



# Clinical profile and in-hospital outcomes of patients hospitalised for bronchiectasis exacerbation

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## To the Editor:

Exacerbations play a pivotal role in the natural history of bronchiectasis, driving symptom worsening, accelerating lung function decline and increasing mortality risk [1, 2]. Exacerbations requiring hospitalisation have particularly severe consequences – not only for individual patients but also for healthcare systems, due to prolonged admissions, the need for intensive care, and post-discharge complications [3]. These events are frequently associated with complex clinical presentations involving respiratory failure, cardiovascular instability and the need for ventilatory support [1]. Yet, despite their impact, hospitalised bronchiectasis exacerbations remain poorly characterised. Most existing evidence derives from outpatient cohorts or retrospective administrative datasets, which lack the clinical granularity necessary to inform risk stratification and guide therapeutic decisions in acute care settings [1]. Identifying factors that predict poor in-hospital outcomes is essential to improve acute management, guide resource allocation, and ultimately prevent long-term sequelae in this vulnerable population.

We conducted a multicentre, retrospective, observational study across four Italian hospitals to characterise adults with bronchiectasis who were hospitalised between January 2013 and August 2023 for an exacerbation, and to identify clinical factors associated with adverse in-hospital outcomes. Adults ( $\geq 18$  years) with clinically and radiologically confirmed bronchiectasis and an acute exacerbation were included [4]. Cases were first identified via ICD-9-CM codes 494.0 (bronchiectasis) and 494.1 (bronchiectasis with exacerbation), and then manually verified by investigators at each site to confirm the diagnosis according to international consensus recommendations for radiological and clinical criteria [4]. Exacerbations were defined according to established criteria: a deterioration in three or more key symptoms (such as cough, sputum volume or purulence, dyspnoea, fatigue, or haemoptysis) lasting at least 48 h and requiring a change in treatment [5]. Data were collected using a standardised case report form and included demographics, comorbidities, presenting symptoms, imaging findings, spirometry (forced expiratory volume % predicted (FEV% pred)), microbiology, arterial blood gases, and clinical outcomes. More precisely, pulmonary function was captured as the most recent FEV% pred measured in clinical stability prior to the index admission; no predefined time-window relative to hospitalisation was applied. Patients with COPD or asthma were not excluded to be closer to what a real life clinic might deal with (although still a stratified analysis as planned) and were recorded as comorbidities together with cardiovascular disease, connective tissue disease, malignancy and others. No additional exclusion criteria were applied, in order to maximise the accurate representation of real-world patients admitted for bronchiectasis exacerbation. The primary endpoint was a composite adverse outcome occurring during hospitalisation, defined as any of the following: all-cause mortality, need for non-invasive ventilation (NIV), or endotracheal intubation and invasive mechanical ventilation. Independent predictors were identified using multivariate logistic regression (ENTER method). Analyses were conducted with SPSS v29.0.1.0. Ethics approval was obtained from the IRCCS Humanitas Ethics Committee (protocol 59/23), with a waiver of informed consent due to data anonymisation.

A total of 318 patients – median (interquartile range (IQR)) age: 72.0 (61.0–78.0) years; 54.7% female – were included, see table 1. 50.3% were current or former smokers. The median (IQR) FEV% pred was 55.5% (41.3–76.0%), and chronic *Pseudomonas aeruginosa* infection was present in 29.2%. The most frequent comorbidities were cardiovascular disease (43.4%), COPD (41.5%) and pulmonary hypertension



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**Patients hospitalised for bronchiectasis exacerbations face significant in-hospital risks. Cardiovascular disease, pulmonary hypertension and low FEV<sub>1</sub> % pred are key predictors of short-term complications and should guide early risk assessment.** <https://bit.ly/42UOpJ3>

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**TABLE 1** Characteristics of the study population and according to the composite adverse outcome occurring during hospitalisation (any of the following: all-cause mortality, need for non-invasive ventilation, or endotracheal intubation and invasive mechanical ventilation)

| Variable                                               | Overall (N=318)    | No negative outcome (N=254) | Negative outcome (N=64) | p-value |
|--------------------------------------------------------|--------------------|-----------------------------|-------------------------|---------|
| Age, years                                             | 72 (61–78)         | 72 (62–78)                  | 71 (56–77)              | 0.251   |
| Male sex                                               | 144 (45.3)         | 108 (42.5)                  | 36 (56.3)               | 0.049   |
| BMI, kg·m <sup>-2</sup>                                | 21.5 (18.4–24)     | 21.5 (18.7–24)              | 21 (16.7–24)            | 0.653   |
| Either current or former smoker                        | 160 (50.3)         | 133 (64.6)                  | 27 (56.3)               | 0.283   |
| Hospitalisations in the previous year                  | 0 (0–1)            | 0 (0–1)                     | 1 (0–1)                 | 0.002   |
| Chronic <i>P. aeruginosa</i> infection                 | 93 (29.2)          | 71 (30.5)                   | 22 (37.3)               | 0.315   |
| Other chronic bacterial infection                      | 69 (21.7)          | 55 (24.8)                   | 14 (26.4)               | 0.805   |
| FEV <sub>1</sub> % pred                                | 55.5 (41.25–76)    | 59.5 (43.3–82.5)            | 47 (35–61.3)            | 0.002   |
| <b>Comorbidity</b>                                     |                    |                             |                         |         |
| COPD                                                   | 132 (41.5)         | 100 (39.4)                  | 32 (50)                 | 0.123   |
| Cardiovascular diseases                                | 138 (43.4)         | 103 (40.6)                  | 35 (54.7)               | 0.041   |
| Connective tissue diseases                             | 14 (4.4)           | 12 (4.7)                    | 2 (3.1)                 | 0.744   |
| Active malignancy                                      | 26 (8.2)           | 21 (8.3)                    | 5 (7.8)                 | 0.905   |
| Inflammatory bowel disease                             | 5 (1.6)            | 5 (2)                       | 0 (0)                   | 0.587   |
| Diabetes mellitus                                      | 45 (14.2)          | 31 (12.2)                   | 14 (21.9)               | 0.047   |
| Pulmonary hypertension                                 | 35 (11.0)          | 21 (8.3)                    | 14 (21.9)               | 0.002   |
| Cognitive impairment                                   | 19 (6.0)           | 15 (5.9)                    | 4 (6.3)                 | 0.917   |
| Chronic liver disease                                  | 18 (5.7)           | 14 (5.5)                    | 4 (6.3)                 | 0.819   |
| Chronic anaemia                                        | 31 (9.7)           | 24 (9.4)                    | 7 (10.9)                | 0.813   |
| Asthma                                                 | 38 (11.9)          | 30 (11.8)                   | 8 (12.5)                | 0.879   |
| Peripheral vascular disease                            | 62 (19.5)          | 51 (20.1)                   | 11 (17.2)               | 0.602   |
| Chronic macrolide therapy                              | 32 (10.1)          | 20 (7.9)                    | 12 (18.8)               | 0.010   |
| LAMA                                                   | 148 (46.5)         | 109 (42.9)                  | 39 (60.9)               | 0.010   |
| LABA                                                   | 158 (49.7)         | 118 (46.5)                  | 40 (62.5)               | 0.022   |
| ICS                                                    | 128 (40.3)         | 98 (38.6)                   | 30 (46.9)               | 0.227   |
| Long-term oxygen therapy                               | 76 (23.9)          | 43 (16.9)                   | 33 (51.6)               | <0.001  |
| Home non-invasive ventilation                          | 20 (6.3)           | 3 (1.2)                     | 17 (26.6)               | <0.001  |
| <b>Signs and symptoms of exacerbation on admission</b> |                    |                             |                         |         |
| Dyspnoea                                               | 235 (73.9)         | 177 (69.7)                  | 58 (90.6)               | <0.001  |
| Cough                                                  | 202 (63.5)         | 162 (63.8)                  | 40 (62.5)               | 0.849   |
| Increased sputum volume                                | 144 (45.3)         | 114 (44.9)                  | 30 (46.9)               | 0.775   |
| Increased sputum purulence                             | 105 (33.0)         | 81 (31.9)                   | 24 (37.5)               | 0.394   |
| Bronchospasm                                           | 95 (29.9)          | 76 (29.9)                   | 19 (29.7)               | 0.971   |
| Haemoptysis                                            | 39 (12.3)          | 34 (13.4)                   | 5 (7.8)                 | 0.288   |
| Chest pain                                             | 41 (12.9)          | 32 (12.6)                   | 9 (14.1)                | 0.755   |
| Fatigue                                                | 115 (36.2)         | 92 (36.2)                   | 23 (35.9)               | 0.966   |
| <b>Vital signs on admission</b>                        |                    |                             |                         |         |
| Heart rate, bpm                                        | 88 (78–100)        | 87 (77–100)                 | 90 (80–100)             | 0.120   |
| Systolic blood pressure, mmHg                          | 130 (116–144)      | 130 (119–144)               | 130 (110–142)           | 0.395   |
| Diastolic blood pressure, mmHg                         | 75 (65–83)         | 75 (65–83)                  | 75 (60–84)              | 0.753   |
| Respiratory rate, breaths·min <sup>-1</sup>            | 19 (17–24)         | 18 (16–22)                  | 22 (18–26)              | 0.013   |
| Temperature, °C                                        | 36.5 (36–37.3)     | 36.5 (36–37.3)              | 36.4 (36–37.2)          | 0.252   |
| <b>Arterial blood gas</b>                              |                    |                             |                         |         |
| F <sub>IO<sub>2</sub></sub> , %                        | 21 (21–21)         | 21 (21–21)                  | 21 (21–32)              | <0.001  |
| pH                                                     | 7.45 (7.41–7.47)   | 7.45 (7.42–7.47)            | 7.41 (7.37–7.47)        | <0.001  |
| P <sub>O<sub>2</sub></sub> , mmHg                      | 65 (56–77)         | 65 (57–77)                  | 60 (51–79)              | 0.093   |
| P <sub>CO<sub>2</sub></sub> , mmHg                     | 39 (35–46)         | 38 (35–43)                  | 47 (36–61)              | <0.001  |
| <b>Blood tests</b>                                     |                    |                             |                         |         |
| Haemoglobin, g·dL <sup>-1</sup>                        | 12.5 (11.12–13.6)  | 12.6 (11.3–13.6)            | 12 (10.9–13.3)          | 0.142   |
| WBC count, 10 <sup>3</sup> ·mm <sup>-3</sup>           | 10.09 (7.51–13.02) | 9.92 (7.46–13.08)           | 10.41 (7.96–12.72)      | 0.426   |
| Eosinophils, 10 <sup>3</sup> ·mm <sup>-3</sup>         | 0.1 (0–0.2)        | 0.1 (0–0.2)                 | 0.1 (0–0.2)             | 0.945   |
| Creatinine, mg·dL <sup>-1</sup>                        | 0.83 (0.66–1.07)   | 0.83 (0.67–1.07)            | 0.81 (0.63–1.05)        | 0.661   |
| BNP, pg·mL <sup>-1</sup>                               | 166 (79–361)       | 147 (71–300)                | 216 (97–432)            | 0.181   |
| C-reactive protein, mg·dL <sup>-1</sup>                | 3.54 (0.93–12.30)  | 3.4 (0.83–12.57)            | 3.73 (1.33–11.79)       | 0.415   |
| Procalcitonin, ng·mL <sup>-1</sup>                     | 0.11 (0.05–0.29)   | 0.1 (0.05–0.22)             | 0.22 (0.05–0.47)        | 0.208   |
| <b>Complications at hospital admission</b>             |                    |                             |                         |         |
| Atrial fibrillation                                    | 24 (7.5)           | 16 (6.3)                    | 8 (12.5)                | 0.093   |
| Confusion                                              | 27 (8.5)           | 13 (5.1)                    | 14 (21.9)               | <0.001  |

Continued

TABLE 1 Continued

| Variable                                        | Overall (N=318) | No negative outcome (N=254) | Negative outcome (N=64) | p-value |
|-------------------------------------------------|-----------------|-----------------------------|-------------------------|---------|
| Respiratory distress                            | 85 (26.7)       | 45 (17.7)                   | 40 (62.5)               | <0.001  |
| Pneumonia (consolidation)                       | 123 (38.7)      | 96 (37.8)                   | 27 (42.2)               | 0.519   |
| Pulmonary embolism                              | 5 (1.6)         | 4 (1.6)                     | 1 (1.6)                 | 1.000   |
| <b>Treatment during hospitalisation</b>         |                 |                             |                         |         |
| Systemic corticosteroids                        | 121 (38.1)      | 93 (36.4)                   | 29 (43.8)               | 0.293   |
| Antibiotic therapy                              | 300 (94.3)      | 239 (94.1)                  | 61 (95.3)               | 1.000   |
| Vasopressors                                    | 1 (0.3)         |                             | 1 (100)                 |         |
| <b>Clinical outcomes during hospitalisation</b> |                 |                             |                         |         |
| Non-invasive ventilation                        | 51 (16.0)       |                             | 51 (100)                |         |
| Intubation                                      | 7 (2.2)         |                             | 7 (100)                 |         |
| In-hospital death                               | 10 (3.1)        |                             | 10 (100)                |         |
| Length of stay, days                            | 13 (9–16)       | 13 (9–15)                   | 17 (13–21)              | <0.001  |

Data are presented as median (interquartile range) or n (%). Systemic corticosteroids include intravenous and/or oral administration during hospitalisation. BMI: body mass index; FEV<sub>1</sub>: forced expiratory volume in 1 s; BNP: brain natriuretic peptide; F<sub>IO<sub>2</sub></sub>: fraction of inspired oxygen; ICS: inhaled corticosteroids; LABA: long-acting  $\beta$ -agonists; LAMA: long-acting muscarinic antagonists; P<sub>CO<sub>2</sub></sub>: partial pressure of carbon dioxide; P<sub>O<sub>2</sub></sub>: partial pressure of oxygen; WBC: white blood cell count.

(11%). Chronic respiratory therapies included inhaled agents (long-acting muscarinic agonists: 46.5%; long-acting beta-agonists: 49.7%; inhaled corticosteroids: 40.3%), long-term oxygen therapy (23.9%), and home NIV (6.3%). Chronic macrolide therapy was prescribed in 10.1%. At admission, the most common symptoms were dyspnoea (73.9%), cough (63.5%), increased sputum volume (45.3%) and purulence (33.0%). Concomitant pneumonia was present in 38.7% of cases, and 26.7% had respiratory acidosis. During hospitalisation, 94.3% received antibiotics, 38.1% ( $\approx$ 121/318) received systemic corticosteroids (either intravenous or oral), 16% required NIV and 2.2% required endotracheal intubation and invasive mechanical ventilation. In-hospital mortality was 3.1%, with a median (IQR) time to death of 15.3 (4.6–24.0) days. The composite adverse outcome occurred in 64 patients (20.1%). Compared to those without complications, patients who experienced the composite outcome had significantly lower FEV% pred (median 47% versus 59.5%,  $p=0.002$ ), and higher prevalence of cardiovascular disease (54.7% versus 40.6%,  $p=0.041$ ), pulmonary hypertension (21.9% versus 8.3%,  $p=0.002$ ), and diabetes (21.9% versus 12.2%,  $p=0.047$ ). They also more frequently presented with respiratory acidosis (62.5% versus 17.7%,  $p<0.001$ ) and were more likely to be on domiciliary NIV prior to admission (26.6% versus 1.2%,  $p<0.001$ ). Multivariate analysis identified cardiovascular disease (OR 3.89, 95% CI 1.39–10.90,  $p=0.010$ ), pulmonary hypertension (OR 3.88, 95% CI 1.16–12.97,  $p=0.028$ ), and low FEV% (OR 1.022 per % decrease, 95% CI 1.001–1.044,  $p=0.036$ ) as independent predictors of the composite outcome. Median (IQR) hospital stay was 13 (9–16) days, and significantly longer among those with adverse outcomes (17 versus 13 days,  $p<0.001$ ). In a subgroup analysis excluding COPD, the direction and magnitude of the associations were preserved; cardiovascular disease and pulmonary hypertension remained significantly associated with the composite outcome, whereas FEV% showed a similar inverse trend but was not statistically significant.

Validated bronchiectasis severity scores (*e.g.* BSI, FACED, BRICS) could not be computed in most patients because several components were missing. As a pragmatic proxy of radiological extent, we report the binary Reiff variable (positive if  $\geq 3$  lobes involved or cystic bronchiectasis; negative otherwise); however, radiological severity was not independently associated with the composite outcome in our cohort.

Our findings underscore: 1) the clinical vulnerability of patients hospitalised for bronchiectasis exacerbations, with one in five experiencing significant deterioration during admission; 2) a low overall in-hospital mortality despite a high comorbidity burden, yet frequent need for ventilatory support; and 3) cardiovascular disease, pulmonary hypertension, and impaired lung function as independent predictors of in-hospital complications [6]. While FEV% is a well-established marker of long-term prognosis, our results confirm its relevance in predicting short-term deterioration during hospitalisation. Notably, age, radiological severity and concomitant pneumonia were not independently associated with poor outcomes. Currently, no validated risk stratification tools exist for patients hospitalised with bronchiectasis exacerbations [1]. Our study has important implications. From a clinical point of view, our findings support the adoption of multidimensional risk assessment tools upon admission to promptly identify high-risk patients who may benefit from intensified monitoring or early escalation of care. The strong

prognostic role of cardiovascular comorbidities highlights the need for systematic screening, risk modification strategies, and cardiology involvement during bronchiectasis exacerbations. From a research point of view, while this study identifies key predictors of adverse outcomes, prospective, multicentre validation is required to develop hospitalisation-specific risk models. Moreover, the association between respiratory acidosis, prior home NIV use, and complications suggests that future interventional trials should evaluate the timing of NIV initiation in this population. Finally, as this study focused exclusively on in-hospital outcomes, longitudinal studies are needed to assess post-discharge mortality, readmission rates, functional recovery, and quality of life, thereby informing integrated care models.

This study has several limitations, including its retrospective design, potential underreporting of non-standardised variables (*e.g.* pneumonia definition), and absence of a formal sample size calculation. Moreover, although all cases were manually validated, initial screening *via* ICD–9–CM codes may have underdetected exacerbations among patients without coded bronchiectasis, particularly in high-risk groups such as haematological malignancies or post-transplant recipients [7]. The aetiology of bronchiectasis – which can influence outcomes during exacerbations – was not captured in our case report form. We could not compute validated severity scores because of missing components, relying instead on a simplified Reiff-based extent variable. Finally, background immunosuppression and exacerbation-specific microbiology (sputum and blood cultures) were not systematically collected and the coexistence of COPD/asthma – recorded as comorbidities – may confound attribution of the exacerbation driver in individual cases, which we recognise as an interpretative limitation. Nevertheless, its multicentre nature, large sample size, manual case validation, and real-world focus on hospitalised patients enhance its validity and generalisability. In contrast to prior studies – mostly based on administrative data or small single-centre cohorts lacking outcome analysis [1] – this work provides one of the most detailed clinical profiles of bronchiectasis exacerbations requiring hospitalisation and identifies early predictors of short-term adverse outcomes.

In conclusion, patients admitted for bronchiectasis exacerbations are at substantial risk of in-hospital deterioration. Cardiovascular disease, pulmonary hypertension, and reduced FEV% are key early predictors of adverse outcomes. Recognising these factors at admission may improve risk stratification, optimise resource allocation, and ultimately enhance short-term outcomes in this fragile patient population.

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Conflict of interest: F. Bindo, E. Simonetta, P. Faverio, P. Scarano, V. Polelli, A. Stainer, F. Amati, M. Nigro, A. Tramontano, S. Mirajaj, P. Curci, M. Mancuso and F. Luppi declare no conflict of interest. A. Gramegna has received honoraria from Chiesi, Vertex, and Insmed for lectures outside the submitted work. C. Crimi has received lecture fees from F&P, ResMed, Philips, Vital Aire, GSK, AstraZeneca and Sanofi; and has participated on an advisory board for Vital Aire, outside the submitted work. F. Blasi reports grants from AstraZeneca, Chiesi and Insmed; and honoraria for lectures or advisory boards from AstraZeneca, Chiesi, Boehringer Ingelheim, GSK, Guidotti, Grifols, Insmed, Menarini, Novartis, OM Pharma, Pfizer, Sanofi, Vertex and Zambon, outside the submitted

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