Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Etiology, Clinical Course, and Mortality-Related Factors in Patients with Non-Cystic Fibrosis Bronchiectasis: A Multicenter Observational Study in Türkiye

Şeyma Başlılar[1]

seymabaslilar@yahoo.com

Sağlık Bilimleri Üniversitesi

Gökçe Külah[1]

Sağlık Bilimleri Üniversitesi

Ayşe Çapar[2]

Sağlık Bilimleri Üniversitesi

Eylem Tunçay[3]

Sağlık Bilimleri Üniversitesi

Ebru Özdemir Bek[4]

Sağlık Bilimleri Üniversitesi

Fatma Özbaki[5]

Sağlık Bilimleri Üniversitesi

Hazan Özkoç[1]

Sağlık Bilimleri Üniversitesi

Harun Öztürk[3]

Sağlık Bilimleri Üniversitesi

İsmet Can Duman[3]

Sağlık Bilimleri Üniversitesi

Celal Satıcı[4]

Sağlık Bilimleri Üniversitesi

Research Article

Keywords: Bronchiectasis, Mortality, Pseudomonas aeruginosa, FACED score, Inflammation, Türkiye

Posted Date: September 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11042108/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Bronchiectasis is a chronic and heterogeneous airway disease characterized by recurrent infections, persistent inflammation, and progressive lung damage. Identifying factors associated with mortality is essential for improving patient outcomes. This multicenter study aimed to evaluate etiological, clinical, microbiological, and inflammatory characteristics and to determine predictors of mortality in patients with non-cystic fibrosis bronchiectasis in Türkiye.

Methods

This retrospective, observational study included 479 adult patients with radiologically confirmed non-cystic fibrosis bronchiectasis from five tertiary care centers. We retrieved demographic, clinical, microbiological, and laboratory data from hospital records and the national health database. Systemic inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII), were calculated. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of mortality. Receiver operating characteristic (ROC) analysis was used to assess the predictive performance of inflammatory markers.

Results

The mean age of the cohort was 58.47 ± 15.76 years, and 52.2% of the patients were female. During the follow-up period, mortality occurred in 61 patients (12.7%), predominantly due to respiratory failure and pulmonary infections. Non-survivors were significantly older, presented with higher mMRC dyspnea scores, and exhibited more severely impaired pulmonary function ($p < 0.001$ and $p = 0.006$, respectively). Healthcare utilization parameters, including emergency department visits, hospitalizations, and intensive care unit (ICU) admissions, were markedly higher among non-survivors (all $p < 0.001$). Sputum culture positivity and chronic *Pseudomonas aeruginosa* isolation were significantly more frequent in the mortality group ($p < 0.001$). Inflammatory markers, namely NLR and SII, were also significantly elevated in patients who died ($p < 0.001$ and $p = 0.001$, respectively). In multivariate analysis, reduced FEV1 (OR: 0.242, $p = 0.049$) and prior ICU admission (OR: 12.788, $p < 0.001$) emerged as independent predictors of mortality. ROC analysis demonstrated modest predictive performance for NLR (cut-off: 3.99, AUC: 0.637) and SII (cut-off: 1183.03, AUC: 0.626).

Conclusion

Reduced pulmonary function and prior ICU admissions are independent predictors of mortality in non-cystic fibrosis bronchiectasis. Chronic airway colonization with *Pseudomonas aeruginosa* and elevated

systemic inflammatory markers contribute significantly to adverse clinical outcomes. These findings highlight the necessity of comprehensive etiological screening, early microbiological evaluation, and rigorous risk stratification in clinical practice.

Introduction

Bronchiectasis is a chronic airway disease characterized by irreversible bronchial dilatation, persistent airway inflammation, and recurrent respiratory infections, leading to progressive lung destruction, severe morbidity, and mortality. Despite recent therapeutic advances, bronchiectasis remains a highly heterogeneous condition characterized by diverse clinical trajectories and outcomes [1, 2].

The etiological spectrum of bronchiectasis is exceptionally broad, encompassing post-infectious sequelae, immunodeficiencies, connective tissue disorders, and genetic conditions. However, a substantial proportion of adult patients present with idiopathic disease, reflecting regional variances in healthcare access, diagnostic thoroughness, and socioeconomic standards. In developing nations such as Türkiye, post-infectious etiologies—particularly a history of childhood pneumonia and pulmonary tuberculosis—historically dominate clinical registries, whereas genetic assessments are infrequently performed in routine adult practice[2–4].

Beyond structural and etiological complexity, chronic airway inflammation and spillover systemic inflammation are central drivers of disease progression. Readily accessible hematological biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII), have gained traction as prognostic indicators in various chronic respiratory conditions, including chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and community-acquired pneumonia [5–8]. In bronchiectasis, elevated NLR and SII reflect heightened systemic inflammation associated with exacerbation frequency, lung function decline, and adverse survival outcomes [9, 10].

Furthermore, microbiological factors—most notably chronic colonization and infection with *Pseudomonas aeruginosa*—accelerate functional deterioration and augment mortality risks, necessitating proactive surveillance and eradication regimens [9, 10].

Given the multifactorial determinants of prognosis in this heterogeneous population, this multicenter observational study aims to characterize the etiological, clinical, microbiological, and systemic inflammatory profile of adult patients with non-cystic fibrosis bronchiectasis in Türkiye and to identify independent predictors of all-cause mortality.

Materials and Methods

Study Design and Population

This multicenter, retrospective, observational study evaluated adult patients diagnosed with non-cystic fibrosis bronchiectasis who were followed for at least one year across five tertiary training and research

hospitals in Istanbul, Türkiye (Sultan 2. Abdülhamid Han Training and Research Hospital, Sancaktepe Prof. Dr. İlhan Varank Training and Research Hospital, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, and Ümraniye Training and Research Hospital).

Inclusion and Exclusion Criteria

- **Inclusion Criteria**: Adult patients aged ≥ 18 years with a radiologically confirmed diagnosis of non-cystic fibrosis bronchiectasis via high-resolution computed tomography (HRCT) and a minimum follow-up duration of one year.
- **Exclusion Criteria**: Patients with incomplete medical records (missing laboratory data, pulmonary function tests, imaging, or mortality status) or a confirmed diagnosis of cystic fibrosis.

Data Collection

Demographic parameters, clinical history, radiological findings, etiological investigations, and laboratory variables were extracted retrospectively from hospital records and the national electronic health database (*e-Nabız*). Recorded variables included:

- Age, sex, smoking history (pack-years), and occupational exposure.
- Etiological factors, including prior tuberculosis, childhood pneumonia, primary/secondary immunodeficiencies, connective tissue disorders, and genetic disorders
- High-resolution computed tomography (HRCT) findings (morphological subtype: cylindrical, varicose, or cystic; and anatomical distribution: unilateral vs. bilateral, affected lobe count).
- Alpha-1 antitrypsin (AAT) levels and genotyping results
- Vaccination status against COVID-19, influenza, and pneumococcus.
- Healthcare utilization metrics: frequency of exacerbations, emergency department (ED) visits, hospitalizations, and intensive care unit (ICU) admissions.
- Respiratory support modalities: long-term oxygen therapy (LTOT), home nebulizer therapy, and non-invasive ventilation (NIV).
- Inhaled corticosteroid (ICS) utilization and duration of therapy.
- Microbiological profiles from sputum cultures (pathogen isolation, colonization status).
- Pulmonary function test (PFT) parameters: forced expiratory volume in 1 second (FEV1, % predicted, and liters), forced vital capacity (FVC, % predicted, and liters), and the FEV1/FVC ratio.
- Complete blood count parameters, including neutrophil, lymphocyte, eosinophil, and platelet counts, were utilized to compute the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII = (Platelet count x Neutrophil count) / Lymphocyte count).
- Disease severity stratification using the FACED score (Mild: 0–2, Moderate: 3–4, Severe: 5–7).

Outcomes

- **Primary Outcome**: All-cause mortality, defined as death confirmed via hospital records or the national death notification system.
- **Secondary Outcomes**: Respiratory-related hospitalizations, ICU admissions, emergency department visits, and microbiological isolation patterns.

Ethical Considerations

The study protocol was approved by the Multicenter Ethics Committee of Ümraniye Training and Research Hospital (Date: 18/12/2023, Approval No: B.10.1.TKH.4.34.H.GP.001/382) in adherence to the Declaration of Helsinki. Due to the retrospective design, informed consent was waived.

Statistical Analysis

Analyses were executed using SPSS software. Descriptive statistics for continuous variables are presented as mean ± standard deviation or median (minimum–maximum) based on distribution normality. Categorical variables are reported as frequencies and percentages. Patients were stratified into mortality (+) and mortality (-) groups. Group comparisons utilized Student's t-test or Mann-Whitney U test for continuous variables, and Chi-square or Fisher's exact test for categorical variables. Univariate and multivariate logistic regression analyses were conducted to evaluate independent predictors of mortality. Receiver operating characteristic (ROC) curve analysis determined optimal cut-off values, sensitivity, and specificity for NLR and SII. Statistical significance was established at $p < 0.05$.

Results

Baseline Characteristics

A total of 479 patients with bronchiectasis were included in this multicenter study. The mean age was 58.47 ± 15.76 years, and 250 patients (52.2%) were female. The majority of patients had bilateral disease (66.0%), and cystic bronchiectasis was the most common radiological subtype (45.5%).

According to the FACED score, most patients had mild disease (73.3%), while 20.9% and 5.8% were classified as moderate and severe, respectively. A history of respiratory-related hospitalization was present in 58.5% of patients, and overall mortality was observed in 61 patients (12.7%).

Regarding microbiological evaluation, sputum cultures were obtained in 55.1% of patients, with a positivity rate of 38.2%. *Pseudomonas aeruginosa* was the most frequently isolated pathogen, accounting for 66.8% of positive cultures.

Comparison Between Survivors and Non-Survivors

Patients who died during follow-up were significantly older compared to survivors ($p < 0.001$). They also exhibited more severe dyspnea, as reflected by higher mMRC scores ($p = 0.001$).

Pulmonary function parameters were significantly impaired in the mortality group, with lower FEV1 (L) and FEV1/FVC ratios ($p = 0.006$ for both). In addition, healthcare utilization was markedly higher among non-survivors, including more frequent emergency department visits, higher hospitalization rates, and increased ICU admissions (all $p < 0.001$).

Microbiologically, sputum culture positivity was significantly higher in patients with mortality ($p < 0.001$), and *Pseudomonas aeruginosa* isolation was more frequent in this group (47.5% vs. 22.7%, $p < 0.001$).

Inflammatory Markers and Treatment-Related Findings

Markers of systemic inflammation were significantly elevated in the mortality group. Both NLR and SII were higher among non-survivors ($p < 0.001$ and $p = 0.001$, respectively).

In addition, inhaled corticosteroid (ICS) use was more common and of longer duration in patients with mortality ($p = 0.042$ and $p < 0.001$, respectively). The use of respiratory support devices was also significantly higher in this group ($p < 0.001$).

Interestingly, vaccination rates for COVID-19 and pneumococcal vaccines were significantly lower among patients with mortality ($p < 0.001$ and $p = 0.026$).

Predictors of Mortality

In univariate analysis, multiple factors were associated with mortality, including age, impaired lung function, frequent hospitalizations, ICU admission, sputum culture positivity, *Pseudomonas aeruginosa* infection, and elevated inflammatory markers.

However, in multivariate analysis, lower FEV1 (L) and a history of ICU admission remained independent predictors of mortality ($p = 0.049$ and $p < 0.001$).

ROC analysis demonstrated that both SII and NLR had modest predictive value for mortality. The optimal cutoff value for SII was 1183.03 (AUC: 0.626), while for NLR it was 3.99 (AUC: 0.637), indicating a potential role of systemic inflammation in risk stratification.

Table 1. Demographic, Clinical, and Laboratory Characteristics of the Patients

Discussion

This multicenter observational study provides comprehensive data regarding the clinical, etiological, microbiological, and inflammatory determinants of mortality in a large cohort of adult patients with non-cystic fibrosis bronchiectasis in Türkiye. Our findings demonstrate that impaired pulmonary function, frequent healthcare utilization, chronic bronchial infection, and heightened systemic inflammation are critical drivers of adverse prognosis.

The etiology of bronchiectasis varies greatly from country to country due to differences in socioeconomic status, prevalence of infectious diseases, access to healthcare, and use of diagnostic tests[11-14]. In underdeveloped and developing countries, lower respiratory tract infections, especially tuberculosis, remain the most frequent etiological causes [11], while in countries with high socioeconomic status, non-infectious and idiopathic causes are dominant [1, 13, 14].

In Türkiye, the rate of tuberculosis in the etiology of bronchiectasis differs between pediatric and adult ages, reported as 2.7-34.8% [11]. In addition, childhood lower respiratory tract infections are still an important cause. However, genetic etiologies are reported with relatively low frequency. This situation may reflect insufficient recognition and limited routine screening rather than a true low prevalence.

In our study, investigation for alpha-1 AT deficiency, immunodeficiencies, and genetic diseases was performed in a small number of patients, and these results show that comprehensive etiological evaluation is not sufficiently performed in the adult patient group. However, it has been reported in the literature that the underlying etiological cause can be determined in approximately half of the patients with bronchiectasis[11].

A central finding of our multivariate analysis is that reduced FEV1 (L) and a history of prior ICU admission are independent predictors of mortality. Diminished forced expiratory volume reflects progressive, irreversible airway destruction, trapped secretions, and chronic airflow obstruction. Similarly, a prior ICU admission acts as a strong clinical surrogate for severe exacerbation proneness, physiological instability, and advanced disease stages rather than serving as an isolated modifiable risk factor.

Microbiologically, *Pseudomonas aeruginosa* was isolated in over a quarter of our total cohort and nearly half of the patients who experienced mortality. Chronic bronchial colonization with *P. aeruginosa* accelerates lung function decline, intensifies local neutrophilic inflammation, and substantially increases mortality risks. Although its independent predictive value was attenuated after multivariate adjustment for healthcare utilization and baseline lung function, its strong univariate association confirms its detrimental impact on clinical trajectories [9].

Another key finding of our study is the role of systemic inflammation in disease progression and prognosis. We observed significantly higher NLR and SII values in patients with mortality. These findings support the growing body of evidence suggesting that systemic inflammatory markers are valuable predictors of adverse outcomes in bronchiectasis. Recent studies have shown that elevated NLR is associated with increased risk of hospitalization and disease severity, while SII has been linked to exacerbation risk and overall disease burden[8]. The predominance of neutrophilic inflammation in bronchiectasis further supports the biological plausibility of these findings, as this inflammatory phenotype is associated with more severe disease and frequent infections[15].

Healthcare utilization was markedly higher among patients with mortality, including increased rates of hospitalizations, ICU admissions, and emergency department visits. This finding reflects the clinical

instability of these patients and highlights the importance of early identification of high-risk individuals. Frequent exacerbations and hospital admissions have been shown to negatively impact long term outcomes and are associated with systemic complications beyond the respiratory system[16].

Interestingly, we found that vaccination rates for COVID-19 and pneumococcal vaccines were lower in patients with mortality. Although causality cannot be established due to the observational nature of the study, this finding suggests a potential protective role of vaccination in bronchiectasis patients. Preventive strategies, including vaccination, may reduce infection-related exacerbations and improve clinical outcomes.

Our study has several strengths, including its large sample size and multicenter design, which enhance the generalizability of the results. In addition, the comprehensive evaluation of clinical, microbiological, and inflammatory parameters provides a holistic understanding of factors influencing mortality in bronchiectasis.

Limitations:

This study has several limitations. First, the retrospective design may limit the ability to establish causal relationships and may introduce selection bias. In addition, the inclusion of centers from a single metropolitan area may restrict the generalizability of the findings.

Furthermore, etiological evaluation and microbiological data, particularly sputum cultures, were incomplete in a substantial proportion of patients, which may have led to underestimation of underlying causes and chronic infections. The lack of detailed information on treatment adherence and long-term management strategies represents another limitation that may have influenced the outcomes.

Finally, systemic inflammation was assessed using NLR and SII; however, other inflammatory biomarkers were not evaluated, which may limit a more comprehensive assessment of the inflammatory burden.

Conclusion

In conclusion, bronchiectasis is a heterogeneous disease in which clinical outcomes are strongly influenced by lung function impairment, healthcare utilization, chronic infection, and systemic inflammation. In this multicenter cohort, reduced FEV1 and prior ICU admission emerged as independent predictors of mortality.

The high prevalence of *Pseudomonas aeruginosa* and its association with mortality highlight the importance of early microbiological evaluation and targeted management strategies. In addition, elevated NLR and SII values support the role of systemic inflammation as a clinically relevant marker for risk stratification.

These findings emphasize the need for comprehensive etiological assessment, closer monitoring of high-risk patients, and individualized treatment approaches to improve outcomes and reduce mortality in

bronchiectasis.

Declarations

- **Ethics Approval and Consent to Participate:** Approved by the Multicenter Ethics Committee of Ümraniye Training and Research Hospital (Date: 18/12/2023, Approval No: B.10.1.TKH.4.34.H.GP.001/382). Informed consent was waived due to the retrospective design.
- **Consent for Publication:** Not applicable.
- **Availability of Data and Materials:** Datasets are available from the corresponding author upon reasonable request.
- **Competing Interests:** The authors declare no competing interests.
- **Funding:** This research received no external funding.
- **Authors' Contributions:** ŞB: Conceptualization, methodology, drafting; GK, AÇ, EÖB, FÖ, HÖzkoç, HÖztürk, İCD: Data collection; ET, CS: Supervision and critical revision. All authors read and approved the final manuscript.
- **Acknowledgements:** We thank all healthcare professionals involved in patient care across the participating centers.

References

1. Gómez-Olivas JD, Oscullo G, Martínez-García MÁ. Etiology of bronchiectasis in the world: data from the published national and international registries. J Clin Med. 2023;12(18):5782.
2. Aliberti S, Goeminne PC, O'Donnell AE, Aksamit TR, Al-Jahdali H, Barker AF, Blasi F, Boersma WG, Crichton ML, De Soyza A. Criteria and definitions for the radiological and clinical diagnosis of bronchiectasis in adults for use in clinical trials: international consensus recommendations. Lancet Respir Med. 2022;10(3):298–306.
3. Choi H, Gao Y-H. Phenotypes and endotypes in bronchiectasis: a narrative review of progress toward precision medicine. J Thorac Dis. 2025;17(4):2640–54.
4. Fang L, Zhu J, Fu D. Predictive value of neutrophil-lymphocyte ratio for all-cause mortality in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. BMC Pulm Med. 2025;25(1):206.
5. Monteleone G, Passantino L, Simonetti J, Iovene B, Varone F, Cameli P, Sgalla G, Richeldi L. A simple ratio in a complex disease: exploring the neutrophil-to-lymphocyte ratio in idiopathic pulmonary fibrosis. J Clin Med. 2025;14(14):5100.
6. Tomas G, Ernam D, Aktürk ÜA. Toplum Kökenli Pnömonide Tanı Anında ve Tedavide C-Reaktif Protein Yerine Nötrofil/Lenfosit Oranı Kullanılabilir mi? Maltepe Tıp Dergisi. 2025;17(2):29–35.
7. Martinez-García MÁ, Olveira C, Girón R, García-Clemente M, Máiz-Carro L, Sibila O, Golpe R, Méndez R, Rodríguez Hermosa JL, Barreiro E. Peripheral neutrophil-to-lymphocyte ratio in bronchiectasis: a

marker of disease severity. Biomolecules. 2022;12(10):1399.
8. Kwok WC, Tam TCC, Lam DCL, Ip MSM, Ho JCM. Systemic immune-inflammation index in predicting hospitalized bronchiectasis exacerbation risks and disease severity. J Thorac Dis. 2024;16(5):2767–75.
9. Sun J, Jia Q, Lv W, Zhang S, Liu S, Wang D, Wang L, Tong X, Chen J, Chen X. Mortality and exacerbations in bronchiectasis patients with carbapenem-resistant Pseudomonas aeruginosa isolation: a long-term retrospective cohort study. Ann Clin Microbiol Antimicrob. 2025;24(1):30.
10. Song J, Sin S, Kang H-R, Oh Y-M, Jeong I. Clinical impacts of Pseudomonas aeruginosa isolation in patients with bronchiectasis: findings from KMBARC Registry. J Clin Med. 2024;13(17):5011.
11. Uğur EG, Kurulu TB. Ulusal yayınlar ışığında Türkiye'de bronşektazi. Tuberk Toraks. 2020;68(1):48–65.
12. Olveira C, Padilla A, Martínez-García M-Á, de la Rosa D, Girón R-M, Vendrell M, Máiz L, Borderías L, Polverino E, Martínez-Moragón E. Etiology of bronchiectasis in a cohort of 2047 patients. An analysis of the Spanish historical bronchiectasis registry. Arch Bronconeumol. 2017;53(7):366–74.
13. Chandrasekaran R, Mac Aogáin M, Chalmers JD, Elborn SJ, Chotirmall SH. Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis. BMC Pulm Med. 2018;18(1):83.
14. Lonni S, Chalmers JD, Goeminne PC, McDonnell MJ, Dimakou K, De Soyza A, Polverino E, Van de Kerkhove C, Rutherford R, Davison J. Etiology of non–cystic fibrosis bronchiectasis in adults and its correlation to disease severity. Ann Am Thorac Soc. 2015;12(12):1764–70.
15. Koukaki E, Papaiakovou G, Klironomou A, Theofani E, Matthaiou AM, Liapikou A, Anagnostopoulos N, Stratakos G, Bakakos P, Rovina N. Inflammatory phenotypes of bronchiectasis. J Pers Med. 2025;15(10):499.
16. Kwok WC, Tsui CK, Sze Him Isaac L, Wong CKE, Tam TCC, Ho JCM, Yap DYH. Bronchiectasis Exacerbation Increases the Risk of Adverse Renal Outcomes—Results From a Large Territory-Wide Cohort Study. Clin Respir J. 2025;19(1):e70029.

Tables

Tables are available in the Supplementary Files section.

Figures

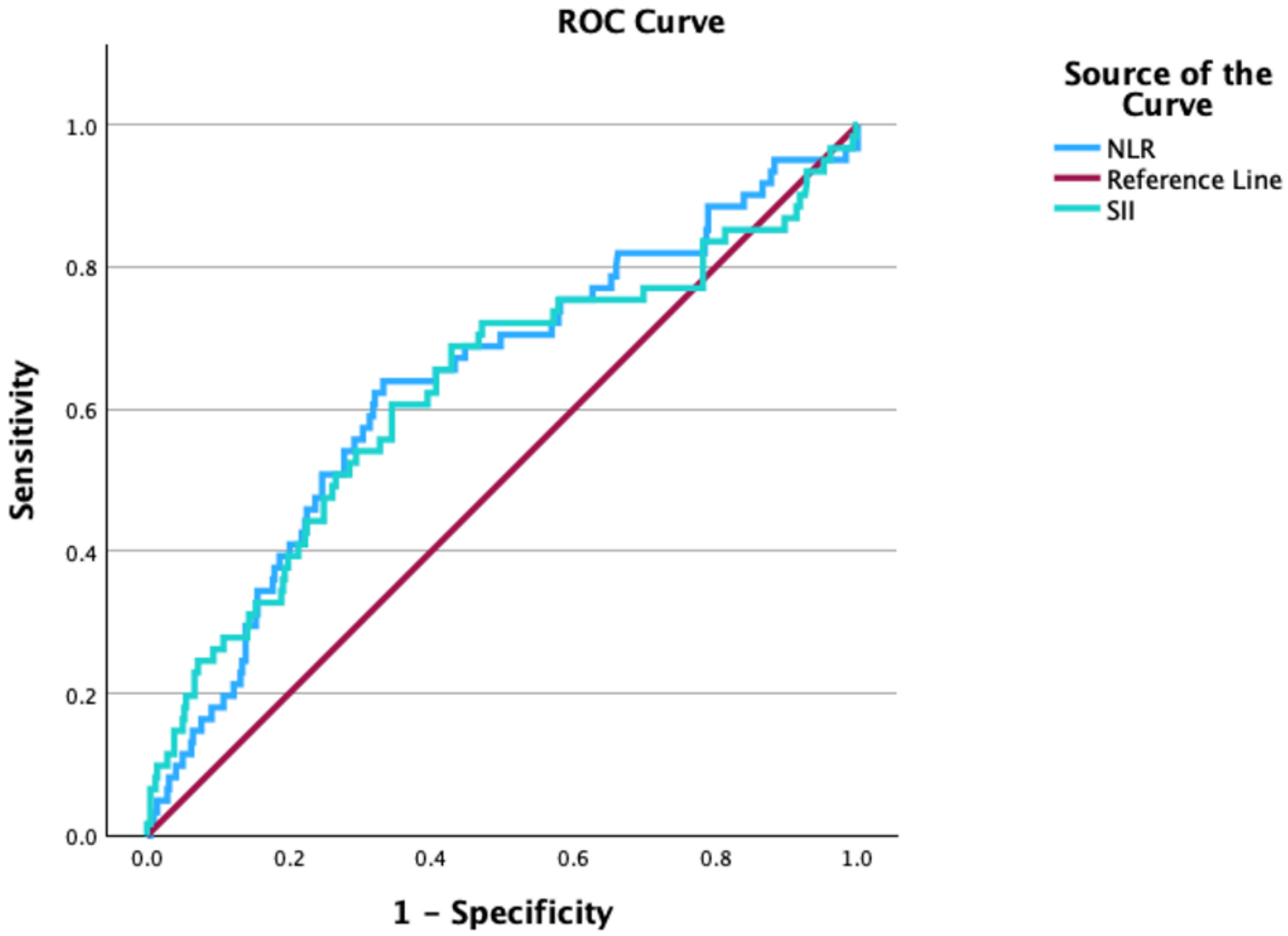


Figure 1

ROC curve analysis for SII and NLR.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.docx