was therefore not randomly assigned; as a result, all patients with a high day-7 bacterial load received longer courses.

Grouping: A total of 102 patients with bronchiectasis were divided into the short-course group (≤ 7 days) and long-course group (> 7 days) according to the duration of antibiotic use. Among them, 42 patients were in the short-course group (18 males and 24 females; mean age, 58.05 years), and 60 patients were in the long-course group (27 males and 33 females; mean age, 60.56 years). Table 1 summarizes the baseline characteristics of the two groups.

The study was approved by the hospital's Ethics Committee (approval no. 2024SW110-01) and conducted per the Declaration of Helsinki. The Committee waived informed consent owing to the retrospective design, use of existing records, and minimal risk. Prior to analysis, all patient identifiers

were removed, and the remaining data were anonymized and handled confidentially per institutional standards.

2. Methods

The reporting of this study followed the STROBE recommendations for observational research [10].

2.1 Data collection

Demographic characteristics (age, sex, smoking and drinking history), presenting symptoms, and day-7 sputum *P. aeruginosa* burden during hospitalization were extracted for all 102 participants. Bacterial burden was quantified by sputum culture and dichotomized at 10^6 colony-forming units (CFU)/mL, a cutoff adopted from prior work [11]. Blood indices—white blood cell (WBC) and neutrophil counts, interleukin-6 (IL-6), serum amyloid A (SAA), C-reactive protein (CRP), and procalcitonin (PCT)—together with spirometric measurements, were recorded before admission and at 1 and 12 months after discharge.

2.2 St. George's Respiratory Questionnaire

Health status was evaluated with the St. George's Respiratory Questionnaire (SGRQ) during the index admission and again 12 months after discharge [12]. This validated instrument quantifies disease burden and health-related quality of life (HRQoL) in adults with chronic respiratory conditions. Scoring followed the developer's official algorithm, which generates three domain scores (symptoms, activity, and impacts); higher values denote worse HRQoL.

2.3 Number of acute exacerbations and use of antibiotics within one year

Follow-up began at the index admission and continued for 12 months through outpatient review or telephone contact. At each contact, we recorded any new hospitalization (date and severity) and the time elapsed before the next respiratory antibiotic course, whether intravenous or oral. In line with established criteria, an exacerbation required acute deterioration of ≥2 of 3 cardinal symptoms—increased dyspnea, sputum volume, or sputum purulence—persisting for at least 48 h; as events were ascertained from readmission records, only hospitalized exacerbations were captured. Antibiotic retreatment was defined as any newly prescribed antibiotic course for a respiratory indication, identified through outpatient logs and telephone interviews.

3. Statistical analysis

Distributional assumptions were checked with the Shapiro–Wilk test. Gaussian data are expressed as mean ± SD and compared with unpaired Student's *t*-tests; skewed data as median (IQR) with Mann–Whitney U tests. Proportions were compared by Pearson's χ^2 test with continuity correction, substituting Fisher's exact test when expected counts fell below 5. Two-sided $P<0.05$ denoted significance. Analyses of covariance (ANCOVA), using the corresponding baseline measurement as covariate, addressed

baseline imbalance for spirometric and SGRQ endpoints. For the secondary endpoint of antibiotic re-initiation interval, Bonferroni adjustment was applied as a sensitivity analysis to control for multiple comparisons across the three bacterial load subgroups; unadjusted *P*-values are also reported for transparency. Between-subgroup contrasts of categorical one-year endpoints (readmission; categorized interval to retreatment) relied on χ^2 or Fisher's exact tests. Given the exploratory nature of this study and the number of comparisons performed, all analyses should be interpreted as hypothesis-generating rather than confirmatory. Computations were performed in GraphPad Prism 7.0.

Results

1. Group comparison of the clinical characteristics

The two treatment arms were comparable for age, sex distribution, and smoking and alcohol history (all $P>0.05$), and presenting symptoms occurred at comparable frequencies in both arms (Table 1).

2. Blood inflammatory markers

We first assessed whether shorter antibiotic duration influenced systemic inflammatory profiles by comparing laboratory parameters between the two groups at baseline, 1 month, and 12 months post-discharge. Despite similar demographic and clinical characteristics, baseline inflammatory markers differed between treatment arms. At admission, the long-course group had higher WBC, neutrophil, and CRP values than the short-course group ($P<0.05$), whereas IL-6, SAA, and PCT levels were comparable ($P>0.05$). At both follow-up timepoints, all measured inflammatory markers were similar between groups ($P>0.05$) (Table 2).

3. Group comparison of pulmonary function indicators

To characterize changes in respiratory function over time, we compared spirometric parameters—FEV_1, FVC, FEV_1/FVC ratio, and PEF—between the two groups at baseline and at 1 and 12 months after discharge. At 12 months, the long-course group had lower FEV_1 and FEV_1/FVC values than the short-course group ($P<0.05$). Although baseline FEV_1/FVC was numerically lower in the long-course group (50.86 ± 6.05% vs. 53.68 ± 5.26%), ANCOVA with baseline FEV_1/FVC as covariate confirmed that the 12-month between-group difference remained statistically significant (adjusted $P<0.05$), indicating that the observed disparity was not solely attributable to the initial imbalance. No between-group differences were observed at admission or 1 month ($P>0.05$) (Table 3). The observed improvement from baseline to 12 months may partly reflect regression to the mean, as baseline measurements were obtained during an acute exacerbation; this alternative explanation cannot be ruled out without a control group.

4. SGRQ scores by group

To evaluate the effect of antibiotic duration on HRQoL, SGRQ domain scores were compared between groups at baseline and 12 months post-discharge. No baseline differences were observed across any

domain (*P*>0.05). At 12 months, the long-course group had higher activity and impact scores than the short-course group (*P*<0.05), while symptom scores remained similar (*P*>0.05) (Table 4). ANCOVA adjusting for the corresponding baseline domain scores confirmed that these between-group differences in activity and impact scores at 12 months remained statistically significant (adjusted *P*<0.05).

5. Bacterial load, rehospitalization, and disease severity

To evaluate the impact of different antibiotic treatment regimens on the one-year prognosis of patients with bronchiectasis, we compared the frequency of rehospitalization, the BSI, and the time to antibiotic reuse in the three groups. Patients were stratified by day-7 sputum *P. aeruginosa* burden into low (≤10^6 CFU/mL) and high (>10^6 CFU/mL) groups. All high-load patients received long-course therapy; thus, load-stratified comparisons are descriptive only and cannot disentangle load effects from treatment duration. The short-course group included 42 low-load patients (no high-load); the long-course group included 32 low-load and 28 high-load patients. Among low-load patients, one-year rehospitalization rates were similar regardless of treatment duration (short-course: 18/42 [42.8%] vs. long-course: 13/32 [40.6%]; *P*=0.749). Within the long-course group, rehospitalization was more frequent in high-load than low-load patients (14/28 [50.0%] vs. 13/32 [40.6%]). BSI severity distribution among low-load patients did not differ by treatment arm (mild-moderate: 40.5% vs. 34.4%; severe: 2.4% vs. 6.3%). In contrast, high-load patients had a greater proportion of severe BSI at readmission (21.4%) than either low-load subgroup (2.4% and 6.3%; Fisher's exact *P*=0.029). Antibiotic re-initiation within 6 months was numerically more frequent in high-load patients than in either low-load group (9.5% and 9.4%), but the overall three-group comparison showed only a trend (*P*=0.052); in the Bonferroni-adjusted sensitivity analysis, this difference did not reach statistical significance. The two low-load subgroups did not differ (*P*>0.05), indicating that among low-load patients, antibiotic-free intervals were independent of treatment duration. Full data are shown in Table 5.

Discussion

Among low-load patients, short-course therapy yielded one-year rehospitalization rates (42.8% vs. 40.6%) and antibiotic-free intervals (9.5% vs. 9.4% retreated within 6 months) indistinguishable from those of longer courses, with no inflammatory rebound at either follow-up timepoint. Beyond these equivalence findings, the short-course group demonstrated better 12-month FEV_1, FEV_1/FVC ratio, and SGRQ activity and impact scores—differences that remained statistically significant after ANCOVA adjustment for baseline values, suggesting they are not solely attributable to pre-existing group imbalances. Taken together, these findings support the hypothesis that among *P. aeruginosa*-positive patients who achieve low bacterial burden by day 7, continuing antibiotics beyond that point confers no measurable benefit on exacerbation risk or inflammatory control, and may be associated with worse long-term respiratory outcomes. High-load patients experienced more severe disease trajectories regardless of duration, pointing to bacterial burden—rather than treatment length alone — as the stronger determinant of prognosis.

Managing bronchiectasis with antibiotics involves complex decisions regarding drug selection, duration, and overall strategy—each of which can significantly influence clinical trajectories. Patients frequently experience recurrent exacerbations; among those with *P. aeruginosa* colonization in particular, infection by this organism is a major driver of disease progression and exacerbation frequency. This organism is often initially susceptible to antibiotics yet difficult to eradicate, with a pronounced tendency to acquire multidrug resistance, thereby perpetuating disease recurrence [13]. Biofilm formation further complicates treatment, as conventional systemic agents may not achieve adequate concentrations at the infection site; inhaled formulations can deliver higher local drug levels with reduced systemic exposure, and have accordingly garnered increasing interest [14]. Extended or excessive antibiotic use not only promotes resistance but also elevates the risk of adverse events [15]. One proof-of-concept randomized trial demonstrated the feasibility of shortening intravenous antibiotic courses in bronchiectasis when guided by bacterial load, without evidence of accelerated clinical deterioration after discontinuation [16]. For mild exacerbations, particularly in the absence of *P. aeruginosa*, shorter antibiotic courses have been proposed as potentially sufficient, given that extended therapy may offer diminishing microbiological returns [8, 11]. Conversely, longer regimens (e.g., 14 days) have been associated with greater reductions in exacerbation frequency and severity among high-burden patients [11], and have been shown to lower sputum bacterial loads and improve lung function. These divergent observations likely reflect underlying differences in bacterial burden, with high-load patients more reliant on sustained antibiotic pressure. In this hypothesis-generating retrospective analysis, day-7 bacterial load appeared more strongly associated with the antibiotic-free interval than did treatment duration: among low-load patients, the proportion requiring retreatment within 6 months was nearly identical regardless of whether therapy lasted ≤ 7 or > 7 days (9.5% vs. 9.4%).

Beyond the comparison of continuous versus intermittent schedules, the broader evidence on antibiotic strategies in bronchiectasis also includes intermittent intravenous regimens and long-term macrolide therapy. Intermittent intravenous antibiotic regimens have been reported as potentially beneficial for critically ill patients with frequent bronchiectasis exacerbations [17, 18]. One study found that administering targeted intravenous therapy every 8 weeks to patients experiencing at least five exacerbations annually significantly reduced exacerbation frequency and improved HRQoL [19], suggesting that appropriately timed antibiotic courses may aid disease control. Macrolides remain a therapeutic option in bronchiectasis [20], owing not only to their antimicrobial properties but also to immunomodulatory effects; long-term low-dose macrolide therapy has been associated with fewer exacerbations [21]. Nevertheless, prolonged antibiotic exposure carries risks of microbiome disruption and adverse effects. In the present cohort, all high day-7 bacterial load patients received extended therapy, precluding reliable assessment of optimal strategies for this subgroup. Although direct evidence that shortening treatment prolongs the antibiotic-free interval is lacking, rational antibiotic use—tailored to individual patient characteristics, disease severity, and causative pathogens—may reduce exacerbations and extend treatment-free periods. Our findings indicate that among low-load patients, ≤7-day therapy was not associated with any inflammatory rebound at follow-up, supporting its short-term safety in this subgroup. A recent report [20] corroborates this direction, noting that prolonged therapy

benefits high-load patients but concurrently increases resistance risk, and recommending regular bacterial load monitoring to guide treatment adjustments. Collectively, these observations support an individualized, bacterial load-informed approach to antibiotic duration as a clinically rational alternative to uniform fixed-course regimens.

Several limitations should be acknowledged. First, all high-load patients (> 10^6 CFU/mL) received long-course therapy because clinicians extended treatment in response to persistent infection. Although ANCOVA adjustment was applied to mitigate baseline imbalances in pulmonary function and HRQoL analyses, residual confounding from unmeasured factors cannot be entirely excluded. Consequently, the unadjusted comparisons in Tables 2–4 should be interpreted with this treatment allocation mechanism in mind; the comparison least affected by confounding is that between the two low-load subgroups (Table 5). Second, the sample size was modest, with no a priori power calculation; the study may therefore have been underpowered for some comparisons, and negative findings should be interpreted cautiously (type II error). Third, as a retrospective single-center study, it is susceptible to selection and information biases. Fourth, requiring hospitalization to define exacerbations likely underestimates the true event rate, as outpatient-managed episodes were not captured. Fifth, specific antibiotic agents, doses, and routes of administration were not systematically recorded in this retrospective dataset and could therefore not be analyzed. The heterogeneity of prescribed regimens may have influenced outcomes, though this limitation is inherent to the study design and reflects real-world clinical practice. Sixth, the number of statistical comparisons performed across multiple outcomes and timepoints increases the probability of false-positive findings; all analyses should be regarded as exploratory and hypothesis-generating rather than confirmatory. Seventh, time-to-event data were dichotomized rather than analyzed as survival-time endpoints. Finally, day-7 bacterial load measurements were taken after 7 days of therapy, introducing reverse causality. Future prospective multicenter studies with larger samples and standardized protocols are needed to validate these exploratory observations.

Conclusion

In this retrospective cohort of mild-to-moderate *P. aeruginosa*-positive bronchiectasis, day-7 sputum bacterial load correlated with disease severity and merits further evaluation as a potential treatment guide. Among low-load patients (≤ 10^6 CFU/mL), short-course (≤ 7 days) and longer-course therapy yielded similar one-year rehospitalization rates, inflammatory profiles, and antibiotic-free intervals; the short-course group additionally showed better 12-month pulmonary function and HRQoL scores, differences that persisted after ANCOVA adjustment for baseline values. High-load patients (> 10^6 CFU/mL), who uniformly received longer courses, experienced more severe disease progression, though load and duration effects could not be disentangled. Univariate analyses suggested associations between higher BSI, lower FEV_1, and increased rehospitalization risk. These observations support further exploration of bacterial load-guided, individualized antibiotic strategies over fixed-duration regimens. Given the retrospective design, the non-randomized treatment allocation, and modest sample size, these findings are hypothesis-generating and require prospective validation.

Declarations

Acknowledgements

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YW and HW conceived and designed the study. JJ and YW designed the methodology and performed the statistical analyses. YW JM and LG drafted the manuscript and confirmed the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study complied with the tenets of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Jiaxing University (approval no. 2024SW110-01; Jiaxing, China). The Ethics Committee waived the requirement for individual informed consent given the retrospective design of the study, the use of pre-existing data, the absence of direct patient contact, and the minimal risk involved. All patient data were anonymized before analysis, and confidentiality was rigorously maintained in compliance with institutional and ethical standards.

Conflicts of Interest

L.G. is an employee of AigenX Biosciences. The authors declare no other competing interests.

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Tables

Tables 1 to 5 are available in the supplementary files section

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