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Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Türkiye
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ABOUT

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Editorial

Artificial Stone Silicosis: Understanding an Emerging Occupational Epidemic

Ozlem Kar Kurt

Clinic of Occupational Medicine, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Türkiye

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Documented as early as ancient Egypt and formally defined by the first international scientific consensus at the 1930 Johannesburg Conference on Silicosis, silicosis is among the oldest recognized occupational diseases. For much of its documented history, it was predominantly associated with well-known traditional industries and generally diagnosed in older workers after prolonged exposure. This epidemiological profile began to change in the early 2000s with the outbreak of denim sandblasting-associated silicosis, which was first brought to the attention of the international scientific community through reports from Türkiye. That outbreak—characterized by exceptionally intense exposure, short latency, rapidly progressive disease, and a strikingly young affected population— now finds a troubling parallel in the artificial or engineered stone industry, a relatively new but highly hazardous sector producing similarly aggressive disease among young workers exposed to extraordinarily high concentrations of respirable crystalline silica (RCS). In this issue of *Thoracic Research and Practice*, the review entitled "Artificial Stone Silicosis: New Face of an Old Disease" provides a timely and clinically oriented synthesis of the occupational context, pathogenesis, clinical manifestations, diagnostic challenges, management, and prevention of this emerging disease.[1]

Since its introduction in Italy in the early 1970s, artificial stone (AS) has evolved into a global industry, increasingly displacing natural materials such as marble and granite in kitchen and bathroom surfaces, interior finishes, and decorative applications, while production and demand continue to expand despite the considerable occupational health burden associated with its fabrication.[2] Parallel to the expansion of the industry, the number of reported patients has increased steadily, with case series, cross-sectional studies, and epidemiological reports now emerging from a growing number of countries. In the most recent American Thoracic Society workshop report summarizing the available evidence, at least 6,351 cases of AS silicosis had been identified worldwide.[3] However, this figure almost certainly represents only the tip of the iceberg, as the true global burden remains unknown and is likely to be substantially underestimated. Much of the literature, from a limited number of countries, consists of case reports, case series, registry analyses, selected screening cohorts, and retrospective studies. Differences in case definitions, exposure characterization, imaging protocols, follow-up periods, and reporting systems complicate comparisons across studies. Underestimation is likely to be greatest in countries where fabrication occurs in small workshops with limited regulatory oversight.

Understanding why AS silicosis has become an increasingly important occupational respiratory health problem requires more than merely documenting new cases. Although its pathogenesis shares the core mechanisms of conventional silicosis, including macrophage activation, oxidative injury, inflammasome signaling, and progressive fibrosis, AS dust is a complex mixture rather than pure crystalline silica.[4] Polymeric resins, pigments, transition metals, and other additives may modify particle toxicity and intensify inflammatory and fibrogenic responses. Experimental studies increasingly suggest that the distinctive toxicity of AS dust is not solely determined by its high crystalline silica content (over 90%), but may also reflect the contribution of metals and other non-silica constituents that amplify inflammatory, cytotoxic, and oxidative responses and disrupt epithelial barrier integrity.[5,6] The current epidemic is simultaneously a consequence of hazardous material

Corresponding author: Ozlem Kar Kurt, MD, PhD, e-mail: okarkurt@gmail.com

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composition, uncontrolled high-intensity exposure, fragmented occupational surveillance, delayed clinical recognition, and inadequate regulatory action. The review emphasizes that exposure is not limited to workers directly operating cutting tools; cleaners, installers, drivers, and other workers in poorly controlled environments may also experience substantial secondary exposure.

Histopathological observations of mixed patterns, including silicotic fibrosis alongside silicoproteinosis, further support the concept that AS-related disease may extend beyond the conventional categories of acute, accelerated, and chronic silicosis. This mixed phenotype may also contribute to the rapid clinical progression observed in some workers. Another intriguing feature is the occurrence of radiological patterns that may mimic sarcoidosis, particularly in patients with chronic silicosis; such diagnostic overlap appears to be encountered more frequently in AS silicosis than in more traditional forms of the disease.[7]

The limitations of conventional chest radiography also deserve emphasis. Although chest radiographs and the International Labour Organization classification remain important in occupational health practice, they may fail to detect early disease associated with AS. High-resolution computed tomography is more sensitive in detecting early nodules, ground-glass opacities, conglomerate fibrosis, emphysema, and mixed radiological patterns. However, the optimal role and frequency of computed tomography in worker surveillance remain unresolved because of radiation exposure, cost, accessibility, and the absence of universally accepted screening protocols. The review therefore highlights an important gap: improved sensitivity must be balanced against feasibility and potential harm, particularly when screening young workers repeatedly over many years.

In our clinical experience, although many patients demonstrate the conventional radiological features of silicosis—including upper-lobe-predominant centrilobular or perilymphatic nodules, coalescent opacities, progressive massive fibrosis, and calcified or non-calcified mediastinal and hilar lymphadenopathy—some cases appear to show a less typical distribution. In particular, confluent mass-like opacities and consolidations may predominate in the middle lung zones, sometimes extending to the upper zones and abutting the pleural surface. Whether this pattern represents part of the broader radiological spectrum of AS silicosis remains uncertain. Nevertheless, it raises the possibility that the complex composition of AS dust—including finely and freshly fractured crystalline silica, resin-derived emissions, adhesives, additives, pigments, and metals—may influence not only disease severity but also its radiological phenotype. This hypothesis requires confirmation through larger, systematically characterized cohorts with detailed exposure, radiological, pathological, and mineralogical assessments.

Therapeutic uncertainty further strengthens the case for prevention. Supportive treatment, management of complications, whole-lung lavage in selected cases of silicoproteinosis, and experimental antifibrotic or immunomodulatory approaches may provide benefit in specific situations, but none currently offers a reliable means of reversing established fibrosis. Lung transplantation remains the only definitive option for advanced disease, yet access is limited, and it cannot compensate for a preventable exposure that continues to cause new cases. Therefore, the most important message of this review is not merely that clinicians should recognize AS silicosis earlier. The hazard posed by AS is already well established, and the priority must be to prevent disease before it develops through rigorous application of the hierarchy of controls. The most effective approach is control at the source, through elimination or substitution of high-silica materials with lower-silica or silica-free alternatives, complemented by rigorously implemented engineering controls such as wet cutting, effective local exhaust ventilation, and appropriate dust containment. Regulatory action is increasingly reflecting this principle. Australia has taken the most decisive step by prohibiting the manufacture, supply, processing, and installation of AS benchtops, panels, and slabs since July 2024.[3] California has also moved in this direction: following the adoption of strengthened silica standards, the state is now advancing rulemaking aimed at prohibiting the fabrication and installation of AS containing more than 1% crystalline silica, a potentially major step forward in primary prevention.[3,8]

Recognition must also trigger action. Each diagnosis should be considered a sentinel event requiring removal from exposure, notification to the relevant authorities, evaluation of coworkers, workplace investigation, and reassessment of exposure controls. Medical surveillance should complement, not replace, primary prevention. Respiratory protective equipment alone is insufficient when elimination, substitution, enclosure, automation, wet methods, and effective local exhaust ventilation have not been implemented.

Available screening studies suggest that the burden of AS silicosis is substantial, with reported prevalence ranging from approximately 12% in a small United States cohort to 23–28% in Australian screening programmes.[1,4] These figures likely still underestimate the true burden, particularly in countries without systematic surveillance.

In parallel, systematic characterization of the clinical and radiological spectrum of AS silicosis—including both the similarities to and the differences from conventional silicosis—may help improve recognition, phenotyping, and early diagnosis. Prevention must remain central to this agenda, with particular emphasis on primary prevention and effective engineering controls rather than reliance on personal protective equipment alone. Finally, future research should focus on quantifying the true burden of AS silicosis, clarifying how AS exposure differs from more traditional sources of RCS, and developing validated approaches for early detection, including biomarkers and low-dose computed tomography-based screening strategies.

Conflict of Interest: Ozlem Kar Kurt, MD, serves as the Editor of the journal. She was not involved in the peer review or editorial decision-making process for this manuscript and had no access to any information regarding its review.

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Original Article

Investigation of the Relationship Between the Daily Physical Activity Level, Smoking Status, and Nicotine Dependence

Yaren Ören[1], Zeynep Nilay Yılmaz[1], Esma Elif Karabulut[1], Nida Nur Karadağ[1], Nisa Nilay Bodur[1], Cahidenur Koçak[2], Esra Pehlivan[1]

[1]Department of Physiotherapy and Rehabilitation, University of Health Sciences Türkiye, Hamidiye Faculty of Health Sciences, İstanbul, Türkiye
[2]Department of Physiotherapy and Rehabilitation, İstanbul Esenyurt University Faculty of Health Sciences, İstanbul, Türkiye

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ABSTRACT

OBJECTIVE: This study aims to assess the relationships among physical activity levels, smoking status, and nicotine dependence in university students enrolled in health sciences programs.

MATERIAL AND METHODS: Between March and April 2025, the study included 164 healthy individuals aged 18 and over, comprising 59 smokers and 105 non-smokers. The "Fagerström test for nicotine dependence" and the "international physical activity questionnaire-short form" were used to evaluate nicotine dependence and to determine daily physical activity levels, respectively.

RESULTS: Non-smokers had higher median walking scores ($P = 0.09$) and slightly higher total physical activity levels ($P = 0.20$) than smokers. However, this difference was not statistically significant and should be interpreted with caution. Spearman correlation analysis showed small correlation coefficients between nicotine dependence and physical activity; the highest coefficient was observed for moderate-intensity activity (r = 0.104).

CONCLUSION: Non-smokers exhibited higher physical activity scores, particularly for walking; however, the differences between groups were not statistically significant. This study highlights the potential relationship between physical activity and nicotine dependence among young adults. Further studies are needed to reduce tobacco use and promote physical activity among university populations.

KEYWORDS: Tobacco use, healthy individuals, motor activity

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INTRODUCTION

Nicotine is a highly addictive substance found in tobacco products. The World Health Organization and recent reviews note that regular (habitual) daily smoking is strongly associated with nicotine dependence and is commonly used as an indicator of dependence in population studies.[1] Globally, cigarette smoking represents one of the leading preventable causes of non-communicable diseases and related mortality. It was responsible for approximately 8.71 million deaths and 229.77 million DALYs worldwide in 2019, with cardiovascular disease, neoplasms, and chronic respiratory diseases among the top causes.[2,3] In Türkiye, tobacco use continues to contribute substantially to morbidity and mortality, aligning with trends seen globally. Cigarette smoking is associated with numerous life-threatening health conditions —including cancers, respiratory disorders, cardiovascular diseases, infections, and neurological dysfunctions —thereby contributing to widespread systemic health deterioration.[2,4] Individuals who smoke are generally less likely to engage in regular physical exercise. Recent studies have found that even among smokers without chronic airflow obstruction, skeletal muscle endurance and ventilatory efficiency are significantly impaired during exercise compared to non-smokers[5] and that physical fitness levels are consistently lower among smokers across adult and elderly populations.[6] A 2024 study in Türkiye found that smokers had reduced exercise capacity and shorter breath-holding times than non-smokers.[7]

Corresponding author: Prof. Esra Pehlivan, PhD, e-mail: fztesrakambur@yahoo.com

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Empirical evidence suggests that regular physical activity contributes to reduced smoking behavior and supports efforts to quit. For instance, a large-scale study conducted in China found that individuals aged 16 and older who engaged in exercise were significantly less likely to smoke.[8] Beyond its role in addiction-related behavior, maintaining a routine of daily physical activity is pivotal for disease prevention, rehabilitation, and chronic disease management among healthy individuals.[9] Given the well-documented health risks associated with tobacco use, the proven benefits of physical activity, and the modifiable nature of both behaviors, exploring the interaction between smoking and physical activity remains crucial for the development of effective tobacco control strategies.[10]

This study aims to contribute to a deeper understanding of the interaction between physical activity and smoking behavior by examining how daily physical activity may influence smoking behavior. By shedding light on the potential relationship between these two modifiable behaviors, these findings may help to raise awareness and to support behavioral strategies aimed at reducing tobacco use. Specifically, this research aimed to investigate whether physical activity levels differ by smoking status and whether physical activity is associated with nicotine dependence among smokers. The ultimate goal is to inform the development of more personalized and effective interventions for individuals who smoke.

MATERIAL AND METHODS

Study Design

This research was a non-randomized, controlled, cross-sectional study. Data were collected using standardized questionnaires. The primary objective was to investigate, using data gathered through validated measurement tools, the association between smoking behavior and physical activity levels among individuals. The study was conducted among students of the University of Health Sciences Türkiye.

Study Population and Sampling

The study sample consisted of 164 participants, including 59 individuals who reported smoking and 105 individuals who identified as non-smokers. The required sample size was determined using an a priori power analysis performed with G*Power software. Based on the chi-square test parameters —effect size (w = 0.3), significance level (α = 0.05), statistical power (1-β = 0.80), and degrees of freedom (df = 4)—the minimum required sample size was calculated as 133.[11] The analysis assumed equal group sizes; however, in practice, exact group matching was not achieved due to the voluntary nature of participation.

Main Points

- Non-smokers may have higher physical activity levels, particularly in walking.
- Higher nicotine dependence may be related to lower physical activity levels.
- Physical activity could be considered a supportive strategy in smoking-related interventions.

Participants were included in the study based on the following criteria: identifying as male or female, being 18 years of age or older, and having no known medical conditions, i.e., being classified as healthy. Smoking status was categorized as current smokers, former smokers, or never smokers. Exclusion criteria included a history of cardiovascular disease, cancer, or serious pulmonary conditions; pregnancy; or age under 18. After applying these inclusion and exclusion criteria, 164 eligible participants were enrolled in the study (Figure 1).

Data Collection Instruments

In this study, data were collected using the Fagerström test for nicotine dependence (FTND) to assess the level of nicotine addiction and the International Physical Activity Questionnaire Short Form (IPAQ-SF) to evaluate participants' physical activity levels.

International Physical Activity Questionnaire

The IPAQ-SF is designed to assess individuals' levels of physical activity, including walking, moderate-intensity activities, and vigorous-intensity activities, as well as time spent sitting. The total physical activity score is calculated in metabolic equivalent of task (MET)-minutes per week, based on the duration and frequency of reported activities. Standardized MET values are assigned as follows: 3.3 MET-min for walking, 4.0 MET-min for moderate-intensity activity, 8.0 MET-min for vigorous-intensity activity, and 1.5 MET-min for sitting. Based on these scores, physical activity levels are categorized into three groups: Category 1: Inactive – individuals who do not meet the minimum activity criteria; Category 2: Minimally Active – individuals who engage in moderate-to-vigorous activities, achieving at least 600 MET-min/week; Category 3: Highly Active – individuals who meet at least 1500 MET-min/week of vigorous activity or accumulate a total of 3000 MET-min/week through various activities.[12]

Fagerström Test for Nicotine Dependence

The FTND is a widely used six-item questionnaire designed to assess the severity of nicotine addiction. It serves as a practical tool for evaluating the degree of dependence and guiding individualized treatment planning. The test provides a classification based on total scores, offering valuable insights for clinical decision-making. Typically administered as a self-report survey, the FTND collects information on smoking habits and behavioral patterns related to nicotine use. Evidence suggests

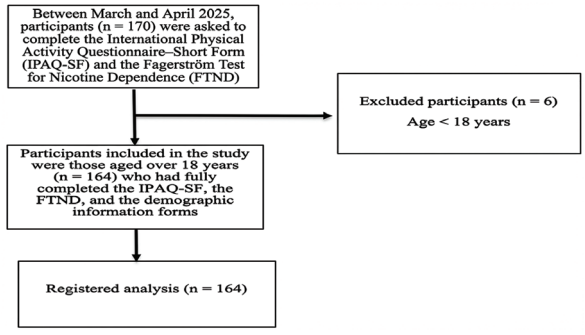


Figure 1. Flow diagram of the study process

that the six-item format enhances the test's ability to accurately determine levels of nicotine dependence. According to the scoring system, total scores of 0–3 indicate low dependence, 4–6 indicate, and 7 or higher indicate high dependence.[13]

In this study, smoking was assessed using participants' smoking status and nicotine dependence level, measured by the FTND.

Ethical Considerations

Ethical approval for this study was obtained from the Hamidiye Non-Interventional Scientific Research Ethics Committee (approval date: 29.05.2025, approval no: 25/488).

Prior to participation, all individuals were informed about the purpose of the study, and it was emphasized that their participation was entirely voluntary. Participants were assured that they could withdraw from the study at any time without any consequences, that their responses would be used solely for scientific purposes, and that all personal data would be kept confidential. Written informed consent was obtained from all participants. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. This study was registered at ClinicalTrials.gov (registration number: NCT07043920).

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The normality of the data distribution was evaluated using the Shapiro–Wilk test, which indicated that the data were not normally distributed ($P < 0.001$). Descriptive statistics were presented as frequencies (n) and percentages (%) for categorical variables. For comparisons of continuous variables between two independent groups, the Mann–Whitney U test was applied, whereas comparisons involving more than two independent groups were analyzed using the Kruskal–Wallis H test. In addition, the Spearman rank-order correlation coefficient was used to examine the relationships between measurement scales. A two-tailed P value of less than 0.05 was considered statistically significant in all tests.[14]

RESULTS

The distribution of participants by gender and smoking status is presented in Table 1. According to the study findings, 36.0% of the 164 participants were identified as smokers, while 64.0% were non-smokers. When gender distribution was examined, 31.9% of female participants and 45.8% of male participants reported smoking. The smoking rate was higher among male participants than among female participants. The chi-square test revealed a statistical trend in the association between gender and smoking status (χ^2: 2.863; $P = 0.09$), which did not reach conventional levels of statistical significance.

Participants' daily physical activity levels were evaluated using the IPAQ-SF, and the results are presented as medians with minimum and maximum values (Table 2). When comparing vigorous physical activity levels between smokers and non-smokers, both groups exhibited a median value of 0.00 MET-min/week, with no statistically significant difference observed ($P = 0.79$). The median moderate physical activity level was similar between smokers and non-smokers, recorded as 120.00 (0–1440) MET-min/week, and showed no significant difference ($P = 0.55$). No significant difference was found, and thus these results should not be overinterpreted. Walking activity levels were 594.00 (0–10,395) MET-min/week in smokers and 891.00 (0–19,635) MET-min/week in non-smokers, demonstrating a trend toward statistical significance ($P = 0.09$). A non-significant trend suggested higher walking activity levels among non-smokers. These findings should be interpreted with caution, as they did not reach statistical significance. For total

Table 1. Sociodemographic characteristics of participants stratified by smoking status

	Total participants (n = 164)	Smokers (n = 59)	Non-smokers (n = 105)	Statistic	*P*
Gender					
Female	116 (70.7%)	37 (31.9%)	79 (68.1%)	2.863[a]	0.09
Male	48 (29.3%)	22 (45.8%)	26 (54.2%)		
Age, years (mean ± SD)	21.9±1.4	22.02±1.6	21.98±1.3		0.6

[a]Chi-square test. Data are presented as number (n) and percentage (%). Statistical significance was set at $P < 0.05$
SD: standard deviation

Table 2. Distribution of participants' physical activity levels according to smoking status

Variables	Total participants (n = 164)	Smokers (n = 59)	Non-smokers (n = 105)	P
IPAQ-SF				
Vigorous physical activity (MET-min/week)	0.00 (0–2880)	0.00 (0–2880)	0.00 (0–2880)	0.79
Moderate physical activity (MET-min/week)	120.00 (0–1440)	120.00 (0–1440)	120.00 (0–1440)	0.55
Walking activity (MET-min/week)	792.00 (0–19,635)	594.00 (0–10,395)	891.00 (0–19,635)	0.09
Total physical activity (MET-min/week)	1188.00 (0–5508)	1158.00 (0–5508)	1188.00 (0–5508)	0.20

Data are presented as median (min–max). Mann–Whitney U test was used. Statistical significance was set at $P < 0.05$
IPAQ-SF: International Physical Activity Questionnaire Short Form, min: minimum, max: maximum, MET: metabolic equivalent of task

physical activity, median values were 1158.00 (0–5508) MET-min/week for smokers and 1188.00 (0–5508) MET-min/week for non-smokers; there was no statistically significant difference between the groups ($P = 0.20$).

The relationship between the level of nicotine dependence among smokers and their physical activity levels was examined using Spearman's correlation analysis. The correlation coefficients were r = 0.098 for vigorous physical activity, r = 0.000 for walking activity, and r = 0.072 for total physical activity. The correlation coefficient was highest for moderate physical activity (r = 0.104) (Table 3).

The distribution of participants' nicotine dependence across categorical physical activity groups was evaluated (low, moderate, high). Among individuals with low nicotine dependence, the majority (n = 28) engaged in moderate physical activity (Table 4). Within this group, only 11 participants reported low physical activity levels, and 4 reported high levels. Conversely, among those with high nicotine dependence (n = 2), one exhibited low physical activity and the other high physical activity. Participants with moderate dependence were predominantly classified in the moderate (n = 9) and low (n = 3) physical activity categories. Because the high-dependence group included only two participants (n = 2), no clear pattern could be identified. These findings should therefore be interpreted with caution.

Figure 2 illustrates the relationship between participants' physical activity levels and their scores on the FTND. Examination of this figure reveals that participants with low nicotine dependence predominantly fall within the moderate physical activity category. While the majority of individuals with low dependence engaged in moderate physical activity, increasing dependence corresponded with a shift toward lower physical activity.

Figure 3 presents the distribution of total physical activity scores from the IPAQ-SF according to smoking status. Analysis of the scatter plot indicates that non-smokers tend to have higher physical activity levels than smokers. Notably, walking scores, which represent low-intensity physical activity, were higher among non-smokers and approached statistical significance.

DISCUSSION

This study investigated whether physical activity levels differed by smoking status and whether physical activity was associated with nicotine dependence among smokers. The main findings showed that non-smokers had higher scores than smokers, particularly in walking and total physical activity; however, these differences were not statistically significant. Furthermore, the correlation between nicotine dependence and physical activity levels was found to be weak and not statistically significant. However, participants with low nicotine dependence were mostly in the moderate physical activity category. Therefore, these findings should be considered trends rather than definitive demonstrations of a relationship.

The existing literature consistently emphasizes the impact of physical activity on overall health status. Several recent reviews and meta-analyses have demonstrated that reductions in physical activity are associated with the emergence and progression of chronic diseases.[15] Another study highlighted the significant role of physical activity in individuals' lives, concluding that consistent exercise programs strengthen the immune system and mitigate adverse effects on physical, mental, psychological, and spiritual health.[16] Tobacco use is another major factor contributing to health problems. Previous research has shown that smokers are less physically active than non-smokers.[17,18] Our findings are consistent with this pattern, as non-smokers report higher levels of physical activity, particularly in walking. However, these differences did not reach statistical significance and should be interpreted with caution. Another notable finding of our study was that the total physical activity score assessed by the IPAQ-SF was higher among non-smokers. Nonetheless, the observed tendency aligns with previous studies suggesting that physical activity may help mitigate smoking behavior.[19]

Although the relationship between smoking behavior and physical activity levels has been extensively investigated, further studies are warranted to support new research in this area. In our study, participants' smoking status and dependence levels were similarly categorized into low, moderate, and high. In our sample, no significant association was observed between gender and smoking status, which contrasts with findings that

Table 3. Relationship between level of nicotine dependence and level of physical activity

Variables		Vigorous physical activity	Moderate physical activity	Walking activity	Total physical activity
FTND	r	0.098	0.104	0.000	0.072
	n	59			

FTND: Fagerström test for nicotine dependence; r: Spearman's correlation coefficient

Table 4. Relationship between nicotine dependence categories and physical activity levels according to IPAQ-SF

		IPAQ-SF category (n)			Total
		Low	Moderate	High	
FTND-category (n)	Low	11	28	4	43
	Moderate	3	9	2	14
	High	1	0	1	2
Total (n)		15	37	7	59

FTND: Fagerström test for nicotine dependence, IPAQ-SF: international physical activity questionnaire-short form

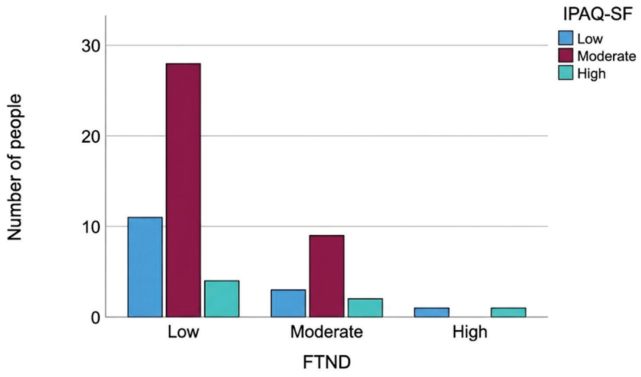


Figure 2. Distribution of physical activity levels based on nicotine dependence categories

IPAQ-SF: International Physical Activity Questionnaire Short Form, FTND: Fagerström test for nicotine dependence

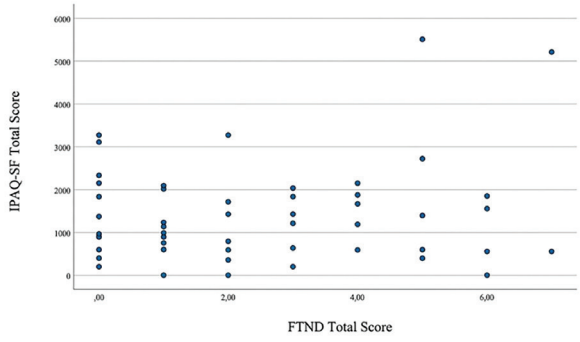


Figure 3. Total IPAQ-SF score according to smoking status

IPAQ-SF: International Physical Activity Questionnaire Short Form, FTND: Fagerström test for nicotine dependence

smoking prevalence may vary by gender depending on cultural and social contexts.[20]

The detrimental effects of nicotine dependence on health are well documented, and its impact on physical activity levels has been examined in various studies. Our study offers a different perspective: it did not demonstrate a strong relationship between nicotine dependence and physical activity levels. Furthermore, analysis of IPAQ-SF and FTND scores in our study revealed that individuals with low nicotine dependence predominantly engaged in moderate physical activity; however, this association did not reach statistical significance and should be interpreted with caution. In contrast, participants with high dependence levels were more frequently clustered within the low physical activity category across subdomains. Similarly, more recent studies report that higher levels of nicotine dependence are associated with lower levels of physical activity and reduced exercise capacity, suggesting a behavioral and physiological link between the severity of nicotine dependence and participation in physical activity.[5,14,21] Our study further indicates that physical activity levels may vary with the degree of nicotine dependence, highlighting the potential role of such activity in behavioral interventions aimed at preventing nicotine addiction. This implies that physical activity could be considered a lifestyle habit that contributes to reduced dependence. Among participants with high nicotine dependence, physical activity levels did not show a clear pattern. Similar findings in the literature have identified physical activity as a protective behavioral factor against smoking.[14] Supporting this, another study reported that low-intensity activities, such as walking, are negatively associated with smoking behavior, and participation in such activities reduces the likelihood of smoking.[9]

Study Limitations

While this study offers a degree of innovation and relevance, it is subject to several limitations. First, as data were collected at a single point in time, causality between smoking behavior and physical activity levels cannot be established. The findings reflect only a cross-sectional snapshot, making it impossible to observe changes over time. Another limitation is that only two participants were classified as having high nicotine dependence. This limits the reliability of comparisons between subgroups and reduces the generalizability of findings related to this category. Future studies could benefit from objective tools such as accelerometers or biochemical markers to verify physical activity and smoking status. Additionally, the influence of psychological or environmental factors, such as stress, peer pressure, or personal motivation, was not evaluated. Investigating these elements could offer a more complete understanding of the behavioral patterns linking smoking and physical activity. However, due to the cross-sectional design, causal inferences cannot be drawn, and the findings should be interpreted with caution.

CONCLUSION

Promoting physical activity may serve as an effective supportive component in smoking cessation efforts and addiction management. Accordingly, physical activity should be incorporated into public health intervention programs aimed at improving overall community well-being. However, the cross-sectional design of this study does not allow causal inferences, which should be acknowledged when interpreting the results.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Hamidiye Non-Interventional Scientific Research Ethics Committee (approval date: 29.05.2025, approval no: 25/488).

Informed Consent: Written informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Concept: Y.Ö., E.P., Design: Y.Ö., E.P., Data Collection or Processing: Y.Ö., Z.N.Y., E.E.K., N.N.K., N.N.B., Analysis or Interpretation: Y.Ö., C.K., E.P., Literature Search: Y.Ö., Writing: Y.Ö., C.K., E.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Original Article

Rifabutin Cross-resistance and Associated *rpoB* Mutations in Rifampicin-resistant *Mycobacterium tuberculosis* Complex Isolates

Nalan Sürücüoğlu[1], Süheyla Sürücüoğlu[2], Nuri Özkütük[2]

[1]Clinic of Medical Microbiology, Manisa City Hospital, Manisa, Türkiye
[2]Department of Medical Microbiology, Manisa Celal Bayar University Faculty of Medicine, Manisa, Türkiye

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ABSTRACT

OBJECTIVE: This study aimed to phenotypically evaluate rifabutin susceptibility in rifampicin-resistant *Mycobacterium tuberculosis* complex isolates and to identify, through DNA sequence analysis of the rifampicin resistance-determining region (RRDR), specific *rpoB* mutations associated with rifabutin susceptibility.

MATERIAL AND METHODS: A total of 43 rifampicin-resistant and 23 rifampicin-susceptible (control) *Mycobacterium tuberculosis* complex isolates, collected between 2000 and 2020 at the Mycobacteriology Laboratories of Manisa Celal Bayar University and Ege University Faculty of Medicine, were included. Phenotypic drug susceptibility testing was performed using the MGIT 960 system. Mutations in a 682-bp fragment encompassing the 81-bp RRDR of the *rpoB* gene were investigated by Sanger sequencing.

RESULTS: Among the 43 rifampicin-resistant isolates, 39 (91%) were resistant to rifabutin, while four (9%) remained susceptible. All rifampicin-susceptible isolates were also susceptible to rifabutin. A total of 44 non-synonymous single nucleotide polymorphisms were detected in rifampicin-resistant isolates, whereas no mutations were observed in the control group. Seven distinct mutation patterns were identified, including one isolate with a double mutation. The most common mutations were S531L (76%), H526Y (12%), and D516Y (4%). The mutations D516Y, L511P, and L533P, as well as the M515I+D516Y double mutation, were associated with rifabutin susceptibility.

CONCLUSION: Early identification of *rpoB* mutations associated with rifabutin susceptibility may allow substitution of rifampicin with rifabutin in selected rifampicin-resistant cases, potentially improving treatment outcomes and limiting the emergence of resistance to second-line drugs. Further *in vitro* studies, including minimum inhibitory concentration testing, and additional clinical data on rifabutin-containing regimens are needed.

KEYWORDS: *Mycobacterium tuberculosis* complex, rifampicin resistance, rifabutin, *rpoB*, mutation

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INTRODUCTION

Tuberculosis (TB) remains one of the most significant infectious diseases threatening global public health. According to the World Health Organization (WHO) Global TB Report 2025, an estimated 10.7 million individuals developed TB in 2024, and there were 1.23 million TB-related deaths worldwide.[1] One of the major obstacles to successful TB control is drug resistance. While the successful treatment rate for drug-susceptible TB remained high at 88% in 2024, it was lower at 71% for rifampicin-resistant TB.[1]

Corresponding author: Nalan Sürücüoğlu, MD, e-mail: surucuoglunalan@gmail.com

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Rifampicin is a cornerstone of TB treatment due to its potent sterilizing activity, and rifampicin resistance is monitored by the WHO as a proxy for multidrug-resistant TB.[1] Rifabutin, a rifamycin derivative with similar antimycobacterial activity, induces cytochrome P450 enzymes to a lesser extent and is therefore preferred in patients co-infected with human immunodeficiency virus or receiving immunosuppressive therapy.[2,3]

In most rifampicin-resistant *Mycobacterium tuberculosis* complex isolates, resistance-conferring mutations occur within the rifampicin resistance-determining region (RRDR) of the *rpoB* gene.[4] Although these mutations frequently result in cross-resistance to rifabutin, certain substitutions—particularly those affecting codons 511, 516, and 533—have been associated with retained *in vitro* susceptibility to rifabutin.[5] Identifying such mutations in rifampicin-resistant isolates may enable the use of rifabutin-containing regimens without resorting to second-line drugs. The present study aimed to phenotypically assess rifabutin cross-resistance in rifampicin-resistant isolates and to characterize the accompanying *rpoB* mutations.

MATERIAL AND METHODS

Mycobacterium tuberculosis Complex Isolates

The study included 43 rifampicin-resistant and 23 rifampicin-susceptible *Mycobacterium tuberculosis* complex isolates collected between 2000 and 2020 at the Mycobacteriology Laboratories of Manisa Celal Bayar University and Ege University Faculty of Medicine. Only one isolate per patient was analyzed. *M. tuberculosis* H37Rv was used as the reference strain.

Phenotypic Drug Susceptibility Testing

Stock isolates were subcultured in MGIT liquid medium, and rifabutin susceptibility was determined using the MGIT 960 automated mycobacterial culture system (Becton Dickinson, USA). Rifabutin (CAS no 72559-06-9, Sigma-Aldrich, USA) was prepared in methanol and diluted to achieve a final critical concentration of 0.5 µg/mL, in accordance with Clinical and Laboratory Standards Institute recommendations.[6] Following completion of the drug susceptibility test, cultures were processed for DNA extraction.

Main Points

- A subset (9%) of rifampicin-resistant *Mycobacterium tuberculosis* isolates remained susceptible to rifabutin, demonstrating that rifampicin resistance alone should not preclude the use of rifabutin.
- Borderline *rpoB* mutations (D516Y, L511P, M515I, L533P) are often associated with a higher probability of rifabutin susceptibility, although they may lead to phenotypic false-susceptibility in rifampicin testing. In contrast, high-level mutations (S531L, H526Y) consistently confer resistance to both rifamycins.
- Molecular identification of *rpoB* mutation profiles can enable personalized rifamycin selection, potentially improving treatment outcomes and preserving second-line drug options.

DNA Extraction, Polymerase Chain Reaction and Sequencing

Genomic DNA was extracted from bacterial suspensions using the GeneMark Bacteria DNA Purification Kit (DP025, GeneMark Technology Co. Ltd., Taiwan) and stored at –20 °C. The genome of *M. tuberculosis* H37Rv (NC_000962.3) was retrieved from the NCBI database and a 682-bp fragment encompassing the *rpoB* RRDR sequences was selected as the target region. Primers were designed in-house using the NCBI Primer-BLAST tool. The primer sequences were as follows: F: 5′-GTCAGACCACGATGACCGTT-3′ and R: 5′-TAGTCCACCTCAGACGAGGG-3′. Polymerase chain reaction (PCR) was performed with an initial denaturation at 94 °C for 2 min, followed by 30 cycles (94 °C for 30 s, 58 °C for 20 s, and 72 °C for 40 s) and a final extension at 72 °C for 5 min. Amplicon integrity was confirmed by agarose gel electrophoresis, and the amplicons were visualized under ultraviolet light before storage at –20 °C for sequencing.

PCR amplicons targeting the *Mycobacterium tuberculosis rpoB* RRDR were sequenced using the BigDye™ Terminator v3.1 kit. Reactions were performed using the original PCR primers and analyzed by capillary electrophoresis on an Applied Biosystems 3730 DNA Analyzer.

Raw chromatograms (AB1) were processed for base calling and quality trimming using the sangerseqR v1.40.0 package. Sequences were aligned to the H37Rv reference (NC_000962.3) using Biostrings and Pwalign packages, with results independently validated via MEGA software. Rifampicin resistance-associated mutations were identified through visual inspection of high-quality consensus sequences and their corresponding chromatograms using the *Mycobacterium tuberculosis* H37Rv (NC_000962.3) strain as the reference sequence.

This study was conducted with the approval of the Health Sciences Ethics Committee of Manisa Celal Bayar University Faculty of Medicine (ref: 1656, date: 01.02.2023).

Statistical Analysis

The frequency of mutations in the study was calculated using percentage values.

RESULTS

Phenotypic susceptibility results for the 43 rifampicin-resistant isolates showed that rifabutin resistance was detected in 39 (91%), while 4 isolates (9%) were found to be rifabutin-susceptible. All 23 rifampicin-susceptible control isolates were also found to be susceptible to rifabutin.

A total of 44 non-synonymous mutations were detected in the rifampicin-resistant isolates. No mutations were observed in the control isolates. The identified mutations resulted in seven distinct genetic variants, with a double mutation observed in one variant. The mutations observed in rifampicin-resistant cases, in order of frequency, were: S531L (76%), H526Y (12%),

D516Y (4%), H526D (2%), L511P (2%), M515I (2%), and L533P (2%).

Among these, the mutations D516Y, L511P, and L533P were identified as associated with rifabutin susceptibility. In addition, one rifabutin-susceptible isolate harbored the M515I+D516Y double mutation. In the four isolates found to be rifampicin-resistant but rifabutin-susceptible, the mutations GAC516TAC, CTG511CCG, ATG515ATC, and CTG533CCG were present; one strain harbored a double mutation of ATG515ATC and GAC516TAC. While the most frequently observed mutation in the 39 isolates phenotypically resistant to both drugs was TCG531TTG (85%, 33/39), the most common mutation in the four rifabutin-susceptible isolates was GAC516TAC (50%, 2/4) (Table 1).

DISCUSSION

Cross-resistance between rifampicin and rifabutin is a well-recognized phenomenon in *Mycobacterium tuberculosis* complex isolates and is largely driven by mutations in the *rpoB* RRDR. However, increasing evidence indicates that not all rifampicin resistance-conferring mutations result in uniform cross-resistance to rifabutin, highlighting a clinically relevant heterogeneity within rifampicin-resistant isolates. In the present study, susceptibility to rifabutin was observed in 9% of phenotypically rifampicin-resistant isolates. Although this proportion is lower than the 13–28% range reported in previous studies, this finding should not be interpreted solely as a limitation.[7-9] Rather, it underscores the population-specific distribution of *rpoB* mutations and reinforces the concept that rifabutin susceptibility is restricted to a molecularly defined subset of rifampicin-resistant isolates. From a clinical perspective, even a relatively small proportion of rifabutin-susceptible isolates may represent a meaningful therapeutic opportunity, particularly in settings where preserving first-line drug backbones is desirable. However, the presence of borderline *rpoB* mutations (often located outside the core 81-bp hot spot) presents a diagnostic challenge, as they frequently confer low-level rifampicin resistance that may lead to phenotypic false-susceptibility in conventional tests.[10]

The WHO's 2023 "Catalogue of Mutations in *Mycobacterium tuberculosis* Complex and Their Association with Drug Resistance" provides a robust framework for interpreting the clinical relevance of *rpoB* mutations by stratifying them according to the strength of evidence linking genotype to phenotypic resistance.[10] Within this framework, the majority of mutations identified in our study—namely S531L, H526Y, H526D, D516Y, L511P, and L533P—are classified as Group 1 mutations associated with rifampicin resistance. The predominance of these mutations among rifabutin-resistant isolates in our cohort is therefore concordant with both molecular expectations and prior epidemiological data. Studies covering the Aegean, Marmara, and Central Anatolia regions of Türkiye indicate that mutations responsible for rifampicin

Table 1. Observed mutations and phenotypic resistance patterns in *Mycobacterium tuberculosis* complex isolates

Codon*	Nucleotide substitution	Amino acid change		Number (%)**	Phenotypic resistance
531	TCG→TTG	S531L	Ser - Leu	33 (75%)	R^R/RFB^R
526	CAC→TAC	H526Y	His-Tyr	5 (11%)	R^R/RFB^R
526	CAC→GAC	H526D	His-Asp	1 (2%)	R^R/RFB^R
516	GAC→TAC	D516Y	Asp-Tyr	2 (5%)	R^R/RFB^s
511	CTG→CCG	L511P	Leu-Pro	1 (2%)	R^R/RFB^s
533	CTG→CCG	L533P	Leu-Pro	1 (2%)	R^R/RFB^s
515+516	*ATG→ATC*	M515I	Met-Ile	1 (2%)	R^R/RFB^s
	GAC→TAC	D516Y	Asp-Tyr		
Wild type				23	R^S/RFB^s

*Based on *Escherichia coli* numbering system[10], **Number (%) indicates the number and percentage of mutation events (n = 44), not the number of isolates
RFB: Rifabutin, ^{R}: Rifampicin, ^{r}: Resistant, ^{s}: Susceptible

Table 2. Grading of identified mutations according to the WHO catalogue

Variant	*E. coli* numbering	Reliability grading	Additional criteria*	Group
rpoB_S450L	S531L	Associated with resistance		1
rpoB_H445D	H526D	Associated with resistance		1
rpoB_H445Y	H526Y	Associated with resistance		1
rpoB_D435Y	D516Y	Associated with resistance	Borderline resistance	1
rpoB_L452P	L533P	Associated with resistance	Borderline resistance	1
rpoB_L430P	L511P	Associated with resistance	Borderline resistance	1
rpoB_M434I	M515I	Associated with resistance-interim		2

*Additional criteria were evaluated in accordance with the Catalogue of Mutations in *Mycobacterium tuberculosis* Complex and Their Association with Drug Resistance, second edition
WHO: World Health Organization

resistance are primarily concentrated in codons 531, 526, 516, and 513, although their frequency distribution varies by region. Among the specific alterations identified in these regions, the Ser531Leu mutation has been reported as the most prevalent variant.[11-14]

In contrast, mutations such as D516Y, L511P, and L533P occupy distinct positions within the resistance spectrum. These substitutions are also categorized as group 1 mutations, but are widely recognized as "borderline" or "disputed" mutations and are often associated with minimum inhibitory concentrations close to the critical threshold.[10] Importantly, multiple *in vitro* and clinical studies have demonstrated that isolates harboring these mutations may retain susceptibility to rifabutin despite being classified as rifampicin-resistant by standard phenotypic methods.[10,15-17] The observation that all isolates carrying these mutations in our study were susceptible to rifabutin provides further support for this genotype-phenotype dissociation and reinforces the biological plausibility of the use of rifabutin in this subset.

In this study, a double mutation (M515I and D516Y) was detected in one isolate, and this variant was found to be susceptible to rifabutin. In contrast, a study conducted by Jing et al.[18] reported that while single mutations at codons 511, 516, 526, and 533 were associated with rifabutin susceptibility, isolates harboring double mutations at these positions exhibited a rifabutin-resistant phenotype. This finding suggests that rifabutin susceptibility or resistance is determined not by the number of mutations but rather by the specific mutation pattern present. Table 2 presents the reliability grading of the mutations identified in this study according to the WHO mutation catalogue. In line with recent advancements, next-generation sequencing technologies are increasingly utilized for TB diagnosis and comprehensive drug resistance profiling, as outlined in current WHO guidelines.[19] Although next-generation sequencing is primarily employed for research purposes, it is anticipated to transition into routine commercial *in vitro* diagnostic use in the near future, offering a higher-throughput approach to identifying complex mutation patterns.

Study Limitations

The most important limitations of this study are the absence of minimum inhibitory concentration analysis and the limited number of isolates included. In addition, the recent WHO recommendation to lower the critical concentration for rifampicin to 0.5 µg/mL may alter phenotypic resistance profiles and increase the rate of false-positive rifampicin resistance. Therefore, further studies incorporating minimum inhibitory concentration testing, multiple culture systems, and sequencing of *rpoB* regions outside the RRDR are required.

CONCLUSION

Nine percent of phenotypically rifampicin-resistant isolates in this study were susceptible to rifabutin. High-level resistance mutations (S531L, H526Y, H526D) were associated with resistance to both rifampicin and rifabutin, whereas borderline resistance mutations (D516Y, L533P, L511P) were associated with susceptibility to rifabutin. The inclusion of rifabutin in treatment regimens for such cases may improve treatment outcomes and help prevent the rapid emergence of resistance to second-line drugs. Larger *in vitro* studies incorporating minimum inhibitory concentration data, together with additional clinical evidence on rifabutin-containing regimens, are required.

Ethics

Ethics Committee Approval: This study was conducted with the approval of the Health Sciences Ethics Committee of Manisa Celal Bayar University Faculty of Medicine (ref: 1656, date: 01.02.2023).

Informed Consent: Patient informed consent was not obtained because the research was retroactively performed on stored laboratory bacterial strains, ensuring complete patient anonymity.

Footnotes

Authorship Contributions

Concept: N.S., S.S., N.Ö., Design: N.S., S.S., Data Collection or Processing: N.S., Analysis or Interpretation: S.S., N.Ö., Literature Search: S.S., Writing: N.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Presented in: This study was presented as an oral presentation at the 8th National Mycobacteriology Symposium (6–7 June 2024, Ankara) and received an award for best presentation.

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Original Article

Pulmonologist-performed Ultrasound-guided Transthoracic Biopsy of Pleural-based Lung Masses: Diagnostic Yield and Safety, a Retrospective Study

Hemant Kumar[1], Pulkit Gupta[1], Sulakshana Gautam[1], Ruth Shifa Hari[2], Sagar Jain[1], Saumya Shukla[3], Sanjay Singhal[4], Mrityunjaya Singh[1], Vineeta Mittal[5], Ajay Kumar Verma[1]

[1]Department of Pulmonary Medicine, Dr. Ram Manohar Lohia Institute of Medical Sciences, Uttar Pradesh, India
[2]Department of Pathology, Career Institute of Medical Sciences and Hospital, Uttar Pradesh, India
[3]Department of Pathology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Uttar Pradesh, India
[4]Department of Pulmonary Medicine, T.S. Misra Medical College and Hospital, Uttar Pradesh, India
[5]Department of Microbiology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Uttar Pradesh, India

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ABSTRACT

OBJECTIVE: Ultrasound-guided transthoracic lung biopsy is a well-established, minimally invasive technique for evaluating peripheral and pleural-based lung lesions. Its use by trained pulmonologists has expanded in recent years; however, evidence from tuberculosis-endemic regions remains limited. This study aimed to assess the diagnostic yield and safety profile of pulmonologist-performed ultrasound-guided transthoracic biopsy of pleural-based lung masses.

MATERIAL AND METHODS: This retrospective study included patients who underwent ultrasound-guided transthoracic biopsy of pleural-based lung lesions. Of 129 eligible patients, 6 did not undergo the procedure, and 7 were excluded because histopathology was unavailable, resulting in 116 patients included in the final analysis. All biopsies were performed by pulmonologists who had formal interventional pulmonology training or who were under direct supervision. Diagnostic yield, histopathological findings, and procedure-related complications were evaluated.

RESULTS: The overall diagnostic yield was 97.4% (113/116). Malignancy was identified in 72.4% of patients, with adenocarcinoma (39.7%) as the most frequent subtype, followed by squamous cell carcinoma (15.5%). Tuberculosis was diagnosed in 9.5% of cases, while 2.6% remained inconclusive. Notably, 29.3% of patients were already receiving anti-tuberculosis therapy at presentation. The overall complication rate was 10.3%. Pneumothorax occurred in 3.4% of patients, and minor hemoptysis occurred in 2.6%; all events were managed conservatively. No procedure-related mortality was recorded.

CONCLUSION: Pulmonologist-performed ultrasound-guided transthoracic biopsy of pleural-based lung lesions yields high diagnostic yield with a low complication rate when conducted by formally trained operators. In tuberculosis-endemic settings, histopathological confirmation is critical to differentiate malignancy from infectious etiologies. Structured interventional pulmonology training may further optimize procedural outcomes and enhance patient safety.

KEYWORDS: Ultrasound-guided biopsy, transthoracic lung biopsy, interventional pulmonology, pleural-based lung mass, diagnostic yield, pneumothorax, lung cancer, tuberculosis, safety

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Corresponding author: Hemant Kumar, DM, e-mail: drhemantkumar14@gmail.com

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INTRODUCTION

Pleural-based lung masses are commonly encountered in clinical practice and may represent primary malignancy, metastatic disease, tuberculosis, or benign inflammatory conditions. Establishing an accurate tissue diagnosis is crucial to guide appropriate therapeutic decision-making.[1,2]

Computed tomography (CT)-guided transthoracic biopsy has traditionally been the preferred technique for sampling peripheral lung lesions because of its high diagnostic accuracy. However, this approach is associated with radiation exposure, higher costs, and reliance on radiology infrastructure and personnel.[3] In contrast, ultrasound-guided transthoracic biopsy offers a real-time, radiation-free, and cost-effective alternative, particularly for pleural-based lesions that abut the chest wall.[4]

Previous studies have reported diagnostic yields ranging from 80% to 95%, with low complication rates, most commonly pneumothorax and hemoptysis.[4,5] Although the majority of published data pertain to procedures performed by radiologists, emerging evidence suggests that pulmonologists can achieve comparable diagnostic performance and safety outcomes.[6,7]

Given the expanding scope of interventional pulmonology, further evaluation of the effectiveness and safety of pulmonologist-performed ultrasound-guided transthoracic lung biopsy is warranted. Accordingly, we conducted this retrospective study to assess the diagnostic yield and complication profile of ultrasound-guided biopsy, performed by pulmonologists, of pleural-based lung masses at a tertiary care center.

MATERIAL AND METHODS

Study Design and Setting

This retrospective observational study was conducted in the Department of Pulmonary Medicine at a tertiary care teaching hospital in North India. All consecutive patients who underwent ultrasound-guided transthoracic biopsy for pleural-based lung masses between 1 January 2024 and 31 December 2025 were included in the study.

The study was approved by the Dr. Ram Manohar Lohia Institute of Medical Sciences Ethics Committee (IEC no: 168/25 dated 30.01.2026).

Main Points

- Ultrasound-guided transthoracic biopsy is a highly effective and safe method for diagnosing pleural-based lung masses when performed by trained pulmonologists.
- Early histopathological confirmation is crucial, particularly in tuberculosis-endemic regions, to avoid misdiagnosis and inappropriate empirical treatment.
- Proper training in interventional pulmonology and real-time ultrasound guidance significantly enhance diagnostic accuracy and minimize complications.
- As this was a retrospective analysis of anonymized data, the requirement for informed consent for study participation was waived. However, written procedural consent had been obtained from the patients or their legally authorized representatives at the time of the procedure.

Study Population (Table 1)

Inclusion criteria

- Adult patients (≥18 years).
- Presence of a pleural-based lung mass abutting the chest wall on imaging.
- Cases in which a definitive diagnosis could not be established by non-invasive methods.
- All consecutive patients with peripheral lung masses who underwent ultrasound-guided transthoracic lung biopsy during the study period.

Exclusion criteria

- Lesions not accessible by ultrasound guidance.
- Uncorrected coagulopathy (international normalized ratio >3 or platelet count <50,000/mm^3).
- Incomplete medical records.
- Cases in which biopsy samples could not be submitted for histopathological or microbiological evaluation.
- Reports that were unavailable or uninterpretable due to reasons such as inadequate sample, specimen loss, or processing errors.
- Patients who did not provide informed consent for procedure.

Procedure Technique

All procedures were performed by pulmonologists with formal training in interventional pulmonology (Doctorate of Medicine Pulmonary Medicine) or with documented prior experience in ultrasound-guided thoracic interventions. The biopsy was either performed directly by these trained pulmonologists or conducted under their strict real-time supervision.

Pre-procedure imaging, including chest radiography and CT of the thorax, was reviewed to confirm pleural contact with the lesion and to determine the optimal entry site (Figure 1).

Ultrasound-guided transthoracic lung biopsies were performed as part of routine clinical care in a dedicated procedure room. Written informed consent was obtained from the patient or their legal guardian prior to the procedure. Intravenous access was secured, and continuous monitoring of vital parameters—including pulse rate, blood pressure, and oxygen saturation—was maintained throughout the procedure.

Thoracic ultrasound was performed using a high-frequency linear or curvilinear transducer. The lesion was localized, and its size, depth, and vascularity were assessed (Figure 2). The biopsy site was marked and prepared under strict aseptic precautions. Local anesthesia was administered by infiltrating 10–15 mL of 1% lidocaine to the level of the parietal pleura. A 16-gauge tru-cut biopsy needle was used to obtain multiple core tissue samples under real-time ultrasound guidance (Figures 3 and 4).

Table 1. STROBE flow diagram of patient inclusion and exclusion

Stage	n	Details
Total patients eligible for USG-guided lung biopsy	129	
Biopsy not performed	6	No consent (n = 2) for procedure TB confirmed on sputum (n = 1) Lidocaine hypersensitivity (n = 1) Lesion not visualized due to scapular shadow (n = 2)
Patients who underwent USG-guided biopsy	123	
Excluded after biopsy	7	Histopathology reports not traceable despite best efforts
Patients included in final analysis	**116**	

USG: Ultrasonography

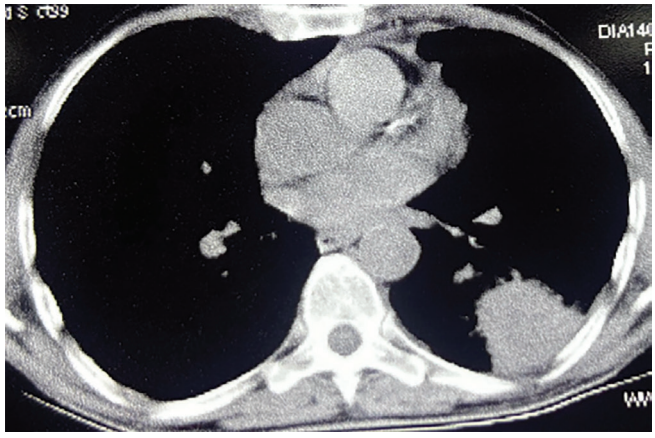


Figure 1. Computed tomography thorax showing pleural-based lung mass in left lower lobe

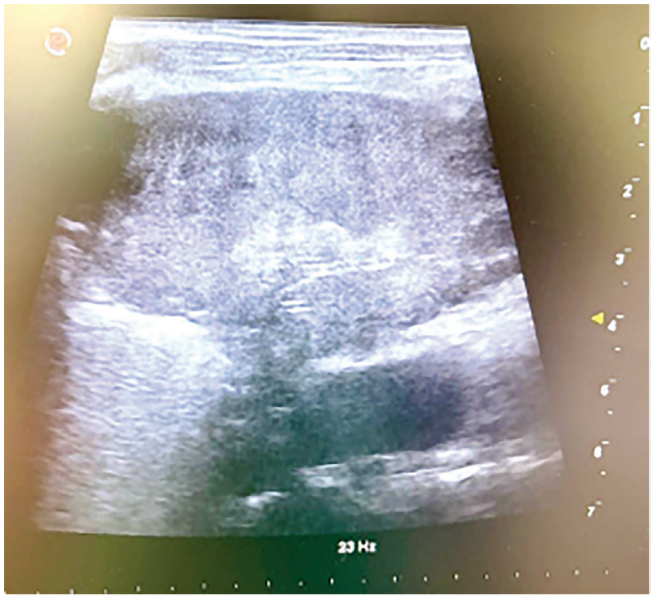


Figure 2. Ultrasound showing pleural-based hyperechoic shadow suggestive of a lung mass

Biopsy specimens were preserved in formalin for histopathological examination, and in normal saline for GeneXpert testing and for acid-fast bacilli mycobacterial growth indicator tube culture. A chest radiograph was obtained 2 hours after the procedure, or earlier if clinically indicated, to evaluate for pneumothorax or other complications.



Figure 3. 16-gauge biopsy gun with needle

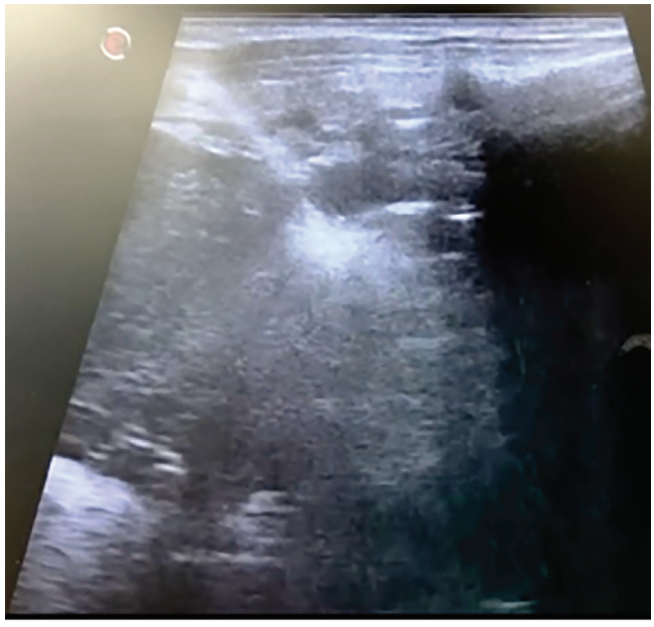


Figure 4. Needle tracking inside the lung mass during ultrasound-guided biopsy

Outcome Measures

Primary outcome

- **Diagnostic yield:** Defined as the proportion of biopsies that provided a definitive pathological diagnosis.

Secondary outcomes

- **Complication rate:** Including pneumothorax, hemoptysis, chest pain, vasovagal episodes, and requirement for any medical or interventional management.
- **Tissue adequacy:** Assessment of whether the biopsy specimen was sufficient for histopathological examination.

Data Collection

Demographic data, radiological characteristics (including lesion size and location), number of biopsy passes, histopathological findings, and procedure-related complications were extracted from medical records using a structured data collection form.

Statistical Analysis

Data were analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate, while categorical variables were presented as frequencies and percentages.

RESULTS

A total of 129 patients were screened during the study period; biopsy was not performed in six. Of the 123 patients who underwent ultrasound-guided transthoracic biopsy, seven were excluded due to unavailable histopathology reports. Ultimately, 116 patients were included in the analysis (Table 1).

The mean age of the study population was 55.15 ± 5.6 years (range 18–85 years), and the majority were male (78.4%). Tobacco exposure was common, with 58.6% reporting tobacco chewing, 24.1% reporting current smoking, and 20.7% reporting former smoking. Alcohol consumption was noted in 27.6% of patients.

Hypertension (23.3%) and diabetes mellitus (18.1%) were the most frequent comorbidities. A prior history of anti-tuberculosis therapy (ATT) was present in 17.2% of patients, while 29.3% of patients were on ATT for the same lesion at presentation. A small proportion had underlying extrapulmonary malignancies (Table 2).

Lesions were more frequently located in the right lung (48.3%) than in the left lung (41.4%); 10.3% involved the mediastinum (Table 1). On ultrasonography, 54.3% of lesions were located at a depth greater than 4 cm from the skin surface. Pleural contact exceeding 3 cm was observed in a substantial proportion of lesions. The majority (70.7%) exhibited heterogeneous echotexture, including areas of necrosis (Table 3).

Histopathological examination revealed malignancy in 84 patients (72.4%). Adenocarcinoma was the most common subtype (39.7%), followed by squamous cell carcinoma (15.5%) and small cell carcinoma (5.2%). Other malignant diagnoses included lymphomas and sarcomas. Non-malignant lesions were identified in 29 patients (25.0%), with tuberculosis accounting for 9.5% and organizing pneumonia for 7.8%. Three cases (2.6%) were inconclusive (Table 4). In the three cases that remained inconclusive (2.6%), a repeat ultrasound-guided lung biopsy was performed. However, the repeat histopathology was again non-diagnostic, showing either fibrosis or normal lung tissue with fibrotic bands. These patients were subsequently kept under clinical and radiological observation without further invasive investigation. At three-month follow-up imaging, the lesions remained stable or showed slight regression, and no clinical progression was noted.

Table 2. Baseline epidemiological and clinical profile of patients

Parameters	n = 116 n (%)
Age	
Mean ± SD	55.15±5.6
Range (years)	18–85
Sex	
Male	91 (78.4%)
Female	25 (21.6%)
Addiction	
Ex smoker	24 (20.7%)
Current smoker	28 (24.1%)
Tobacco chewer	68 (58.6%)
Alcoholic	32 (27.6%)
Comorbidity	
Diabetes	21 (18.1%)
Hypertension	27 (23.3%)
Coronary artery disease	12 (10.3%)
Chronic kidney disease	8 (6.9%)
Chronic liver disease	3 (2.6%)
Anti-tuberculosis therapy (ATT) status	
Past history of ATT	20 (17.2%)
Currently on ATT for same lesion	34 (29.3%)
Underlying malignancy	
Lung carcinoma	8 (6.9%)
Breast carcinoma	3 (2.6%)
Gastrointestinal tract malignancy	2 (1.7%)
Buccal mucosa carcinoma	2 (1.7%)
Genitourinary carcinoma	1 (0.9%)
Location of mass	
Left lung	48 (41.4%)
Right lung	56 (48.3%)
Mediastinum	12 (10.3%)
Peripheral <1/3rd area	35 (30.2%)
Peripheral <2/3rd area	28 (24.1%)
Peripheral >2/3rd area	25 (21.6%)
Extends from hilum to peripheral	16 (13.8%)

SD: Standard deviation

The overall diagnostic yield of ultrasound-guided biopsy was 97.4% (113/116). Procedure-related complications occurred in 12 patients (10.3%). Pneumothorax was observed in four patients (3.4%), one of whom required intercostal tube drainage and a 48-hour hospitalization. Minor hemoptysis occurred in three patients (2.6%) and did not require intervention. Bleeding at the biopsy site and post-procedure pain were each observed in 1.7% of patients. One patient developed a vasovagal episode requiring intensive care unit observation for 24 hours. No procedure-related mortality was reported (Table 5).

Table 3. Ultrasound characteristics of lung masses

	n (%)
Depth of mass	
<2 cm	10 (8.6%)
2–3 cm	19 (16.4%)
3–4 cm	24 (20.7%)
>4 cm	63 (54.3%)
Contact with pleura	
<2 cm	14 (12.1%)
2–3 cm	23 (19.8%)
3–4 cm	44 (37.9%)
>4 cm	35 (30.2%)
Architecture of mass	
Homogeneous	34 (29.3%)
Heterogeneous	82 (70.7%)

Table 4. Histopathological diagnosis in lung biopsy

Histopathological examination		n (%)
Malignancy (84)	**Adenocarcinoma**	46 (39.7%)
	Squamous cell carcinoma	18 (15.5%)
	Small cell carcinoma	06 (5.2%)
	Non-Hodgkin lymphoma	4 (3.4%)
	Pleomorphic sarcoma	2 (1.7%)
	Malignant phylloid tumor	1 (0.9%)
	Spindle cell tumor likely neural tumor	2 (1.7%)
	Seminoma	1 (0.9%)
	Schwannoma	1 (0.9%)
	Undifferentiated carcinoma	1 (0.9%)
	Plasmacytoma-lambda restricted	1 (0.9%)
	Osteosarcoma	1 (0.9%)
Non-malignancy (29)	Tuberculosis	11 (9.5%)
	Organizing pneumonia	9 (7.8%)
	Coagulative necrosis	1 (0.9%)
	Fibrosing pleuritis	1 (0.9%)
	Non-tubercular mycobacteria, *Mycobacterium abscessus*	1 (0.9%)
	Non-specific inflammation	6 (5.2%)
Inconclusive		3 (2.6%)
Total		116

DISCUSSION

In this retrospective study of 116 patients undergoing pulmonologist-performed ultrasound-guided transthoracic biopsy of pleural-based lung masses, we observed a high diagnostic yield of 97.4%, an overall complication rate of 10.3%, and no procedure-related mortality. These findings underscore the effectiveness and safety of thoracic ultrasound-guided biopsy when performed by trained interventional pulmonologists.

The diagnostic yield in our cohort is comparable to or higher than previously reported yields of 80–93% in PubMed-indexed series evaluating ultrasound-guided transthoracic biopsies (Table 6).[4-8] For instance, Portela-Oliveira et al.[4] reported a diagnostic accuracy of 90.5% in thoracic ultrasound-guided biopsies of pleural and peripheral lung lesions, while Khan et al.[5] demonstrated a yield of 88.3% for peripheral pulmonary lesions using ultrasound-guided tru-cut biopsy. In a series involving respiratory physicians, Laursen et al.[6] documented a diagnostic rate of 76.9% for malignant lesions. More recent pulmonologist-led studies have reported yields approaching 88–93% with low complication rates.[7] The higher yield observed in our study may reflect careful patient selection, inclusion of only pleural-based lesions with adequate pleural contact, and the use of real-time imaging guidance.

Table 5. Complications of USG-guided lung biopsy

SN	Complications	n
1	Post procedure pneumothorax required observation	3 (2.6%)
2	Pneumothorax required admission and ICTD	1 (0.9%)
3	Post procedure hemoptysis	3 (2.6%)
4	Bleeding from biopsy site	2 (1.7%)
5	Post procedure pain at biopsy site	2 (1.7%)
6	Vasovagal shock required ICU	1 (0.9%)
7	Death	0 (0%)
	Total	12 (10.3%)

USG: Ultrasonography, SN: Serial number, ICTD: Intercostal tube drainage, ICU: Intensive care unit

A key strength of our study is the standardized operator criteria. All procedures were performed or directly supervised by pulmonologists with formal training in interventional pulmonology (Doctorate of Medicine Pulmonary Medicine) or structured prior experience in ultrasound-guided thoracic interventions. Operator expertise is known to significantly influence procedural success and safety outcomes.[6,7] Unlike earlier studies where operator experience varied, our structured approach likely minimized the procedural learning curve, contributing to both the high tissue adequacy rate (97.4%) and the relatively low pneumothorax rate (3.4%). The absence of procedure-related mortality further supports the safety of performing this intervention within a specialized pulmonology unit.

Malignancy accounted for 72.4% of diagnoses, consistent with previous thoracic ultrasound biopsy series in which malignant etiologies predominate.[4,5] Adenocarcinoma was the most common histological subtype (39.7%), followed by squamous cell carcinoma (15.5%), reflecting contemporary trends in lung cancer epidemiology.[9] An important contextual factor is the tuberculosis-endemic setting of India: 29.3% of patients were already receiving ATT for the same lesion at presentation. In endemic regions, peripheral lung opacities are often treated empirically for tuberculosis before tissue confirmation is obtained, and patients who fail to respond are referred to tertiary centers for definitive diagnosis. This referral pattern likely enriched our cohort with malignant cases, contributing to a higher proportion of malignant diagnoses compared with some international series.

Table 6. Comparative analysis of USG-guided transthoracic lung biopsy

Parameter	Present study (2025)	Portela-Oliveira et al.[4] 2021	Khan et al.[5] 2019	Laursen et al.[6] 2016	Kumar et al.[7] 2025	Li and Kong[11] 2023 (meta-analysis)
Operator	**Pulmonologist**	**Radiologist**	**Radiologist**	**Respiratory physician**	**Pulmonologist**	**Mixed**
Sample size (n)	116	89	85	215	88	1200+
Diagnostic yield (%)	97.4	90.5	88.3	76.9	88.5	92 (pooled)
Adenocarcinoma (%)	39.7	35	32	34	38	NA
Squamous cell carcinoma (%)	15.5	18	20	16	14	NA
Tuberculosis (%)	9.5	NA	6	NA	5	NA
Inconclusive (%)	2.6	8	7	9	6	5–10
Pneumothorax (%)	3.4	5.6	1.5	2.5	2.3	4.5 (pooled)
Overall complications (%)	10.3	9	6	8	7	8–12

USG: Ultrasonography, NA: Not available

Tuberculosis was diagnosed in 9.5% of cases, aligning with reports from other Indian and tuberculosis-endemic settings.[5,10] The low inconclusive rate (2.6%) compares favorably with previously reported rates of 5–12%,[4,6] likely reflecting the use of a 16-gauge tru-cut needle and multiple core sampling under real-time visualization.

The overall complication rate of 10.3% is consistent with prior studies reporting complication rates between 5% and 15% for ultrasound-guided transthoracic biopsy.[4-8] Pneumothorax occurred in 3.4% of patients, with only one patient (0.9%) requiring intercostal tube drainage. These rates are substantially lower than those commonly reported for CT-guided transthoracic biopsy, where pneumothorax may occur in 15–25% of cases.[3] Minor hemoptysis and local bleeding were self-limiting and required no major intervention. A recent meta-analysis comparing ultrasound- and CT-guided biopsies confirmed lower pneumothorax rates with ultrasound guidance, supporting its favorable safety profile.[11]

Study Limitations

This study has several limitations. The retrospective design introduces potential selection bias, and the single-center experience may limit generalizability. A direct comparison with CT-guided biopsy was not performed. Nevertheless, the relatively large sample size, the standardized procedural protocol, and procedures performed exclusively by trained interventional pulmonologists strengthen the validity of our findings.

Our results support the expanding role of pulmonologists in performing ultrasound-guided transthoracic biopsy of pleural-based lung masses by demonstrating high diagnostic accuracy and acceptable safety, particularly in tuberculosis-endemic and resource-constrained settings.

CONCLUSION

Pulmonologist-performed ultrasound-guided transthoracic biopsy of pleural-based lung masses demonstrates a high diagnostic yield and an acceptable safety profile. Structured interventional training and adherence to strict operator criteria appear to enhance both tissue adequacy and procedural safety. In regions endemic for tuberculosis, this modality is especially valuable for patients who do not respond to empirical therapy. Thoracic ultrasound-guided biopsy should therefore be considered an essential component of contemporary interventional pulmonology practice.

Ethics

Ethics Committee Approval: The study was approved by the Dr. Ram Manohar Lohia Institute of Medical Sciences Ethics Committee (IEC no: 168/25 dated 30.01.2026).

Informed Consent: As this was a retrospective analysis of anonymized data, the requirement for informed consent for study participation was waived. However, written procedural consent had been obtained from the patients or their legally authorized representatives at the time of the procedure.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.K., P.G., S.G., S.J., S.S., V.M., Concept: H.K., P.G., S.G., R.S.H., S.J., S.Sh., V.M., A.K.V., Design: H.K., P.G., S.G., R.S.H., S.S., A.K.V., Data Collection or Processing: H.K., P.G., S.G., R.S.H., S.J., S.Sh., S.S., M.S., V.M., A.K.V., Analysis or Interpretation: H.K., P.G., S.G., S.J., S.S., M.S., V.M., Literature Search: H.K., P.G., S.G., S.J., S.Sh., S.S., M.S., V.M., Writing: H.K., P.G., S.G., R.S.H., S.S., M.S.

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Original Article

Occupational Respiratory and Cutaneous Allergic Diseases in Hairdressers: A Two-center Study

Nazan Beyhan[1], Gülden Paçacı Çetin[2], Bahar Arslan[2], Ebru Dumlupınar[3], Zeynep Çelebi Sözener[1], İnsu Yılmaz[2], Ömür Aydın[1], Dilşad Mungan[1]

[1]Division of Immunology and Allergy, Department of Pulmonary Diseases, Ankara University Faculty of Medicine, Ankara, Türkiye
[2]Division of Immunology and Allergy, Department of Pulmonary Diseases, Erciyes University Faculty of Medicine, Kayseri, Türkiye
[3]Department of Biostatistics, Ankara University Faculty of Medicine, Ankara, Türkiye

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ABSTRACT

OBJECTIVE: Hairdressers are frequently exposed to various allergens in hair products, placing them at high-risk for occupational allergic diseases such as allergic contact dermatitis (ACD) and occupational asthma (OA). Despite the large number of hairdressers in Türkiye, data on occupational allergy risk are limited. This study aimed to investigate the occurrence of occupational allergic diseases in hairdressers presenting with skin or respiratory complaints and to identify common workplace allergens.

MATERIAL AND METHODS: We conducted a prospective, descriptive study of hairdressers aged 18 years or older with suspected occupational allergic disease who attended outpatient allergy clinics between 2020 and 2023. Participants underwent diagnostic tests, including skin prick tests, patch tests, pulmonary function tests, and specific inhalation challenges (SIC).

RESULTS: Thirty hairdressers (female/male: 18/12) were included. Although 93% of participants reported using personal protective equipment, allergic diseases remained prevalent. Participants had an average of 15.1 years of professional experience, worked nearly 11 hours per day, and spent the most time per day on hair dyeing (3.1 hours/day). Among the 21 participants (70%) with ACD symptoms, ammonium persulfate, potassium persulfate, cocamidopropyl betaine (CAPB), and nitro-p-phenylenediamine were the most common allergens. Ten participants (33%) were diagnosed with asthma, and SIC confirmed OA and/or occupational rhinitis in 3 cases (10%).

CONCLUSION: A considerable frequency of OA and ACD was observed among symptomatic hairdressers. Ammonium persulfate, CAPB, and nitro-p-phenylenediamine were identified as common triggers. The persistence of allergic diseases despite the use of protective equipment highlights the need for improved occupational health strategies, stronger regulations, and enhanced preventive measures in the hairdressing sector in Türkiye.

KEYWORDS: Hairdressers, allergic contact dermatitis, occupational allergic diseases, occupational asthma, occupational rhinitis

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Corresponding author: Prof. Ömür Aydın, MD, e-mail: mdomuraydin@gmail.com

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INTRODUCTION

Occupational allergic diseases are a major concern in professions with frequent exposure to sensitizing agents. These include allergic contact dermatitis (ACD), occupational asthma (OA), occupational rhinitis (OR), and urticaria. Hairdressers are at particularly high-risk due to frequent and prolonged contact with shampoos, conditioners, hair dyes, and bleaching agents, both through skin contact and inhalation.[1] Previous studies indicate that work-related skin damage, especially hand eczema (HE), affects a large proportion of hairdressers and has a significant negative impact on career longevity.[2,3]

Routine exposure to these allergens damages the epidermal barrier and creates a pro-inflammatory environment, increasing the risk of occupational contact dermatitis. The transition from irritant contact dermatitis to allergic HE can occur rapidly as allergens penetrate the weakened skin barrier.[4,5] Repeated exposure to water, cleaning agents, and other chemical substances, exacerbates irritation and accelerates sensitization, further worsening the condition.[6] This process may lead to hypersensitivity reactions such as contact urticaria, protein contact dermatitis, and ACD.[7,8] These reactions are not limited to the skin: respiratory and ocular symptoms such as rhinitis, conjunctivitis, and asthma have also been observed, particularly following exposure to persulfate salts (PS) used in hairdressing and cosmetic products.[7,9] Although PS are water-soluble and unlikely to become airborne unless aerosolized, they have been identified as primary contributors to OR and asthma among hairdressers, representing a significant occupational respiratory hazard.[9,10]

There are limited studies on the prevalence of allergic skin and respiratory diseases among hairdressers in Türkiye; however, no data are available on specific sensitizing factors or on the adequacy of protective measures in this professional group.[11]

Hairdressing is a widespread profession in our country, employing a large workforce. According to the "Barbering and hairdressing occupational guide" published in 2021, there are 37,846 individuals employed in the hairdressing profession across Türkiye.[12] All procedures, including styling, waving or relaxing hair, and dyeing or bleaching, are carried out intensively during long working hours. Many salons are poorly ventilated, and personal protective measures are either not widely used or inadequate. Consequently, hairdressers are heavily exposed to hair cosmetic products in our country.

Because hairdressing is a common profession in our country, and because data are lacking and protection measures are inadequate, this study was required. We aimed to investigate the occurrence of occupational allergic diseases in hairdressers with skin and respiratory complaints and to identify the occupational allergens commonly encountered in the workplace. Additionally, we planned to assess the subjects' protective attitudes and the preventive measures implemented in the salons. We anticipate that this study will provide a snapshot of the occupational allergic conditions among hairdressers in our country.

Main Points

- This prospective study evaluated, in hairdressers who presented with work-related symptoms, occupational respiratory manifestations, including occupational asthma and occupational rhinitis, and occupational skin diseases.
- Respiratory symptoms were highly prevalent, with asthma symptoms reported by the majority of participants and objective confirmation of asthma and/or rhinitis obtained through pulmonary function testing, bronchial provocation, and specific inhalation challenge procedures.
- Persulfate salts were identified as the principal occupational agents responsible for both lower and upper airway diseases and as a leading cause of concomitant skin sensitization.
- Allergic contact dermatitis was frequently observed, with ammonium/potassium persulfate, cocamidopropyl betaine, and aromatic amines emerging as the most common sensitizing agents.
- The findings highlight the coexistence of occupational respiratory and cutaneous allergic diseases and underscore the need for integrated preventive strategies, including exposure reduction, adequate personal protective equipment, and improved workplace conditions among hairdressers.

MATERIAL AND METHODS

Study Design and Population

This prospective descriptive study, conducted at two allergy clinics of Erciyes University Medical Faculty and Ankara University Medical Faculty between 2020 and 2023, included hairdressers over 18 years old who presented to the clinics with respiratory and/or skin complaints suggestive of occupational allergic disease. Informed consent was obtained from all participants, and the study was approved by the Ethics Committee of Erciyes University Medical Faculty on October 7, 2020 (authorization no: CE 2020/499).

Data Collection

The demographic and disease characteristics of the participants, the relationship between symptoms and professional procedures, workplace conditions, and the use of personal protective equipment were recorded using a detailed questionnaire. For participants with skin complaints, skin patch and skin prick tests (SPT) were performed. For those with respiratory complaints, SPT, pulmonary function testing (PFT), and methacholine challenge testing were conducted. Patients diagnosed with asthma underwent serial peak expiratory flow (PEF) monitoring and/or specific inhalation challenges (SIC) with the suspected agent to confirm the diagnosis of OA. The overall diagnostic workflow for the study participants, including evaluation pathways for skin, nasal, and respiratory complaints, is presented in Figure 1.

Diagnostic Procedures

SPTs for common inhalant allergens *(Dermatophagoides pteronyssinus, Dermatophagoides farinae, tree pollens, weed pollens, mixtures of grass pollens, Alternaria, Aspergillus fumigatus, cat and dog epithelia,* and *latex*) were performed

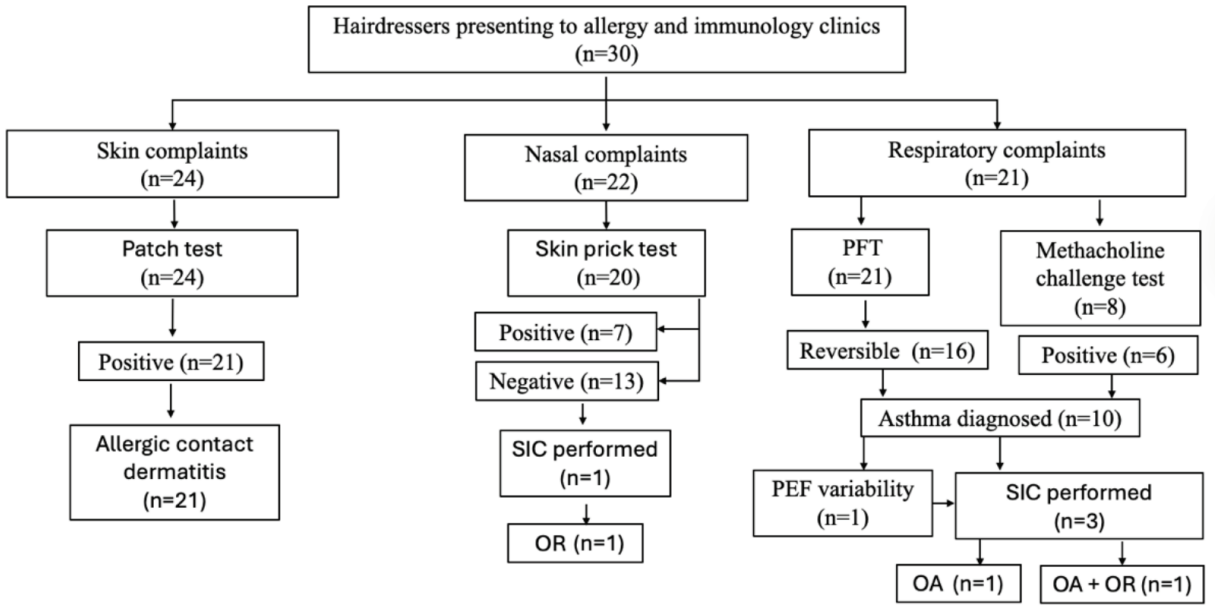


Figure 1. Flow diagram of the diagnostic assessment of hairdressers with occupational allergic disease symptoms

SIC: specific inhalation challenge, OR: occupational rhinitis, PFT: pulmonary function test, PEF: peak expiratory flow, OA: occupational asthma

using commercial extracts (ALK, Abello, Spain). Histamine and saline solution were used as positive and negative controls, respectively. After 20 minutes, a positive reaction was defined as a wheal diameter ≥3 mm with no reaction to the negative control and a positive reaction to histamine. Atopy was defined as at least one positive SPT response to allergens.

Patch tests were performed according to the European Society of Contact Dermatitis patch test guidelines.[13] Patch tests were conducted by placing allergen extracts from a set of 20 hairdresser series (ammonium persulfate/potassium persulfate, ammonium thioglycolate, captan 0.5%, cocamidopropyl betaine (CAPB), cysteamine HCl, disperse orange, disperse yellow, formaldehyde, glycerylthioglycolate, hydroquinone, hydroxyethyl methacrylate, m-aminophenol, methylchloroisothiazolinone, methylisothiazolinone, N,N-bis(2-hydroxyethyl)-p-phenylenediamine sulfate, nickel sulfate, nitro-p-phenylenediamine, quaternium-15, resorcinol thiuram mix, toluen-2,5-diamine sulfate) on the patient's back (ALK, Abello, Madrid, Spain). The test was evaluated at 48, 72, and 96 hours. Reaction intensity was recorded in four categories (negative, 1+, 2+, and 3+); doubtful reactions (?+) were considered negative. A positive patch test result in the presence of dermatitis was used to diagnose allergic occupational dermatitis.

Pulmonary function tests, reversibility tests, and methacholine challenge tests were performed in patients with respiratory symptoms. Reversibility was tested with 400 mcg salbutamol inhalation; an increase in forced expiratory volume in one second (FEV_1) ≥12% and ≥200 mL after 15 minutes was considered positive. Methacholine challenge tests were performed in individuals who had normal lung function but reported respiratory symptoms. Aerosolized methacholine was generated using a pressurized nebulizer, and inhalations were administered at 5-min intervals with increasing concentrations (0.25, 0.5, 1, 2, 4, 8, and 16 mg/mL) until a positive reaction occurred or the maximum dose was reached. A provocative concentration causing a 20% (PC20) fall in FEV_1 below 8 mg/mL was considered positive.

For OA diagnosis, 15-day PEF monitoring during at-work and off-work periods was planned; however, due to demanding working conditions in hairdressing salons, only one participant completed the monitoring. In addition, SIC with persulfate was conducted in selected participants. Four participants underwent SIC in a 7 m^3 cabinet. Participants were asked to simulate a workplace situation by inhaling persulfate powder while mixing it in a bowl. Subjects were closely monitored during the challenge procedure. Study participants were exposed to bleaching powder in a controlled manner for 5, 10, 15, 30, and 60 minutes. A ≥20% decrease in FEV_1 measurements after each exposure period was considered a positive test. At the same time points, the same physician assessed nasal symptoms (itching, congestion, sneezing, rhinorrhea) and recorded total nasal symptom scores. An increase in rhinitis symptom scores at posttest was also recorded.

Statistical Analysis

Descriptive statistics were presented as mean ± standard deviation (SD) for the variables with normal distribution and as median (minimum, maximum, and interquartile range) for the variables without normal distribution, whereas they were presented as number and percentage (%) for nominal variables. Differences in median values between groups were analyzed using the Mann-Whitney U test. Categorical variables were evaluated using Fisher's exact test. A *P* value of less than 0.05 was considered statistically significant, and the analyses were conducted using the Statistical Package for Social Sciences (SPSS, Version 30.0, Chicago, IL).

RESULTS

Thirty patients (female/male: 18/12) were included in the study with a mean age of 34.53±11.23 (mean ± SD) years. The average duration of employment as a hairdresser was 15.08±11.06 years. Patient demographics and disease characteristics are shown in Table 1.

Hairdressers reported that they work 6 days a week for 10 hours per day. They spent the most time performing hair

Table 1. The demographics and disease characteristics of the patients

Variable	Category	Value
Sex	Female, n (%)	18 (60.00)
	Male, n (%)	12 (40.00)
Age (years), mean ± SD		34.53±11.23
Age (years), median (min-max, IQR)		35 (18–57, 15.25)
Smoking history	Never, n (%)	15 (50.00)
	Ex-smoker/active smoker, n (%)	15 (50.00)
Occupational exposure (years), mean ± SD		15.08±11.06
Occupational exposure (years), median (min-max, IQR)		14.5 (1–45, 18.5)
Allergic comorbidities	Drug allergy, n (%)	4 (13.33)
	Urticaria, n (%)	4 (13.33)
Increased work-related complaints	Skin symptoms, n (%)	26 (86.66)
	Asthmatic symptoms, n (%)	21 (70.00)
	Nasal symptoms, n (%)	22 (73.33)
Skin prick test	Negative, n (%)	19 (63.33)
	Positive, n (%)	9 (30.00)
FEV_1 (L), mean ± SD		3.26±0.72
FEV_1 (L), median (min-max, IQR)		3.08 (2.3–4.69, 1.06)
FEV_1 (%), mean ± SD		97.84±12.82
FEV_1 (%), median (min-max, IQR)		96 (82–134, 17)
FVC (L), mean ± SD		4.03±0.87
FVC (L) , median (min-max, IQR)		3.71 (2.55–5.82, 1.41)
FVC (%), mean ± SD		105.4±13.8
FVC (%), median (min-max, IQR)		100 (88–137, 15)
FEV_1/FVC (%), mean ± SD		82.12±10.90
FEV_1/FVC (%), median (min-max, IQR)		79 (65–105, 15.25)
Pulmonary function test	Reversible, n (%)	5 (16.66)
	Normal, n (%)	16 (53.33)
Methacholine challenge test	Negative, n (%)	2 (6.66)
	Positive, n (%)	6 (20.00)
Confirmed to have asthma, n (%)		10 (33.33)
PEF variability n (%)		1 (3.33)
SIC	Negative, n (%)	1 (3.33)
	Positive, n (%)	3 (10.00)
OA, n (%)		1 (3.33)
OR, n (%)		1 (3.33)
OA + OR, n (%)		1 (3.33)
Of the 26 patients with cutaneous symptoms, 24 underwent patch testing	Negative, n (%)	3 (10.00)
	Positive, n (%)	21 (70.00)
Confirmed to have ACD, n (%)		21 (70.00)

SD: standard deviation, min-max: minimum-maximum, IQR: interquartile range, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, PEF: peak expiratory flow, SIC: specific inhalation challenge, OA: occupational asthma, OR: occupational rhinitis, ACD: allergic contact dermatitis

dyeing (3.10±1.17 hours/day), hair cutting (2.47±0.89 hours/day), and blow drying (2.45±1.09 hours/day). Most complaints were related to hair dyeing: 13 participants (38.2%) reported general dyeing complaints, and 17 (50%) reported complaints related to bleaching/lightening procedures. Most participants (93%) reported using personal protective equipment, including gloves and masks. In general, gloves were used during dyeing procedures and, less frequently, for other wet work.

Eighty-six percent (n = 24) of the patients reported skin symptoms, while 70% and 73% of them complained of asthma and nasal symptoms, respectively. Symptoms worsened at work in 93% of participants and improved on days off in 86% of participants.

Patch testing was performed in 24 patients presenting with dermatologic complaints. ACD was diagnosed in 21 participants based on sensitivity to one or more allergens. Among the 21 hairdressers diagnosed with ACD, the most frequently sensitizing allergens were ammonium persulfate/potassium persulfate (n = 11, 52%), CAPB (n = 6, 28%), and nitro-p-phenylenediamine (n = 6, 28%).The frequency of sensitization detected in the patch test is summarized in Figure 2.

Respiratory symptoms were reported by 21 participants (70%). Ten patients were diagnosed with asthma based on PFTs and/or methacholine challenge tests.

Pulmonary function test results were compared between female and male participants; no significant differences were observed in FEV_1 (%), forced vital capacity (FVC) (%), or the FEV_1/FVC ratio. Similarly, no significant sex-based differences were observed in SPT or patch-test positivity (Table 2).

SIC was performed in four subjects; one was diagnosed with OA, one with OR, and one with both OR and OA. No participants exhibited a delayed decrease in FEV_1 during the 24-hour follow-up after exposure to PS. The characteristics of patients who underwent SIC are listed in Table 3.

DISCUSSION

This study investigated the occurrence and spectrum of occupational allergic diseases among hairdressers and identified the specific sensitizing agents responsible for both cutaneous and respiratory manifestations. In contrast to earlier Turkish studies, which were primarily limited to questionnaire-based or survey-derived prevalence data, our findings provide a detailed allergen-specific diagnostic assessment in a cohort of patients presenting with symptoms related to workplace exposure.[11] Consistent with international evidence, our results indicate that hairdressers remain highly vulnerable to occupational allergic risks, despite their reporting adequate implementation of personal protective measures.[14,15]

Hairdressers are among the occupational groups most affected by contact dermatitis due to repeated exposure to various chemicals.[16] The cohort's average professional experience was approximately 15 years, suggesting that prolonged exposure substantially increases health risks. These results are consistent with findings from a 24-year Turkish cohort in İstanbul, which also identified ammonium persulfate as the leading allergen among hairdressers.[15] Similarly, a recent systematic review by Havmose et al.[17] reported a lifetime prevalence of HE of 38.2%, with a 1-year prevalence of 20.3%. In our study, the majority of participants reported skin-related complaints, all of which were exacerbated in the workplace. This finding is consistent with the high prevalence reported in the literature and underscores the significance of occupational skin exposure in hairdressers.[18] Notably, hair-dyeing procedures, which account for, on average, more than three hours per day, represent a major source of such exposure. These results indicate that the high rate of self-reported protective measures

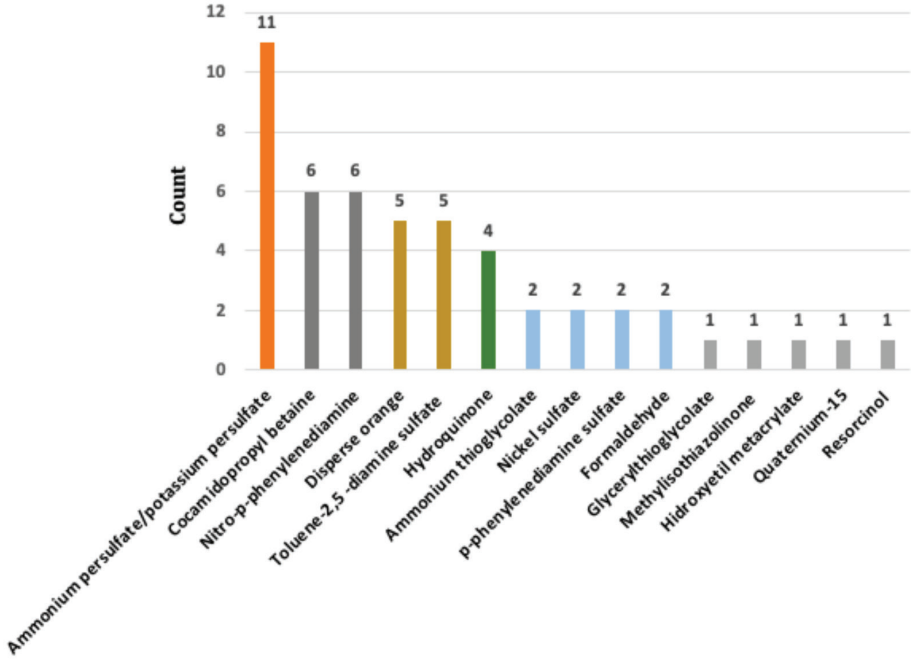


Figure 2. Frequency of sensitization to haptens in patch tests conducted on hairdressers

should be questioned, as such measures are insufficiently implemented in practice.

Patch testing remains essential for diagnosing ACD and should ideally incorporate hairdresser-specific test series.[19] In our cohort, ACD was diagnosed in 70% of hairdressers and in 87% of those presenting with dermatitis. Patch testing of hairdressers with dermatitis revealed a high frequency of sensitization to ammonium persulfate and potassium persulfate. Ammonium persulfate, potassium persulfate, and p-phenylenediamine (PPD) were the most frequent sensitizing agents, consistent with both international studies and previous Turkish retrospective data.[15,20] Our findings demonstrate that contact allergies to ammonium persulfate and potassium persulfate, which are widely used in hair-bleaching and lightening products, remain highly prevalent among hairdressers. The persistent and extensive occupational exposure to these agents likely contributes to the elevated sensitization rates, rendering ACD an ongoing occupational health concern within this profession.

Although other studies report lower rates, our analysis found that 28% of hairdressers with ACD were sensitised to CAPB.[20,21] CAPB, a surfactant derived from coconut oil, is widely used in personal care products and can cause skin irritation, eye irritation, and skin sensitization.[22] A meta-analysis found that hairdressers had a 1.7-fold higher risk of developing contact allergy to CAPB compared with non-hairdresser controls.[23] According to data from the North American Contact Dermatitis Group, CAPB was identified as a common allergen, accounting for 5.9% of positive patch-test reactions associated with hair-care products; notably, 71% of patients who developed ACD related to hair-care products were hairdressers or cosmetologists.[24]

Table 2. Comparison of clinical test results by sex

Parameter	Female	Male	*P* value
Pulmonary function tests*			
FEV_1 (L)	2.78 (2.30–3.17, 0.46)	3.81 (2.76–4.69, 0.81)	**<0.001**
FEV_1 (%)	96 (82–109, 16.75)	96 (82–134, 21)	0.968
FVC (L)	3.39 (2.55–4.27, 0.41)	4.78 (3.63–5.82, 0.86)	**<0.001**
FVC (%)	98 (88–128, 4)	108 (93–137, 21)	0.412
FEV_1/FVC (%)	80 (68–105, 23.5)	78 (65–97, 13.5)	0.73
Skin prick test positivity†, n (%)			
Negative	13 (68.4)	6 (31.6)	0.677
Positive	5 (55.6)	4 (44.4)	
Patch test positivity‡, n (%)			
Negative	2 (66.7)	1 (33.3)	0.999
Positive	12 (57.1)	9 (42.9)	

*Pulmonary function test data are presented as median (min-max, interquartile range) and were compared using the Mann-Whitney U test
†Skin prick test
‡Patch test data are presented as n (%) and were compared using Fisher's exact test
A *P* value <0.05 was considered statistically significant
FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, min-max: minimum-maximum

Table 3. Characteristics of patients undergoing specific inhalation challenges

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Age	39	32	38	35
Gender	Male	Male	Female	Female
ACD	No	Yes	No	Yes
PFT	Normal	Normal	Normal	Normal
Eosinophil count cells/μL (%)	280 (5.9)	390 (4.6)	120 (2.1)	20 (0.3)
SPT	Negative	Positive	Positive	Negative
Methacholine challenge test (PC20 mg/mL)	Negative	Positive (4.38)	Positive (0.51)	Positive (4.09)
Asthma	No	Yes	Yes	Yes
PEF variability	Not performed	Yes	Not performed	Not performed
SIC	+ (rhinitis)	+ (asthma)	+ (asthma and rhinitis)	-
OA	No	Yes	Yes	No
OR	Yes	No	Yes	No

ACD: allergic contact dermatitis, PFT: pulmonary function test, SPT: skin prick test, PC20: provocative concentration causing a 20%, PEF: peak expiratory flow, SIC: specific inhalation challenge, OA: occupational asthma, OR: occupational rhinitis, +: indicates a positive test, -: indicates a negative test

Given the relatively high rate of CAPB sensitization observed in our cohort, we suggest including CAPB in routine patch testing panels for all hairdressers diagnosed with eczema.

In our study, PPD, a key intermediate used in oxidative hair dyes, was identified as another allergen through patch testing. An analysis of 271 allergic reactions diagnosed among 4,314 patients between 2008 and 2013 revealed that approximately 80% of those who tested positive for PPD had previously dyed their hair, of whom half developed scalp dermatitis.[25] Alongside PPD, toluene-2,5-diamine (TDA), another aromatic amine widely used in permanent hair dyes, was detected in 16% of our patients. In contrast to some reports in the literature, co-sensitization to TDA among PPD-positive individuals was relatively infrequent, suggesting that patterns of cross-reactivity may vary between populations.[26]

Despite the use of gloves and masks by 93% of participants, these measures appear to be insufficient to prevent allergic diseases. The fact that hairdressers in this study work for prolonged periods under intensive conditions, together with their perception of being adequately protected by using gloves only during selected wet work procedures, may partially explain this discordance. In addition to individual compliance, factors such as glove quality, replacement frequency, and workplace ventilation should be considered key preventive strategies. Enhanced occupational health training for hairdressers would also help increase awareness of chemical hazards and promote more effective and consistent use of protective measures.

Respiratory health is another critical issue in this profession. Hairdressers are frequently exposed to ammonia, volatile organic compounds, and persulfates, all of which are known to induce OA and OR.[7,27,28] In our study, 70% of participants reported asthma-related symptoms, and asthma was confirmed in 33% of participants. Among those who underwent SICs, two were diagnosed with OA; both were atopic, suggesting that atopic status may increase susceptibility to persulfate-induced asthma. Supporting our findings, a retrospective Italian cohort study reported that over half of hairdressers evaluated for OA were diagnosed with the condition, with persulfates responsible for nearly 90% of cases.[29] A meta-analysis showed that hairdressers have a 20-fold higher risk of respiratory symptoms from bleaching powders compared with controls.[7] In Spain, persulfates accounted for 12.1% of occupational respiratory diseases, making them the second most common cause of OA.[30] Provocation studies have further confirmed that persulfates can induce both lower and upper airway symptoms, including asthma and rhinitis.[31] Taken together, these data highlight persulfates as a major occupational respiratory hazard and underscore the urgent need for safer bleaching formulations, improved salon ventilation, and strict adherence to comprehensive protective measures. In our cohort, patch test results were comparable between female and male participants, and no significant sex-based differences were observed in FEV_1 (%), FVC (%), or FEV_1 /FVC ratio.

Serial PEF monitoring is a valuable method for demonstrating work-related variability in airway obstruction and is commonly used in the diagnostic evaluation of OA. In the present study, PEF monitoring could be performed on only one hairdresser. The demanding working conditions in hairdressing salons made it difficult for most participants to take approximately 15 days off work, which are typically required for reliable serial PEF measurements. As a result, PEF monitoring could not be applied to all asthmatic participants. Nevertheless, clinical evaluation together with PFT, methacholine challenge, and SIC testing provided important diagnostic information for identifying occupational respiratory disease in this cohort.

Nasal symptoms were observed in 73% of patients, with two patients diagnosed with OR through SIC. In one patient, a positive SIC despite a negative inhalant-allergen SPT highlights the importance of obtaining a detailed occupational history in patients presenting with rhinitis symptoms. Previous studies have reported that OR occurs in approximately half of OA cases caused by ammonium persulfate, and that exposure to persulfates is strongly associated with an increased risk of developing OR.[32,33] Provocation tests that simultaneously assess upper and lower airways are more time- and cost-efficient than separate airway tests and have high diagnostic specificity for detecting persulfate-induced asthma and rhinitis.[31]

The strengths of our study include the comprehensive identification of allergic sensitization and respiratory diseases in a high-risk occupational group such as hairdressers. A wide range of standardized diagnostic procedures was employed to identify specific allergens and respiratory conditions. This study provides valuable and clinically relevant insights into occupational allergic diseases and associated health risks among hairdressers, highlighting the importance of implementing more effective and targeted protective measures in our country. However, the relatively small sample size may limit the generalizability of the findings and restrict the ability to establish definitive causal relationships. Because the study population consisted of symptomatic hairdressers presenting to allergy clinics, the findings reflect a selected clinical sample rather than a representative occupational cohort of hairdressers and should therefore be interpreted with caution when generalizing to the broader population of hairdressers. Furthermore, serial PEF monitoring could only be performed in one participant due to the demanding working conditions that limited the ability of most hairdressers to take time away from work. An additional limitation of the study is the inability to perform SIC in all patients diagnosed with asthma. Nevertheless, these findings have important implications for occupational health practice and underscore the need for larger, multicenter studies to further clarify occupational risks in this profession.

CONCLUSION

This study indicates a considerable frequency of ACD and OA among symptomatic hairdressers evaluated in allergy clinics for suspected occupational allergic diseases; ammonium persulfate/potassium persulfate, PPD, and CAPB are the predominant allergens. The high rates of occupational diseases among hairdressers indicate that protective measures are not always fully implemented. These findings underscore the need for stronger protective strategies, regulatory measures, and improved educational programs in the hairdressing sector in our country.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Erciyes University Medical Faculty on October 7, 2020 (authorization no: CE 2020/499).

Informed Consent: Informed consent was obtained from all participants.

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Footnotes

Authorship Contributions

Concept: N.B., Z.Ç.S., İ.Y., Ö.A., D.M., Design: N.B., Z.Ç.S., İ.Y., Ö.A., D.M., Data Collection or Processing: N.B., G.P.Ç., B.A., Ö.A., Analysis or Interpretation: N.B., E.D., Literature Search: N.B., G.P.Ç., B.A., Z.Ç.S., İ.Y., Ö.A., D.M., Writing: N.B., G.P.Ç., B.A., E.D., Z.Ç.S., İ.Y., Ö.A., D.M.

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Original Article

Clinical Characteristics and Treatment Outcomes After First *Achromobacter* Isolation in Children with Cystic Fibrosis (Pre–CFTR Modulator Era)

Şeyda Karabulut[1], Merve Selçuk Balcı[1], Mine Yüksel Kalyoncu[1], Aynur Gulieva[1], Mürüvvet Yanaz[1], Cansu Yılmaz Yeğit[1], Almala Pınar Ergenekon[1], Burcu Uzunoğlu[2], Gamze Taştan[2], Özgenur Demirkol[3], Ela Erdem Eralp[1], Yasemin Gökdemir[1], Ayşegül Karahasan[3], Fazilet Karakoç[1], Bülent Karadağ[1]

[1]Division of Pediatric Pulmonology, Marmara University Faculty of Medicine, İstanbul, Türkiye
[2]Selim Coremen Cystic Fibrosis Center, Marmara University Faculty of Medicine, İstanbul, Türkiye
[3]Department of Medical Microbiology, Marmara University Faculty of Medicine, İstanbul, Türkiye

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ABSTRACT

OBJECTIVE: We aimed to describe the clinical and demographic characteristics of children with cystic fibrosis (cwCF) diagnosed with a first *Achromobacter* (Ach) isolation, and to evaluate treatment outcomes at our CF center during the pre-modulator era.

MATERIAL AND METHODS: We retrospectively reviewed children followed at a single CF center (2014–2021) with at least four respiratory cultures per year and ≥12 months of follow-up after first Ach isolation. Eradication was defined as no Ach isolation for 12 months after the first detection; persistent infection was defined as intermittent or chronic isolation according to the Leeds criteria. We compared clinical characteristics and 12-month outcomes between the eradicated and non-eradicated groups.

RESULTS: Forty children were included; mean age at first isolation was 10.9±7.0 years, and eradication was achieved in 19/40 (47.5%). The non-eradicated group was older at first isolation (12.7±8.0 vs. 8.5±5.1 years; $P = 0.04$), had more pulmonary exacerbations (Pex) in the preceding year (median 4 vs. 2; $P = 0.01$), and more frequent prophylactic azithromycin use (67% vs. 21%; $P = 0.01$). Airway colonization patterns changed significantly over 12 months in the non-eradicated group ($P < 0.001$), with increased colonization by *Pseudomonas aeruginosa* (PA); changes were not significant in the eradicated group. Among those with available spirometry, 12-month forced expiratory volume in one second (FEV_1) z-scores did not differ by eradication status after adjustment for the baseline FEV_1 z-score.

CONCLUSION: In this pre–cystic fibrosis transmembrane conductance regulator modulator study, persistence of Ach was associated with older age, higher Pex burden before first isolation, and clinically relevant shifts in airway microbiology, including increased PA colonization. Our findings suggest that cwCF with frequent exacerbations or a worsening clinical course may warrant closer attention to Ach, and eradication of Ach may be considered at first detection.

KEYWORDS: *Cystic* fibrosis, *Achromobacter*, children, emerging pathogens, pulmonary infection, treatment

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INTRODUCTION

Achromobacter species (Ach) are opportunistic, non-fermentative, Gram-negative pathogens that are increasingly isolated in people with cystic fibrosis (pwCF) and can cause pulmonary exacerbations (Pex).[1-6] According to the 2022 records of the Cystic Fibrosis Foundation (CFF), it was reported as the fourth most commonly detected pathogen in the respiratory tract of pwCF.[7] In the 2021 European Cystic Fibrosis Society (ECFS) data, the prevalence of Ach was 3% among cwCF and 6.4% among adults.[8] In the same registry, the prevalence of Ach in Türkiye was reported to be 1.1% among cwCF and 3.1% among adults.[8]

Corresponding author: Şeyda Karabulut, e-mail: seydakarabulut@yahoo.com.tr

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More recent registry data suggest a stabilization of Ach prevalence. According to the 2024 CFF patient registry,[9] Ach is now the fifth most frequently detected respiratory pathogen, with a prevalence of approximately 2%. The 2023 ECFS registry data report an overall European prevalence of 1.6%, with lower rates observed in Türkiye (0.9%).[10] Taken together, contemporary CFF and ECFS data indicate that, although Ach remains a clinically relevant pathogen in pwCF, its prevalence appears to have stabilized at lower levels in recent years, with notable regional variation.

In this context, a recent study suggests that highly effective cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy may have influenced the epidemiology of Ach in CF. This longitudinal comparison between the year preceding initiation and the first year following initiation of elexacaftor/tezacaftor/ivacaftor therapy demonstrated a reduction in Ach positivity from 7.8% to 5.6%.[11] However, this apparent decline may not reflect the intrinsic clinical behavior of Ach, as access to CFTR modulators remains inequitable and many patients are either ineligible for them or subject to delayed treatment.[12] In Türkiye, CFTR modulators became available only after 2021 and were not reimbursed by the national health insurance system until June 2025, necessitating individual legal action for access.

It remains unclear whether Ach is a cause of more rapid deterioration in lung function or occurs in severe CF disease.[3,13,14] More clinical data are needed to understand how Ach affects lung function, mortality, and morbidity in pwCF worldwide. There are no standard treatment protocols.

In this study, we aimed to describe the clinical and demographic characteristics of cwCF in whom Ach was isolated, and to evaluate treatment outcomes at our CF center during the pre-modulator era.

MATERIAL AND METHODS

This single-center retrospective study was conducted at the Marmara University CF Center between January 2014 and June 2021. A total of 400 pwCF medical records were reviewed.

Data Collection

All sputum and deep pharyngeal swab cultures were reviewed, and cwCF in whom Ach was isolated were included in the study. Gender, age at isolation, forced expiratory volume in one second (FEV_1) z-score, body mass index (BMI) z-score, genotype, pancreatic insufficiency, cystic fibrosis-related diabetes mellitus (CFRD), cystic fibrosis-related liver disease (CFRL), hypertonic saline use, azithromycin use, dornase-alpha use, inhaled corticosteroid use, allergic bronchopulmonary aspergillosis (ABPA), chest physiotherapy techniques, Pex, and eradication regimens were obtained from the medical records. Pex was defined using the criteria modelled by Ng et al.[15] ABPA, CFRD, and CFRL definitions were defined as stated in the relevant literature.[8,16-18] None of these cwCF were treated with a CFTR modulator or high-dose ibuprofen at the time of the study.

Main Points

- This study evaluates the clinical features of *Achromobacter* (Ach) in children with cystic fibrosis (cwCF).
- It underscores the risk of opportunistic infections in cwCF populations without cystic fibrosis transmembrane conductance regulator modulators.
- The study emphasizes the need for careful monitoring of cwCF who have frequent pulmonary exacerbations for Ach colonization.
- The findings suggest that eradication may be considered when Ach is identified in cwCF.

Inclusion Criteria

Forty cwCF were included in the study. The inclusion criteria were as follows: CF diagnosis according to the consensus guidelines from the CFF,[19] regular follow-up in the CF center outpatient clinic, and having at least four sputum or deep pharyngeal swab cultures per year (every 2–4 months). The cwCF were followed up for at least one year after their first isolation of Ach. cwCF with fewer than four respiratory samples in the years before and after Ach isolation were excluded.

Infection State

Initial isolation was defined as the first-ever positive culture or as a new isolation after being Ach-free for the previous 12 months. Ach isolation was determined using the Leeds criteria.[20] Leeds criteria define chronic colonization as isolation of the same pathogen from more than 50% of respiratory tract cultures after the first detection of the microorganism, and intermittent colonization as isolation in less than 50% of respiratory tract cultures. Eradication was defined as no isolation for 12 months after the initial isolation.

In our study, cwCF were divided into eradicated and non-eradicated groups. The non-eradicated group included cwCF with intermittent and chronic colonization. CwCF without Ach isolation for 12 months after the initial isolation were considered eradicated.

Lung Function

For children over six years of age, FEV_1 z-score values measured one year before and one year after the first *Ach* isolation were recorded with the Minispir spirometry device (Medical International Research, Rome, Italy) according to American Thoracic Society/European Respiratory Society technical standards.[21]

Microbiological Studies

Isolates were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (VITEK MS, BioMérieux, France) with a matrix. However, using this method, species differentiation between *Achromobacter xylosoxidans* and *Achromobacter denitrificans* could not be achieved, and therefore species information was not included in the study. Antimicrobial susceptibility tests were conducted on Mueller Hinton agar (BioMérieux, France) using the disk diffusion method in accordance with European Committee on Antimicrobial Susceptibility Testing (EUCAST)

recommendations, and zone diameters were recorded in millimeters.[22] Because the EUCAST guidelines provide zone diameter values only for *Achromobacter xylosoxidans* and no specific criteria are defined for other species, the recommended cut-off values for this species were used.[22]

Antimicrobial Treatment

There was no standard treatment protocol; cwCF received their treatment according to the clinical status and antibiotic susceptibility of their microbial cultures. Treatment was not given to cwCF who had no complaints, even if they were in isolation. The cwCF with fever, low oxygen saturation, and weight loss were hospitalized and treated with intravenous (IV) antibiotics. The cwCF, whose general condition did not require hospitalization, received oral antibiotic treatment.

Among the oral antibiotics, amoxicillin-clavulanic acid, trimethoprim-sulfamethoxazole, and ciprofloxacin were used based on antimicrobial susceptibility testing. Meropenem, meropenem + colistin, and ceftazidime + amikacin were the preferred IV antibiotics. Oral antibiotics were administered for at least 14 days, and IV antibiotics for 14 to 21 days, depending on the clinical condition of the individuals.

Treatment was initiated seven days after sample collection for individuals who did not require hospitalization because the microbiological result was notified within that period.

Official approval for the study was received from the Marmara University Ethics Committee (protocol no: 09.2024.30, decision date: 12.01.2024). Given the retrospective study design and the use of fully anonymized patient data, written informed consent was not required and therefore not obtained in accordance with the ethics committee's decision.

Statistical Analysis

Numerical variables are expressed as mean ± standard deviation or median (Q1-Q3) as appropriate to the distribution of variables. Continuous data were analyzed using the independent-samples t-test or the Mann-Whitney U test for non-parametric data. Categorical data were analyzed using χ^2 or Fisher's exact tests. $P \leq 0.05$ was considered significant.

Changes in airway colonization status before and after Ach isolation were assessed using the Stuart–Maxwell test for marginal homogeneity, applied separately to the eradicated and non-eradicated groups. Exact *P* values were reported given sparse transitions across colonization categories.

To examine whether eradication status was associated with lung function, an analysis of covariance was performed to compare follow-up FEV_1 z-scores between groups, adjusting for baseline FEV_1 z-score. Analyses were restricted to individuals who were able to perform spirometry and who had FEV_1 z-score measurements available at both baseline and follow-up time points. Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 31.

RESULTS

A total of 400 cwCF were screened, and Ach was isolated in 40. Of these, 30 received treatment.

The mean age of the cwCF at the first Ach isolation was 10.9 (±7) years; 8.5 (±5.1) years in the eradicated group and 12.7 (±8) years in the non-eradicated group (*P* = 0.04, Table 1).

Baseline FEV_1 z-scores were similar between the eradicated and non-eradicated groups [−4.82 (±1.61) vs. −5.08 (±1.56); *P* = 0.68]. Over the 12-month follow-up period, lung function declined in both groups; however, there was no significant difference in 12-month FEV_1 z-scores between eradicated and non-eradicated patients [−5.11 (±1.42) vs. −5.42 (±1.35); *P* = 0.59]. After adjustment, eradication status was not independently associated with 12-month FEV_1 z-scores (adjusted means −5.24 vs. −5.32; *P* = 0.63), and similar patterns of lung function change were observed in both groups over the 12-month period (Table 2).

No differences in medication use between the groups were observed, except for azithromycin. The use of azithromycin prophylaxis was higher in the non-eradicated group than in the eradication group (*P* = 0.01). The baseline characteristics of the groups are presented in Table 1.

The number of pre-Ach Pex was higher in the non-eradicated group [median (Q1-Q3): 4 (2–5); *P* = 0.01; Table 1].

Of the 40 cwCF with Ach isolation, eradication was achieved in 19 (47.5%). Twenty-one (52.5%) cwCF were considered non-eradicated. Of these, 14 (35%) had intermittent colonization and 7 (17.5%) had chronic colonization. No treatment was administered to 3 (7.5%) cwCF in the eradicated group and to 7 (18%) cwCF in the non-eradicated group (*P* = 0.3).

Colonization patterns remained stable in the eradicated group, with no statistically significant change over time as determined by the two-tailed exact test (*P* = 0.063). In contrast, the non-eradicated group demonstrated a statistically significant shift in colonization status over time (*P* < 0.001). These transition patterns are illustrated in Figure 1.

The treatment modalities for cwCF are shown in Figure 2. Sixteen cwCF (n = 16/19) in the eradicated group and 14 cwCF (n = 14/21) in the non-eradicated group received IV or oral treatment, according to clinical status and culture-sensitivity results. In the eradicated group, 11 cwCF received only oral treatment, two cwCF received only IV treatment, and three cwCF received combined IV and oral treatment. Spontaneous eradication was observed in three cwCF who did not receive treatment. In the non-eradicated group, six cwCF received oral therapy, five received IV therapy, and three received oral + IV therapy. There was no statistically significant difference in IV and/or oral antibiotic treatment regimens between the groups (*P* = 0.6 in the eradicated group, *P* = 0.5 in the non-eradicated group).

Table 1. The baseline characteristics of the groups (before the first *Achromobacter* isolation) (n = 40)

Baseline characteristics and clinical outcomes	Eradicated (n = 19)	Non-eradicated (n = 21)	*P* value
Ach isolation age (years), mean ± SD	8.5±5.1	12.7±8	0.04*
Female, n (%)	8 (42%)	9 (43%)	0.9
BMI z-score, median (Q1-Q3)	–1 (-2.1 ~ -0.06)	–1 (–2.2 ~ 0)	0.9
CFTR variants, n (%)			
p.Phe508del/p.Phe508del	7 (37%)	3 (14%)	0.2
p.Phe508del/other	5 (26%)	9 (43%)	
Other/other	7 (37%)	9 (43%)	
Pancreatic insufficiency, n (%)	17 (89%)	19 (90%)	0.9
CFRD, n (%)	3 (16%)	6 (29%)	0.4
CFRL, n (%)	7 (37%)	6 (29%)	0.7
ABPA, n (%)	2 (11%)	1 (5%)	0.5
Pulmonary hypertension, n (%)	0 (0%)	2 (10%)	0.4
Inhaled corticosteroid use, n (%)	8 (42%)	10 (48%)	0.7
Chest physiotherapy, n (%)	18 (95%)	18 (86%)	0.6
7% hypertonic saline use, n (%)	15 (79%)	19 (90%)	0.3
Dornase-alpha use, n (%)	15 (79%)	20 (95%)	0.1
Oxygen use, n (%)	2 (11%)	8 (38%)	0.06
Azithromycin prophylaxis, n (%)	4 (21%)	14 (67%)	0.01*
No prior chronic airway colonization before first Ach isolation, n (%)	12 (63%)	18 (85%)	0.4
Pex in prior 12 months, median (Q1-Q3)	2 (1–4)	4 (2–5)	0.01*

*$P < 0.05$

Ach: *Achromobacter*, BMI: body mass index, CFTR: cystic fibrosis transmembrane conductance regulator, CFRD: cystic fibrosis-related diabetes mellitus, CFRL: cystic fibrosis-related liver disease; ABPA: allergic bronchopulmonary aspergillosis, Pex: pulmonary exacerbation, SD: standard deviation

Table 2. Baseline and 12-month FEV_1 z-scores according to *Achromobacter* eradication status

Ach status	Baseline FEV_1 z-score (mean ± SD)	12-month FEV_1 z-score (mean ± SD)	Adjusted 12-month FEV_1 z-score (mean; 95% CI)*
Eradicated (n = 10[a])	−4.82 (± 1.61)	−5.11 (± 1.42)	-5.24 (-5.52; -4.97)
Non-eradicated (n = 14[a])	−5.08 (± 1.56)	−5.42 (± 1.35)	-5.32 (-5.56; -5.10)
P value	0.68†	0.59†	0.63‡

†independent samples t-test, ‡analysis of covariance (ANCOVA) adjusted for baseline FEV_1 z-score, *adjusted means estimated at a baseline FEV_1 z-score of −4.97, [a]analyses were restricted to patients who were able to perform spirometry

FEV_1: forced expiratory volume in one second, SD: standard deviation, CI: confidence interval

DISCUSSION

In this single-center retrospective study, we evaluated the demographic and clinical characteristics of cwCF according to the treatment outcomes after initial Ach isolation. We observed that eradication was less likely among children who were older at the time of the first Ach isolation. Those in whom Ach persisted experienced a higher burden of Pex in the year preceding detection and were more likely to be receiving long-term azithromycin therapy. Persistent (non-eradicated) Ach was associated with changes in lower airway colonization over time.

The prevalence of Ach has been reported to range from 17.9% to 29.3% in previous studies.[2,23] In our cwCF population, Ach positivity was detected in at least one respiratory culture in 10% of cases.

Kerem et al.[24] evaluated ECFS registry data and reported that the age of Ach occurrence peaked in the third decade of life and increased with advancing age. However, the mean age at first Ach isolation in our cohort was 10.9 years. Notably, more Ach isolates were identified in childhood than expected based on reports from low-income countries.[2,24,25] In such settings, factors, including unfavorable environmental conditions, limited access to adequate nutrition, and suboptimal adherence to treatment, may contribute to earlier lung function decline and increased susceptibility to opportunistic airway pathogens in children.

In our study, consistent with the studies conducted by Lambiase et al.[13] and De Baets et al.[2], our results showed a reduction in FEV_1 z-scores at the 12th month following Ach isolation in both groups, without reaching statistical significance. However, a study conducted in our country by Sunman et al.[26] reported

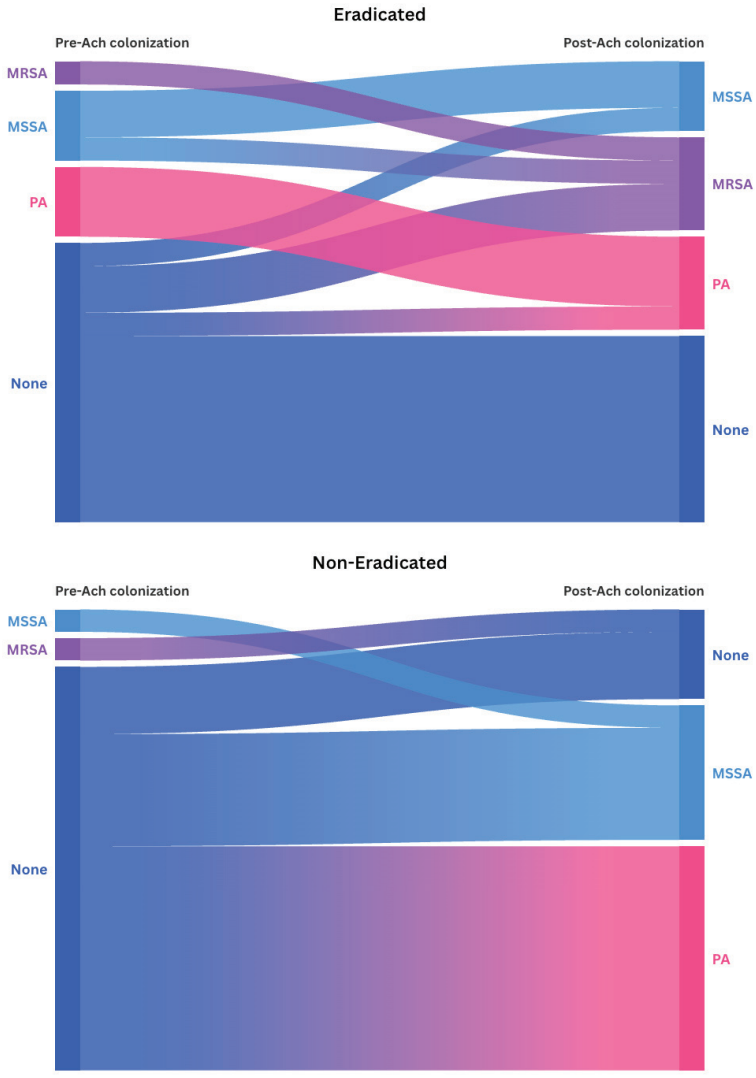


Figure 1. Transitions in airway colonization before and after *Achromobacter* (Ach) isolation stratified by eradication status. Sankey diagrams illustrate changes in airway colonization patterns from pre- to post-Ach isolation in the eradicated (top panel) and non-eradicated (bottom panel) groups. Colonization categories include no bacterial isolation (none), methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), and *Pseudomonas aeruginosa* (PA). In the eradicated group, the pre-Ach categories were none (n = 12), MSSA (n = 3), MRSA (n = 1), and PA (n = 3), while the post-Ach categories were none (n = 8), MSSA (n = 3), MRSA (n = 4), and PA (n = 4). In the non-eradicated group, the pre-Ach categories were none (n = 18), MSSA (n = 1), and MRSA (n = 1), while the post-Ach categories were none (n = 4), MSSA (n = 6), and PA (n = 10). The width of each flow represents the number of individuals transitioning between colonization states

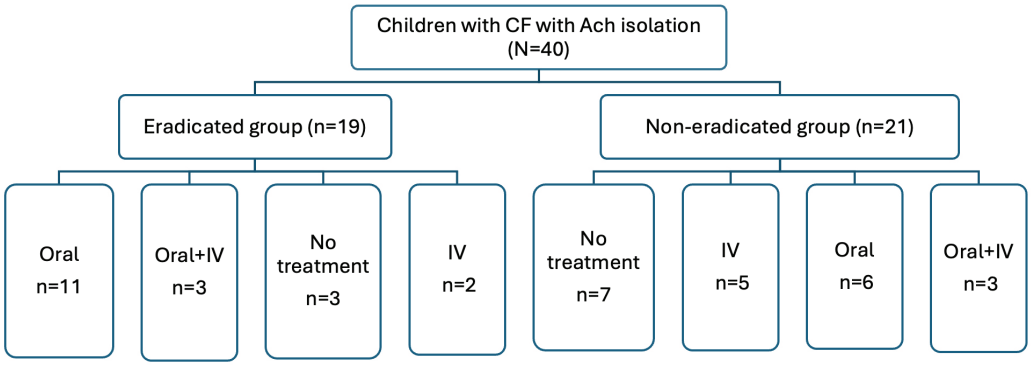


Figure 2. Antibiotic treatment regimens in eradicated and non-eradicated *Achromobacter* infection

CF: cystic fibrosis, Ach: Achromobacter, IV: intravenous

that Ach isolation is associated with a more rapid decline in lung function in cwCF. Although baseline pulmonary function tests and decreases in FEV_1 were not different between the groups, the pre-Ach Pex number was higher in the non-eradicated group, similar to the pediatric study by Marsac et al.[27] They observed that before the initial Ach isolation, patients had more Pex, hospitalizations, IV, and oral antibiotic courses than controls. In our study, FEV_1 z-scores declined over the 12 months following Ach detection in both groups; however, these changes did not reach statistical significance. While this short-term follow-up did not demonstrate a clear difference in lung function trajectories by eradication status, the higher burden of Pex observed in the non-eradicated group may indicate a subgroup at risk for more pronounced functional decline over longer observation periods.

In this study, we found that colonization status changed over time among patients in whom Ach could not be eradicated. The observed changes in Pa colonization patterns following detection of Ach highlight a potential interaction between Ach and other airway pathogens in the CF airway. This result is similar to that of a case-control study conducted at two pediatric CF centers in France, which observed an increased colonization with Pa within 2 years following Ach colonization.[27] Studies have shown that co-infection with Pa + Ach is significantly associated with lower lung function and BMI across all age groups.[24] Additionally, Ach, after its initial colonization of the respiratory tract, induces neutrophilia, cytokine production, and inflammatory responses. We speculate that Ach may create a microenvironment conducive to opportunistic pathogens.[28]

In our study, the non-eradicated group had a higher percentage of azithromycin use in the year prior to initial Ach isolation. The mean age and the number of Pex were higher in this group. Although not statistically significant, the FEV_1 z-score was lower. These clinical factors were indicative of a worse health status that led to treatment with azithromycin. Tan et al.[29] argued that intensive antibiotic usage, such as azithromycin, may be a risk factor for the development of opportunistic infections. In contrast, Cogen et al.[30] stated that long-term use of azithromycin does not increase opportunistic respiratory pathogens in pwCF.

Poor nutritional status in pwCF leads to declines in pulmonary function, more frequent Pex, and increased mortality.[31,32] Studies have demonstrated that pwCF with Ach colonization have lower BMI z-scores than those without Ach colonization.[24,33] We compared the baseline BMI z-scores between the eradicated and non-eradicated groups and found that both groups had low scores. This result may be attributed to challenges accessing adequate nutritional resources for cwCF in our country, independent of microbiological isolation.[34]

Considering the lack of a significant difference in BMI z-scores at the 12th month follow-up between the eradicated and non-eradicated groups, our findings suggest that, in the short-term, Ach alone does not appear to adversely affect the nutritional status. It is crucial to improve the nutritional status of cwCF, regardless of the presence of a specific pathogen.

There are no standardized eradication treatment protocols. Clinicians evaluate each pwCF individually, considering *in vitro* antimicrobial susceptibility reports and post-treatment clinical outcomes.[35] To our knowledge, two studies have evaluated treatment outcomes after Ach isolation in pwCF.[36,37] In a study conducted by Wang et al.[36], meropenem, piperacillin-tazobactam, and trimethoprim-sulfamethoxazole were highly effective against Ach. Additionally, it was concluded that ceftazidime, colistin, and tobramycin were sufficient for inhalation therapy. In a study conducted in the microbiology laboratory of our hospital that presented antimicrobial susceptibility data for all isolates of Ach, we observed high resistance rates to piperacillin-tazobactam, meropenem, and trimethoprim-sulfamethoxazole.[38] In our study, eradication treatments were planned based on antibiogram results. Although the number of uses of meropenem + colistin and trimethoprim-sulfamethoxazole was higher in our study, this difference was not statistically significant. Nebulized antibiotics could not be used for Ach due to reimbursement issues.

Some argue that chronic use of inhaled antibiotics in pwCF may lead to the development of multidrug resistance; however, adding inhaled antibiotics to the eradication protocol can prevent chronic colonization by pathogens, including Ach.[39] Therefore, the likelihood of Ach colonization may decrease, thereby potentially reducing chronic nebulized antibiotics. The traditional approach to eradicating Ach in pwCF involves the use of oral and IV agents, depending on the individuals' clinical status, and our study also included the administration of oral and/or IV antibiotics for Ach.[40] No significant differences were found in oral and/or IV antibiotic use. In the eradicated group, spontaneous eradication of Ach in three cwCF suggested that these cases might involve non-pathogenic strains of Ach.

This study is significant because it assesses the clinical features of Ach in cwCF. The absence of cwCF using CFTR modulators in this cohort underscores the relevance of this research for countries where access to these therapies remains limited, highlighting the risk of opportunistic infections. Furthermore, the study advocates heightened clinical awareness of Ach in cwCF experiencing frequent Pex and suggests that eradication should be considered when Ach is identified.

Study Limitations

Our study has several limitations. This single-center retrospective study included a limited number of cwCF. Although microbial species differentiation of Ach could not be performed, the eradication success rate was high.

CONCLUSION

In this pediatric CF cohort from the pre–CFTR modulator era, non-eradicated Ach was associated with older age at first isolation, a higher Pex burden in the preceding year, and significant shifts in airway microbiology over 12 months, including increased Pa colonization. Although 12-month lung function did not differ by eradication status among those with available spirometry, the observed microbiological transitions underscore the need for careful clinical and microbiological follow-up after the first Ach isolation, especially in children with frequent exacerbations.

Ethics

Ethics Committee Approval: Official approval for the study was received from the Marmara University Ethics Committee (protocol no: 09.2024.30, decision date: 12.01.2024).

Informed Consent: Given the retrospective study design and the use of fully anonymized patient data, written informed consent was not required and therefore not obtained in accordance with the ethics committee's decision.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ş.K., M.S.B., M.Y.K., A.G., M.Y., C.Y.Y., A.P.E., Ö.D., E.E.E., Y.G., A.K., F.K., B.K., Concept: Ş.K., M.S.B., A.P.E., B.U., G.T., Ö.D., E.E.E., Y.G., A.K., F.K., B.K., Design: Ş.K., M.S.B., A.P.E., Ö.D., E.E.E., Y.G., A.K., F.K., B.K., Data Collection or Processing: Ş.K., M.S.B., M.Y.K., A.G., M.Y., C.Y.Y., A.P.E., B.U., G.T., Ö.D., Analysis or Interpretation: Ş.K., M.S.B., A.P.E., E.E.E., Y.G., A.K., Literature Search: Ş.K., M.S.B., M.Y.K., A.G., M.Y., C.Y.Y., A.P.E., Y.G., A.K., F.K., B.K., Writing: Ş.K., Y.G., A.K., F.K., B.K.

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Original Article

Thoracic Surgeon Density in Türkiye in the Global Context: Implications for Workforce Planning

Necati Çıtak

Clinic of Thoracic Surgery, University of Health Sciences Türkiye, İzmir Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, İzmir, Türkiye

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ABSTRACT

OBJECTIVE: Ten years ago, evidence demonstrated that the number of thoracic surgeons in Türkiye was excessive. In the intervening period, health policies have continued to significantly increase the number of thoracic surgeons. It is estimated that this number will almost double within the next ten years. This study aims to investigate, using scientific data, the ideal number of thoracic surgeons required in Türkiye.

MATERIAL AND METHODS: Thoracic surgery workforce requirements were estimated using national data on annual outpatient visits and hospitalization rates; data from the Turkish Statistical Institute; specialist physician growth rates; and international data from Europe, the Americas, and global sources, according to service targets, population growth, high human development index countries, and global benchmarks.

RESULTS: According to Ministry of Health data, 693 licensed thoracic surgeons are currently registered as active physicians in Türkiye. In addition, 353 residents are undergoing specialist training in thoracic surgery. Based on annual outpatient visits (1,100,000) and hospitalization rate (5%), the required number of thoracic surgeons was calculated as 589. Based on specialist physician growth and population growth over the past decade, the required numbers were estimated as 586 and 589, respectively. According to European, American, and global benchmarks, the required numbers were 267, 351, and 102, respectively. Overall, calculations using all methods indicate a workforce excess ranging from 15% to 81.9%.

CONCLUSION: The number of thoracic surgeons in Türkiye is substantially higher than the estimated requirements and is expected to increase further due to ongoing residency training. National workforce planning based on objective criteria is needed to ensure alignment between training capacity and healthcare needs.

KEYWORDS: Thoracic surgery, workforce planning, human resources for health, specialist physician density, health policy

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INTRODUCTION

Safe and timely access to surgical care has been recognized as a fundamental component of universal health coverage.[1] Despite this recognition, the Lancet Commission's Global Surgery 2030 report concluded that approximately 5 billion people worldwide lack access to surgical care, particularly in low- and middle-income countries (LMICs), including for oncological indications.[2] Cancer surgery remains critically under-resourced in LMICs. In 2015, Sullivan et al.,[3] in the Lancet Oncology Commission's Global Cancer Surgery report, estimated that approximately 80% of new cancer cases would require surgical intervention. Lung cancer, as the leading cause of cancer-related mortality worldwide, represents a major component of this surgical burden.

Thoracic surgeon workforce capacity is a key determinant of access to surgical care for lung cancer. However, accurate data regarding the number and density of active thoracic surgeons remain limited due to heterogeneous certification

Corresponding author: Assoc. Prof. Necati Çıtak, MD, e-mail: necomomus@gmail.com

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systems and the absence of a harmonized global registry.[4] Recent international data presented at the International Association for the Study of Lung Cancer (IASLC) 2025 meeting demonstrated substantial disparities in thoracic surgeon density between high-income countries (HICs), MICs, and low-income countries, while projecting workforce declines in several HICs by 2035.[5]

A decade ago, our workforce analysis in Türkiye, utilizing data up to 2013, concluded that the country already had a 28.4% surplus of thoracic surgeons (n = 542 compared with a calculated need of 388) and warned that failure to regulate this increase could lead to underemployment and specialists seeking alternative career paths.[6] Given recent global data and updated national figures, this study aims to re-evaluate thoracic surgeon workforce trends in Türkiye over a 10-year period and contextualize the country within the global thoracic surgical workforce landscape.

MATERIAL AND METHODS

Study Design

This study was designed as a longitudinal, descriptive analysis of the thoracic surgery workforce in Türkiye. The study period spans 2005–2024, with the primary analytical focus on the 2015–2025 period and projections extending to 2028. The methodological framework was based on the workforce planning approach previously described in our 2015 national study and was updated using current national and international data sources.[6]

The analysis aimed to reassess the adequacy of the thoracic surgeon workforce using multiple independent calculation models and comparisons with international benchmarks.

No patient-level data were used. All data were obtained from publicly available national and international sources; therefore, ethics committee approval was not required.

Data Sources

National and International Data

National workforce modeling was performed using the following parameters: the annual number of thoracic surgery outpatient visits reported by the Ministry of Health, the outpatient-to-hospitalization rate, the bed occupancy rate, and the mean length of hospital stay in Ministry of Health hospitals.

In addition, the annual increase rates of specialist physicians and thoracic surgeons, population data obtained from the Turkish Statistical Institute (TÜİK), and the annual number of active thoracic surgeons were included in the analysis.

The 2015 population (78.7 million) was used as the reference year for the population growth model, as it represents the most recent complete dataset available when the original workforce projection was published. The number of individuals per thoracic surgeon was calculated by equating population growth to the increase in the number of thoracic surgeons.

Furthermore, data published in Europe and the United States (U.S.) were considered to determine the population-to-thoracic surgeon ratio in these regions and to adapt them to the national context. International thoracic surgeon density data were obtained from global mapping studies presented at international scientific meetings and published sources.[7-10] Density values were extracted for the global average, the European and American continents, and other World Health Organization regions. All density values were standardized per population unit to ensure comparability.

Workforce Estimation Models

The Service-target-based Model estimates workforce requirements based on parameters of healthcare service delivery. The calculation incorporated annual outpatient visit volume, the proportion of patients requiring hospitalization (5%), and the daily number of outpatient visits (≥25). Because branch-specific annual outpatient visit data published by the Ministry of Health were only available up to 2017,[11] the estimated thoracic surgery outpatient volume for 2025 was extrapolated by adjusting the 2017 value according to the proportional increase in total annual hospital admissions between 2017 and 2025. Annual inpatient workload and required specialist capacity were estimated using these variables, according to service targets defined by national health planning criteria.

Specialist Growth Rate Model: Workforce need was estimated by proportionally adjusting the number of thoracic surgeons according to the national growth rate of specialist physicians during the study period. The annual specialist growth rate was calculated using the methodology for demographic population growth rates. The net annual change in the number of specialists was divided by the mid-year specialist stock and then multiplied by 100 to obtain the annual percentage growth rate.

To integrate both the magnitude and velocity of expansion, a workforce composite growth index (CGI) was constructed as the ratio of the cumulative increase in specialists to the annual growth rate. This approach enabled the evaluation of dynamic expansion patterns rather than static proportional change alone. The CGI was calculated as follows: CGI = cumulative growth ratio (%) / annual growth rate.

Population Growth Model: Thoracic surgeon requirements were recalculated by maintaining the historical thoracic surgeon-to-population ratio and adjusting it according to national

Main Points

- According to multiple independent workforce models, the number of thoracic surgeons in Türkiye exceeds the estimated national requirement by 15% to 81%, indicating a substantial surplus.
- If the current growth trajectory continues, the number of active thoracic surgeons is projected to double within the next decade, potentially exacerbating the mismatch between workforce supply and healthcare demand.
- In international comparisons, Türkiye has nearly seven times the global average for thoracic surgeon density, underscoring the need for evidence-based and structurally informed workforce planning rather than continued numerical expansion of the workforce.

population growth. The 2015 population (78.7 million) was used as the reference year for the population growth model, as it represents the most recent complete dataset available when the original workforce projection was published.

Continental Benchmark Models: Required thoracic surgeon numbers were recalculated by applying thoracic surgeon density values observed in Europe and the Americas to the Turkish population, allowing benchmarking against high-income continental standards.

Global Benchmark Model: Global average thoracic surgeon density was applied to the Turkish population to estimate workforce need using worldwide benchmarks. Using continental and global benchmark models, thoracic surgeon density was standardized per 100,000 population and per 10 million population to enable direct comparisons between Türkiye and global regions.

Weighted Multi-model Estimation: To reduce model-specific bias, an aggregate estimate was generated by averaging the outputs of all independent models.

RESULTS

The number of thoracic surgeons in Türkiye was 256 in 2005 and increased to 380 in 2007, 433 in 2009, 524 in 2011, 542 by the end of 2013, and 693 by the end of 2023. At the beginning of 2024, 353 physicians were undergoing specialist training in thoracic surgery (residents). Accordingly, by 2028, excluding deaths, retirements of specialists, or discontinuations of training among residents, the number of specialist thoracic surgeons is projected to reach at least 1,046.

Service-target-based Model

According to data from the Ministry of Health, the estimated annual number of thoracic surgery outpatient visits in 2025 is approximately 1,100,000. Assuming that outpatient services can provide 5,000 consultations annually over 200 working days (200 working days×25 outpatient visits/day), 220 specialist physicians are required for outpatient services alone (1,100,000 outpatient visits/5,000 annual consultations per physician).

Given that at least 20 outpatient visits are required for each hospitalization (based on a targeted hospitalization rate of 5%), the annual number of inpatients is estimated at 55,000. Assuming a thoracic surgeon manages one inpatient per day, including all interventional procedures, a single surgeon would manage 200 inpatients per year (200 working days×1 patient/day), indicating a need for 275 specialists (55,000 patients/200 patients per physician).

Therefore, a total of 495 thoracic surgeons (220 for outpatient services and 275 for inpatient care) would be sufficient for Ministry of Health institutions. Given that the Ministry of Health manages 84% of the total workload, approximately 589 specialists would be required across all institutions to meet service targets.

Specialist Growth Rate Model

Thoracic surgeons accounted for 0.54% of all specialist physicians in 2005, increasing to 0.70% by 2024. Over the past decade (2013–2023), the number of specialist physicians in clinical and surgical departments in Türkiye increased by 29%, corresponding to an annual growth rate of 2.3%. Based on these results, the CGI was calculated as 12.6% (29/2.3). According to the CGI, the required number of thoracic surgeons was estimated at 586.

Population Growth Model

Over the past 20 years, the national population increased by 27.3%, while the number of thoracic surgeons increased by 170%. According to the TÜİK's Address-Based Population Registration System, the population was 78.7 million at the end of 2015. In the same year, there was one thoracic surgeon per 145,000 individuals (n = 542). Adjusting this ratio for the 2024 population of 85.6 million indicates that the required number of thoracic surgeons would be 589.

Continental and Global Benchmark Models

Thoracic surgeon density per 10 million population is 31.4 in Europe and 41.2 in the Americas, whereas the global average is 12 per 10 million population. In Türkiye, at the end of 2024, thoracic surgeon density was 80.9 per 10 million population. Based on these benchmark values, the required number of thoracic surgeons in Türkiye by the end of 2024 would be 267, 351, and 102, respectively.

Weighted Multi-model Estimation

The required number of thoracic surgeons in Türkiye, estimated as the average of the estimates from all models, was 414. Accordingly, the current workforce exceeds the estimated requirements by 40.2% (n = 279) (Table 1). Because no prior evidence exists to determine the superiority of any single model, equal weighting was applied; however, results are presented individually to allow independent interpretation.

DISCUSSION

A decade ago, our analysis using data up to 2013 demonstrated that Türkiye had a 28.4% surplus of thoracic surgeons (n = 542 compared with a calculated need of 388) and cautioned that failure to regulate the increasing workforce could result in underemployment and specialists seeking alternative career pathways.[6] Notably, this trend has continued unabated. Data presented at the 12th National Thoracic Surgery Congress indicate that the number of board-certified thoracic surgeons in Türkiye reached 693 by 2023, representing a 42% increase over the past decade.[12] Projections suggest that this number may rise to 1,045 by 2028, corresponding to a further 56% increase from 2023 levels. If the rate of increase in the number of thoracic surgeons observed recently continues, the number of active thoracic surgeons will double within 10 years. As shown in Table 1, the current number of thoracic surgeons in Türkiye exceeds the estimated national requirement by between 15% and 81%, depending on the methodology applied.

Table 1. The required number of thoracic surgery specialists, calculated based on specific variables, and its comparison with the current number (n = 693)

	Calculated	Difference from the current situation	Surplus from current workforce (%)
According to targets*	589	104	15.0
According to the growth rate of specialist physicians	586	107	15.4
According to the population growth rate	589	104	15.0
According to the European continent	267	426	61.4
According to the American continent	351	346	49.9
According to global data	102	568	81.9
Weighted average	414	279	40.2

*According to the Ministry of Health hospital data, the number of thoracic surgeons needed for our country is calculated based on the annual number of outpatient visits to thoracic surgery (1,100,000) and hospitalization rate (5%). "Surplus from current workforce (%)" represents the proportion of the current workforce that exceeds the calculated need

This national surplus should be interpreted within a broader global context, as highlighted in a recent presentation at the IASLC 2025 World Conference.[5] While many LMICs face a critical shortage of thoracic surgeons and several HICs anticipate a future workforce decline (e.g., a projected 29% reduction in the U.S. cardiothoracic workforce by 2035), Türkiye appears anomalous, characterized by a substantial oversupply. Recent global data report an average thoracic surgeon density of 12.0 per 10 million population worldwide and 31.4 per 10 million population in Europe. In contrast, the corresponding density in Türkiye is approximately 81 per 10 million population—nearly seven times the global average and 2.6 times the European average.

However, Europe should not be considered a homogeneous entity with respect to healthcare systems, economic development, or workforce distribution. Thoracic surgeon density varies considerably among European countries, with higher densities observed in Southern and Eastern Europe and lower densities in some Western and Northern regions. Consequently, although continental averages provide a useful macro-level benchmark, they may obscure substantial intra-continental heterogeneity. For this reason, the present study incorporated multiple independent estimation models rather than relying solely on European density values.

In contrast, workforce distribution in related specialties demonstrates a markedly different pattern. Whereas the European average density of adult pulmonologists is approximately 4.4 per 100,000 population, the corresponding figure in Türkiye is reported to be nearly half of this value.[13] This discrepancy suggests a potential imbalance in specialty-specific workforce planning within the national healthcare system.

The consequences of this oversupply are becoming increasingly tangible. Performance-based payment data from 2022–2023 indicate that thoracic surgeons' average performance scores rank among the lowest across surgical specialties, directly affecting remuneration.[14] The long-cited aphorism that "being a thoracic surgeon means being labeled as surplus" is, unfortunately, becoming a financial reality for many practitioners.

Concurrently, the Medical Specialty Examination score required for entry into thoracic surgery residency has declined by approximately 20%, and a substantial proportion of residency positions remain unfilled (up to 58.3% in certain chest disease hospitals), indicating waning interest in the specialty despite the continued increase in specialist numbers.[12] A cross-sectional study published in 2023 further reported that none of the surveyed sixth-year medical students in Türkiye expressed an intention to pursue a career in thoracic surgery.[15] This paradox underscores a critical systemic challenge in workforce planning.

Meanwhile, the number of institutions providing thoracic surgery residency training in Türkiye increased by 157%, from 26 in 2012 to 67 in 2022.[16,17] During the same period, the number of thoracic surgery training centers increased by 46% in Spain.[18] In Brazil, a country with approximately three times the population of Türkiye, the number of institutions offering thoracic surgery training is nearly half that of Türkiye (n = 35).[19] In France, which has a similar population size, only 25 thoracic surgery residency positions are offered annually-approximately one-eighth of the number available in Türkiye.[20] These findings underscore the need to reassess national workforce planning policies to ensure alignment between training capacity and projected healthcare demand.

Workforce planning in thoracic surgery should not be limited to determining the required number of specialists based solely on quantitative indicators. In addition to service volume, bed capacity, and population growth, essential factors such as specialist qualifications, job descriptions, healthcare system structure, and governance mechanisms must be considered. Medical science—particularly within academic institutions—extends beyond procedural volume to include research productivity, training quality, and the long-term sustainability of the specialty. Although the present study primarily focuses on quantitative workforce indicators, it aims to stimulate a broader discussion on comprehensive, structurally informed workforce planning.

Study Limitations

A further limitation of this study is the inability to apply the World Health Organization-recommended Workload Indicators of Staffing Need (WISN) methodology because of a lack of up-to-date, publicly available national workload data.

Potentially influential workforce variables such as maternity leave, mortality, retirement, migration abroad, and non-clinical employment patterns could not be evaluated. These factors may substantially affect the active thoracic surgery workforce and should be considered in future workforce planning models. Nevertheless, the use of multiple independent estimation models and international benchmarks provided a pragmatic assessment of thoracic surgery workforce adequacy in Türkiye. Future studies using standardized WISN-based approaches may enable more precise workforce planning.

CONCLUSION

Data from the past decade validate the concerns raised in our original report. The continued expansion of the thoracic surgery workforce in Türkiye has not been aligned with projected healthcare demand, resulting in a substantial surplus of thoracic surgeons, with measurable professional and economic implications for those surgeons. Addressing this imbalance will require a paradigm shift in workforce planning that moves beyond numerical estimations toward a more holistic framework encompassing service characteristics, defined job roles, and the structural features of the healthcare system. Responsible, evidence-based, and centralized planning—developed collaboratively by professional organizations, practicing physicians in the field, and experienced academic experts—will be essential to align training capacity with national needs and to ensure the long-term sustainability, professional satisfaction, and quality of care within the specialty.

Ethics

Ethics Committee Approval: All data were obtained from publicly available national and international sources; therefore, ethics committee approval was not required.

Informed Consent: No patient-level data were used. All data were obtained from publicly available national and international sources. Therefore informed consent was not used for this study.

Footnotes

Conflict of Interest: Necati Çıtak, MD, is an editor of Thoracic Research and Practice. He was not involved in the peer review of this article and had no access to information regarding its peer review.

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Systematic Review

Breathe Easier: Evaluating Serratus Anterior Plane Block for Rib Fracture Analgesia-A Systematic Review and Meta-analysis

Clara Alverina[1], Safina Fairuz Salwaa[2], Syaogi Ahmed 'Azizy[3], Pesta Parulian Maurid Edwar[1]

[1]Department of Anesthesiology and Reanimation, Universitas Airlangga-Dr. Soetomo General Academic Hospital Faculty of Medicine, Surabaya, Indonesia
[2]Department of Thoracic, Cardiac, and Vascular Surgery, Universitas Airlangga Faculty of Medicine, Surabaya, Indonesia
[3]Department of Anesthesiology and Intensive Care, Universitas Gadjah Mada Faculty of Medicine, Public Health, and Nursing, Yogyakarta, Indonesia

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ABSTRACT

OBJECTIVE: Rib fractures may cause severe pain that impairs ventilation, increases pulmonary complications, and lengthens hospitalization. Conventional analgesic techniques have several limitations, whereas the serratus anterior plane block (SAPB) offers a simpler, ultrasound-guided regional anesthesia alternative. This systematic review and meta-analysis examined whether SAPB improves pain control and reduces opioid use and hospitalization duration.

MATERIAL AND METHODS: A systematic review and meta-analysis were performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A literature search of PubMed, Scopus, EBSCO, Taylor & Francis, Web of Science, and ScienceDirect was conducted to identify randomized and observational studies comparing SAPB with opioid-based analgesia or other regional blocks in patients with rib fracture pain. The primary outcome was pain severity visual analogue scale/numeric rating scale (VAS/NRS) at predefined time points, whereas opioid consumption and hospital length of stay (LOS) served as secondary outcomes. Given the variability of pain assessment scales across studies (NRS 0-10 and VAS 0-100), continuous outcomes were pooled as standardized mean differences (SMDs) using a random-effects model. Seven studies comprising 611 patients met the inclusion criteria and were included in the analysis.

RESULTS: The meta-analysis showed that baseline pain scores were broadly comparable between SAPB and comparators, with no statistically significant difference overall (baseline SMD: 0.18; $P = 0.25$) or within either subgroup. Compared with opioids, SAPB was associated with significantly lower pain scores at 3 hours (SMD: –0.40; $P = 0.04$) and, in the opioid subgroup, at 12 hours (SMD: –0.44; $P = 0.002$). Overall pooled estimates at 6, 12, and 24 hours did not reach statistical significance owing to substantial heterogeneity (I^2 87–96%). Compared with other regional blocks, SAPB was associated with higher pain scores at 6 hours (SMD: 0.85; $P = 0.004$), whereas the comparison at 24 hours was inconclusive, with the overall estimate not statistically significant (SMD: –0.76; $P = 0.15$). A pooled analysis also showed a significant reduction in opioid consumption with SAPB (SMD: –0.35; 95% confidence interval: –0.67 to –0.02; $P = 0.04$). Findings on hospital LOS were inconsistent across studies and remain inconclusive.

CONCLUSION: Overall, low-certainty evidence suggests that SAPB may provide effective and longer-lasting analgesia, reduce opioid requirements, and support respiratory function, indicating a potential role as an adjunct in the management of rib fracture pain.

KEYWORDS: Rib fractures, serratus anterior plane block, regional anesthesia, opioids, pain management

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Corresponding author: Pesta Parulian Maurid Edwar, MD, e-mail: edwarnest@yahoo.co.id

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INTRODUCTION

Rib fractures are common thoracic injuries, occurring in more than 50% of blunt trauma cases and associated with significant morbidity, long-term disability, and mortality.[1] The annual incidence of rib fractures is estimated at 4–8 per 10,000 individuals in the United Kingdom.[2] The risk of complications increases proportionally with the number of ribs fractured.[1,3] Multiple rib fractures in elderly patients are more likely to require admission to intensive care and are associated with poor clinical outcomes.[4]

Most complications arise not only from structural injury but also from inadequately controlled pain. Severe pain can lead to impaired alveolar ventilation, manifested by shortness of breath or splinting. This impairment further compromises effective coughing, thereby increasing the risk of atelectasis, pneumonia, and even respiratory failure.[5] Therefore, early and adequate analgesic administration is a cornerstone in the management of patients with rib fractures.[6]

Analgesic treatment typically begins with systemic pharmacological therapy administered orally or intravenously, including paracetamol, nonsteroidal anti-inflammatory drugs, and opioids.[6] However, in patients with more severe injuries or certain comorbidities, systemic analgesics may provide inadequate pain control. Although effective, opioids are associated with well-recognized adverse effects, including respiratory depression, sedation, constipation, nausea and vomiting, delirium in elderly patients, and drug dependence.[3] Consequently, interventional techniques and regional anesthesia have emerged as effective alternatives that provide adequate analgesia while reducing opioid-related side effects.[1,3]

Given these considerations, regional techniques, such as the serratus anterior plane block (SAPB), have attracted increasing interest. The SAPB was first described as a regional analgesic technique for patients undergoing breast surgery by Blanco et al.[7] The technique was developed to provide analgesia for the lateral thoracic wall by blockade of the thoracic intercostal nerves and proposed as a simpler and potentially safer alternative to thoracic epidural analgesia (TEA) and paravertebral blockade. Since its introduction, SAPB has been increasingly adopted for other indications, including rib fracture analgesia, due to its ease of performance, favorable safety profile, and feasibility of bedside administration under ultrasound guidance.[7] SAPB, performed by administering local anesthetic into the plane between the serratus anterior muscle and the lateral thoracic wall, effectively blocks the lateral cutaneous branches of the intercostal nerves (T2–T9), resulting in extensive analgesia of the anterolateral chest wall. Additional advantages include the feasibility of catheter placement for continuous local anesthetic infusion and its reported relative safety in patients with coagulopathy.[8,9]

Early studies suggest that SAPB effectively reduces pain scores and opioid consumption and improves respiratory function.[10-12] However, most available evidence is derived from small-scale studies with heterogeneous designs, and the comparative effectiveness of SAPB versus systemic opioids or other regional analgesic techniques remains controversial. Moreover, data on clinically relevant outcomes such as mortality, hospital length of stay (LOS), and respiratory complications remain limited. To address these limitations, we conducted a systematic review and meta-analysis evaluating the effectiveness and safety of SAPB compared with opioids and other regional block techniques in patients with rib fractures, with particular emphasis on pain control, opioid-sparing effects, and impact on length of hospital stay.

Main Points

- Serratus anterior plane block (SAPB) may provide effective and sustained analgesia in patients with rib fractures, with a favorable safety profile and analgesic efficacy that appears comparable to, and possibly greater than, that of other regional techniques within the first 24 hours.
- SAPB supports pulmonary function and reduces opioid exposure, thereby contributing to improved respiratory outcomes and a meaningful opioid-sparing effect that may reduce opioid-related adverse events.
- The impact of SAPB on hospital length of stay remains inconclusive, with heterogeneous findings across studies. Further large-scale, well-designed randomized controlled trials are required to investigate this outcome.

METHODS

Study Design and Eligibility Criteria

This systematic review was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[13] Eligible studies included randomized controlled trials (RCTs) and observational studies (both prospective and retrospective cohort designs) evaluating the use of SAPB in patients with rib fractures. Studies were required to compare SAPB with other analgesic techniques, including systemic opioid therapy and alternative regional anesthesia approaches, such as TEA, paravertebral block (PVB), intercostal nerve block (ICNB), and erector spinae plane block (ESPB). Case reports, case series, narrative reviews, conference abstracts without full-text availability, and non-English-language publications were excluded. The protocol for this study has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with ID CRD420261287442.

Search Strategy

A comprehensive literature search was conducted across databases, such as PubMed, Scopus, EBSCO, Taylor & Francis, Web of Science, and ScienceDirect, to identify publications from January 2015 to June 2025. The search strategy employed the following keywords: “serratus anterior plane block” AND “rib fractures” AND (“regional anesthesia” OR “paravertebral block” OR “thoracic epidural” OR “erector spinae plane block”). Additionally, reference lists of relevant articles were manually searched to identify eligible studies (Figure 1).

Data Extraction and Statistical Analysis

Article screening and data extraction were performed independently by three authors using a predefined and

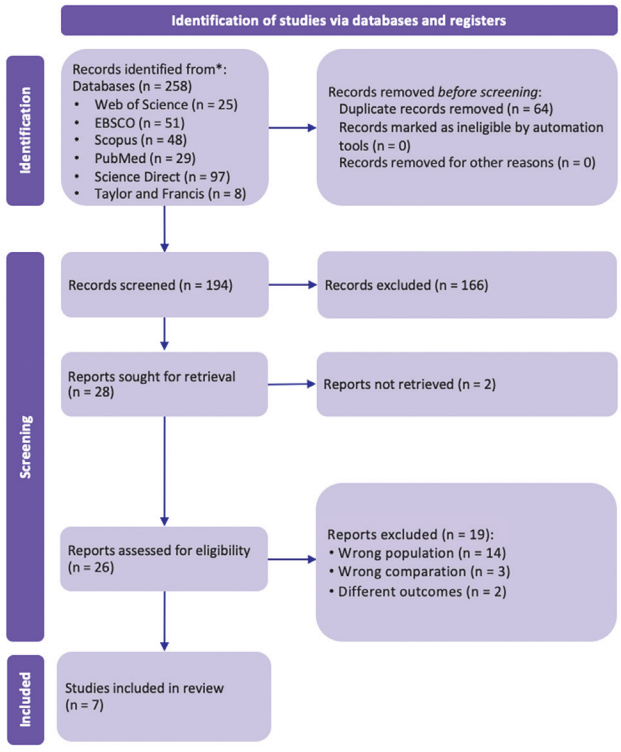


Figure 1. PRISMA 2020 flow diagram for included studies[13]

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

standardized form. The extracted data included study design, patient characteristics, interventions and comparators, and reported outcomes. Any discrepancies during data evaluation were discussed until a consensus was reached.

Quantitative analyses focused on pain scores reported at multiple time points (baseline, 3 hours, 6 hours, 12 hours, and 24 hours). Continuous outcomes were pooled using standardized mean differences (SMDs) with 95% confidence intervals (CIs) under a random-effects model. Because the included studies measured pain on different scales, most using the numeric rating scale (NRS, 0–10) and one[14] using the visual analogue scale (VAS, 0–100), the SMD was selected as the effect measure. Expressing treatment effects in standard deviation (SD) units enabled valid comparison and pooling of outcomes derived from different pain scales within a single analysis. Because opioid consumption was reported in heterogeneous units (tramadol in milligrams and morphine in milligram equivalents), the SMD was selected to standardize effect estimates across studies. Where appropriate, VAS values were rescaled to a common 0–10 metric before standardization. When data were reported only as medians and interquartile ranges, they were converted to means and SDs using the methods described by Luo et al.[15] and Wan et al.[16] Where feasible, subgroup analyses were conducted to compare SAPB with other regional blocks and with opioid-based analgesia. Statistical heterogeneity was assessed using the I^2 statistic, with values greater than 50% considered indicative of substantial heterogeneity. Sensitivity analyses were considered in cases of substantial baseline imbalance or marked heterogeneity. All analyses were performed using Review Manager (RevMan) version 5.4.

Risk-of-Bias Assessment and Quality of Evidence

Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for RCTs and the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool for non-randomized studies.[17,18] The RoB 2 tool assessed bias arising from the randomization process, deviations from intended interventions, the completeness and accuracy of outcome data, and selective reporting. The ROBINS-I tool additionally assessed bias due to confounding and participant selection. All assessments were conducted independently by two reviewers, with disagreements resolved by a third reviewer. The overall quality of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[19]

Interventions

The primary intervention evaluated was SAPB in patients with rib fractures. SAPB is performed under ultrasound guidance, with local anesthetic injected between the serratus anterior muscle and the lateral thoracic wall, with or without the placement of a catheter for continuous infusion. The comparators included systemic opioid therapy and other regional analgesic techniques such as TEA, PVB, ICNB, and ESPB.

Outcomes

The primary outcome was pain intensity, assessed using the VAS or the NRS at multiple time points, including baseline and 3, 6, 12, and 24 hours post-intervention. Secondary outcomes included total opioid consumption within the first 24 hours and hospital LOS.

RESULTS

Study Characteristics

This systematic review includes seven studies, published between 2021 and 2025, that were conducted in Italy, Türkiye, Egypt, the United States, and Australia. Among the included studies, five were RCTs,[11,12,14,20,21] one was a retrospective observational study,[22] and one was a prospective observational cohort study.[23] Sample sizes across the included studies ranged from 38 to 210 patients. All studies investigated SAPB as the primary intervention, including its superficial variant (S-SAPB). Comparator groups included the ESPB, the ICNB, intravenous patient-controlled analgesia (PCA) using tramadol, and standard care (Table 1).

Seven studies included in this review involved sample sizes ranging from 38 to 210 patients, with a balanced distribution between the intervention and control groups. The mean or median age of patients in the SAPB group ranged from 34.4±12.35 years to 71 (54–85) years, while in the control group ranged from 35.8±11.56 years to 71 (58–82) years. The proportion of male patients in the SAPB group ranged from 36.67% to 70.7%, whereas in the control group it ranged from 23.33% to 66.7%. The instruments used to assess pain intensity varied across studies, with most studies employing the NRS and one study using the VAS (Table 2).

In total, 611 patients were analyzed across the seven included studies (SAPB groups, n = 298; comparator groups, n = 313).

Table 1. Characteristics of included studies

No.	First author	Year	Country	Study design	Sample size, n	Intervention	Control
1	El Malla[20]	2022	Italy	Prospective randomized trial	50	SAPB	ESPB
2	Zengin[14]	2025	Türkiye	Prospective, randomized, assessor-blind study	60	SAPB	ICNB
3	Tekşen[11]	2021	Türkiye	Prospective controlled randomized trial	60	SAPB	IV PCA (tramadol)
4	Abu-Elwafa[21]	2021	Egypt	Randomized controlled study	40	SAPB	IV morphine
5	Serra[22]	2024	Italy	Retrospective observational study	156	SAPB	Standard care
6	Sadauskas[23]	2024	United States	Prospective observational cohort study	38	SAPB	Standard care
7	Partyka[12]	2024	Australia	Multicenter, open-label, pragmatic randomized clinical trial	207	SAPB	Standard care

n: number of samples, SAPB: serratus anterior plane block, ESPB: erector spinae plane block, ICNB: intercostal nerve block, IV: intravenous, PCA: patient-controlled analgesia

Table 2. Characteristics of study participants

No	Author, year	Sample size (n)		Age, year*		Male, % (n)		Pain scale
		SAPB	Control	SAPB	Control	SAPB	Control	
1	El Malla et al.[20], 2022	25	25	34.4±12.35	35.8±11.56	68 (17)	80 (20)	NRS
2	Zengin et al.[14], 2025	30	30	53 [18]	44 [27.75]	70 (21)	66.67 (20)	VAS
3	Tekşen et al.[11], 2021	30	30	50.7±18.8	42.4±15.8	36.67 (11)	23.33 (7)	NRS
4	Abu-Elwafa et al.[21], 2021	20	20	NR	NR	NR	NR	VAS
5	Serra et al.[22], 2024	75	81	64 [55–74]	61 [51–74]	70.7 (53)	60.5 (49)	NRS
6	Sadauskas et al.[23], 2024	15	23	58±21	64±19	66 (10)	43 (10)	NRS
7	Partyka et al.[12], 2024	103	104	71 [54–85]	71 [58–82]	65 (67)	60 (62)	NRS

*Data are presented as mean ± SD or median (IQR)

**Partyka et al.[12] baseline characteristics are reported for the analyzed population (103 SAPB, 104 control); 210 patients were initially randomized

n: number of samples, SAPB: serratus anterior plane block, NRS: numeric rating scale, VAS: visual analog scale, SD: standard deviation, IQR: interquartile range

This total reflects the number of participants analyzed in each study, including 207 patients reported by Partyka et al.[12] (103 in the SAPB group and 104 in the comparator group), which is consistent with the baseline characteristics reported in that trial. The 210 patients initially randomized are reported in the study-characteristics table. The same total of 611 is reported consistently across the Abstract, Results section, and the GRADE evidence profile (Supplementary Table 1).

With respect to the local anesthetic used for the block, bupivacaine and ropivacaine were the agents employed across the included studies. Bupivacaine 0.25% was the most frequently used agent: Tekşen et al.[11] administered 30 mL (75 mg), Zengin et al.[14] used 20 mL (50 mg) for the superficial SAPB, and El Malla et al.[20] used a 30 mL mixture of bupivacaine 0.25% (15 mL, 37.5 mg) and lignocaine 1% (15 mL, 150 mg) with added dexamethasone. Abu-Elwafa et al.[21] administered a weight-based volume of bupivacaine 0.25% (0.5 mL/kg). Ropivacaine was used in the remaining studies: Serra et al.[22] administered 30 mL of 0.23–0.33% ropivacaine (median dose 80 mg; range 70–100 mg); Partyka et al.[12] used a high-volume, low-concentration ropivacaine solution as a single-shot block, with a median volume of 40 mL and a median dose of 150 mg; Sadauskas et al.[23] did not report the agent, concentration, or volume in sufficient detail (Supplementary Table 2). The number and anatomical location of fractured ribs (anterior/lateral/posterior; unilateral/bilateral) were inconsistently reported across studies and, therefore, could not be pooled. These gaps were acknowledged as limitations.

Clinical Outcomes

All included studies reported pain intensity as the primary outcome, assessed both at rest and during coughing at various time points within the first 24 hours after the intervention. The timing of assessments varied across studies, with the initial evaluation performed immediately after the procedure (T0; hour 0), followed by serial measurements at T0.5 (30 minutes), T1 (1 hour), T2 (2 hours), T4 (4 hours), T6 (6 hours), T8 (8 hours), T10 (10 hours), T12 (12 hours), T16 (16 hours), T18 (18 hours), T20 (20 hours), and T24 (24 hours) post-procedure. Overall, the SAPB intervention group consistently demonstrated lower pain scores compared with the control group, both at rest and during coughing. This analgesic benefit was most pronounced during the early postoperative period (up to the first 12 hours) and remained evident up to 24 hours.

In addition to pain outcomes, several studies evaluated length of hospital stay and postoperative opioid requirements. Serra et al.[22] reported a median hospital stay of 4 (3–6) days in the SAPB group compared with 5 (4–6) days in the control group. Partyka et al.[12] reported similar findings, with a median LOS of 4.2 (2.2–

7.7) days in the SAPB group versus 5 (3–7.3) days in the control group. Postoperative opioid consumption was also consistently lower in the SAPB group. Tekşen et al.[11] reported a total 24-hour tramadol consumption of 98.33±74.13 mg in the SAPB group, compared with 148.30±87.68 mg in the control group. Consistent results were also reported by Sadauskas et al.[23] and Partyka et al.[12], with lower morphine milligram equivalent (MME) values observed in the SAPB group compared with controls.

Meta-analysis

A total of nine pooled analyses were performed across two primary outcomes: pain score and opioid consumption. Baseline pain scores were comparable between groups (SMD: 0.18, 95% CI −0.13 to 0.49; $P = 0.25$; $I^2 = 77\%$). SAPB significantly reduced pain scores at 3 hours post-intervention (T3; SMD: −0.40, 95% CI: −0.79 to −0.02; $P = 0.04$; $I^2 = 67\%$), whereas no significant differences were observed at 6, 12, or 24 hours (all $P > 0.05$), with substantial heterogeneity across analyses ($I^2 = 88$–96%). A prespecified opioid subgroup analysis at T12 demonstrated a significant benefit favoring SAPB (SMD: −0.44, 95% CI: −0.72 to −0.16; $P = 0.002$; $I^2 = 46\%$); this effect remained unchanged in sensitivity analysis. Exclusion of an outlier study at T24 reduced heterogeneity but did not alter the non-significant result.

Regarding opioid consumption, SAPB was associated with significantly lower opioid requirements compared with the control group (SMD: −0.35, 95% CI: −0.67 to −0.02; $P = 0.04$; $I^2 = 61\%$) (Table 3).

Pain Intensity at Baseline

The forest plot at baseline showed no significant difference in pain intensity between SAPB and comparators overall (SMD: 0.18; 95% CI: –0.13 to 0.49; $P = 0.25$; $I^2 = 77\%$). In the subgroup analysis, no significant baseline difference was found in either subgroup: the opioid-comparator subgroup (SMD: 0.23; 95% CI: –0.19 to 0.64; $P = 0.28$) or the other-regional-block subgroup (SMD: 0.10; 95% CI: –0.37 to 0.57; $P = 0.68$). These findings indicate that the SAPB and comparator groups were broadly comparable at baseline, with no statistically significant imbalance detected (Figure 2).

Pain Intensity at 3 Hours

The forest plot at 3 hours showed that SAPB was associated with significantly lower pain intensity than opioids (SMD: –0.40; 95% CI: –0.79 to –0.02; $P = 0.04$; $I^2 = 67\%$). At this time point, No studies have compared SAPB with other regional block techniques. This result is consistent with an early analgesic effect of SAPB relative to systemic opioid analgesia, although the substantial heterogeneity and the very low certainty of the evidence warrant cautious interpretation (Figure 3).

Pain Intensity at 6 Hours

At 6 hours, the forest plot demonstrated marked heterogeneity between subgroups. Compared with opioids, SAPB was associated with lower pain scores (SMD: –0.57; 95% CI: –0.89 to –0.25; $P = 0.0005$). Conversely, when compared with other regional block techniques, SAPB was associated with higher pain scores (SMD: 0.85; 95% CI: 0.27 to 1.43; $P = 0.004$). The overall pooled result was not statistically significant (SMD: –0.29; 95% CI: –0.85 to 0.27; $P = 0.31$; $I^2 = 94\%$), reflecting opposing effects across subgroups. These findings suggest that, at 6 hours post-intervention, SAPB was associated with greater pain reduction than opioids but with less pain reduction than other regional blocks; given the substantial heterogeneity and low certainty of evidence, this pattern should be interpreted with caution (Figure 4).

Pain Intensity at 12 Hours

At 12 hours, the pooled result was not statistically significant (SMD: –0.37; 95% CI: –0.92 to 0.18; $P = 0.18$; $I^2 = 88\%$). Subgroup analysis showed that SAPB remained associated with significantly lower pain scores than opioids (SMD: –0.44; 95% CI: –0.72 to –0.16; $P = 0.002$; $I^2 = 46\%$), whereas no significant difference was observed between SAPB and other regional blocks (SMD: –0.24; 95% CI: –2.46 to 1.98; $P = 0.83$; $I^2 = 97\%$). These findings suggest that the analgesic effect of

Table 3. Meta-analysis result

Outcome	Time point	Pooled SMD (95% CI)	*P* value	I^2	Interpretation
Pain score	Baseline	0.18 (−0.13 to 0.49)	0.25	77%	Non-significant; groups comparable
Pain score	T3 (3 h)	−0.40 (−0.79 to −0.02)	0.04	67%	Significant; favors SAPB (low certainty)
Pain score	T6 (6 h)	−0.29 (−0.85 to 0.27)	0.31	94%	Non-significant overall; subgroup divergence
Pain score	T12 (12 h)-Main	−0.37 (−0.92 to 0.18)	0.18	88%	Non-significant overall
Pain score	T12-Opioid subgroup	−0.44 (−0.72 to −0.16)	0.002	46%	Significant; favors SAPB (low certainty)
Pain score	T12-Sensitivity (excl. El Malla et al.[20])	−0.44 (−0.72 to −0.16)	0.002	46%	Robust; result confirmed
Pain score	T24 (24 h)-Main	−0.76 (−1.79 to 0.27)	0.15	96%	Non-significant; extreme outlier present
Pain score	T24-Sensitivity (excl. Tekşen et al.[11])	−0.44 (−0.99 to 0.11)	0.12	88%	Still non-significant; I^2 reduced
Opioid consumption	Total	−0.35 (−0.67 to −0.02)	0.04	61%	Significant; SAPB opioid-sparing

CI: confidence interval, SAPB: serratus anterior plane block

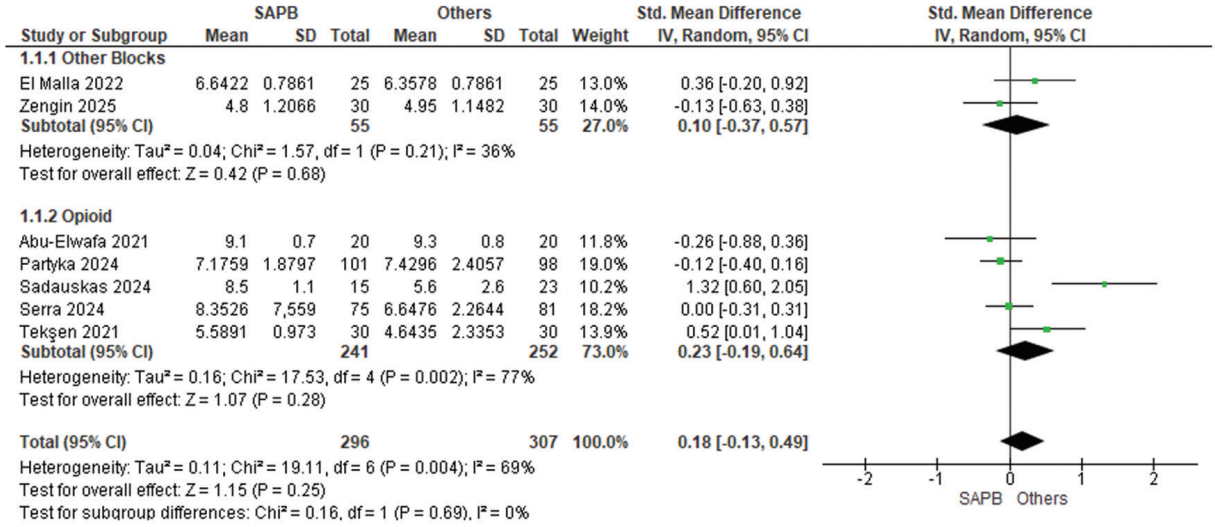


Figure 2. Mean pain intensity between SAPB and comparators at baseline

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

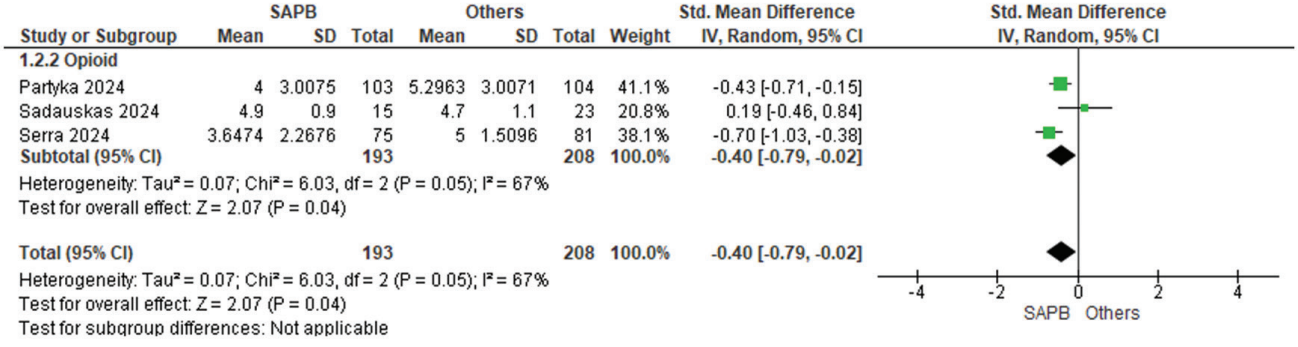


Figure 3. Mean pain intensity between SAPB and comparators at 3 hours

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

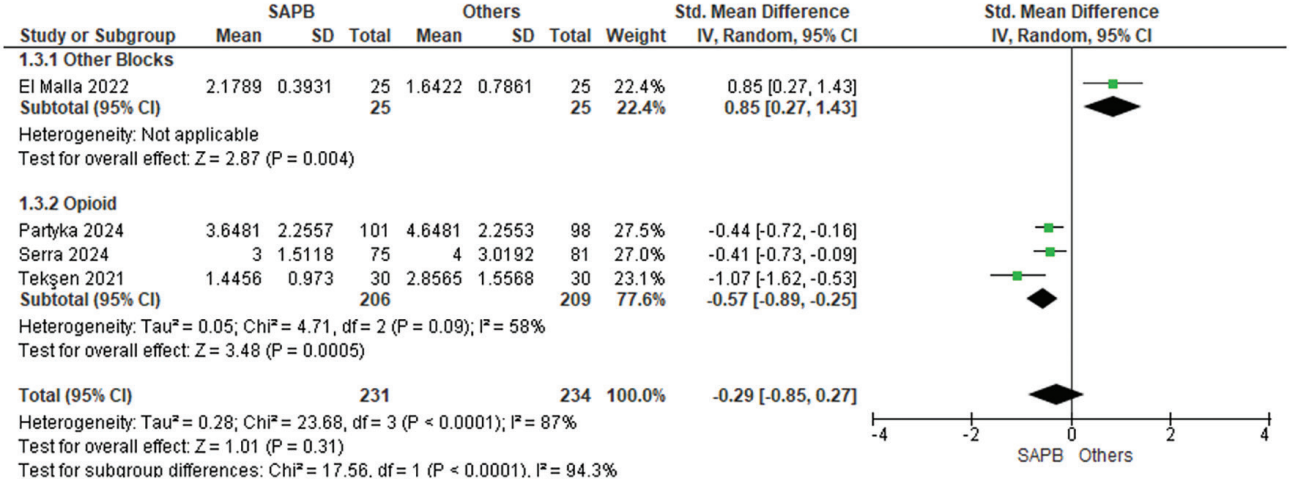


Figure 4. Mean pain intensity between SAPB and comparators at 6 hours

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

SAPB relative to opioids was sustained at 12 hours, whereas comparisons with other regional blocks were inconclusive and highly heterogeneous. Given the low certainty of evidence, these estimates should be interpreted with caution (Figure 5).

Pain Intensity at 24 Hours

At 24 hours, the overall pooled result was not statistically significant (SMD: –0.76; 95% CI: –1.79 to 0.27; $P = 0.15$; $I^2 = 96\%$), with very high heterogeneity. Subgroup analysis was likewise inconclusive: neither the comparison with opioids (SMD: –0.97; 95% CI: –2.28 to 0.35; $P = 0.15$; $I^2 = 97\%$) nor the comparison with other regional blocks (SMD: –0.43; 95% CI: –2.85 to 1.99; $P = 0.73$; $I^2 = 97\%$) reached statistical significance. Although the point estimates favored SAPB, the wide CIs and extreme heterogeneity—largely driven by a single small outlier study[11]—mean that no reliable conclusion about the 24-hour effect can be drawn; a sensitivity analysis excluding this outlier is presented in the Supplementary Figures 1-3 (Figure 6).

Total Opioid Consumption

Total opioid consumption within the first 24 hours was reported by four studies comprising 453 patients. Because the included studies expressed opioid use in different units (24-hour tramadol consumption in milligrams in Tekşen et al.[11] and MME in Sadauskas et al.[23], Partyka et al.[12], and MMEs in Serra et al.[22]), the outcome was pooled using the SMD to allow combination across heterogeneous measurement scales. Compared with

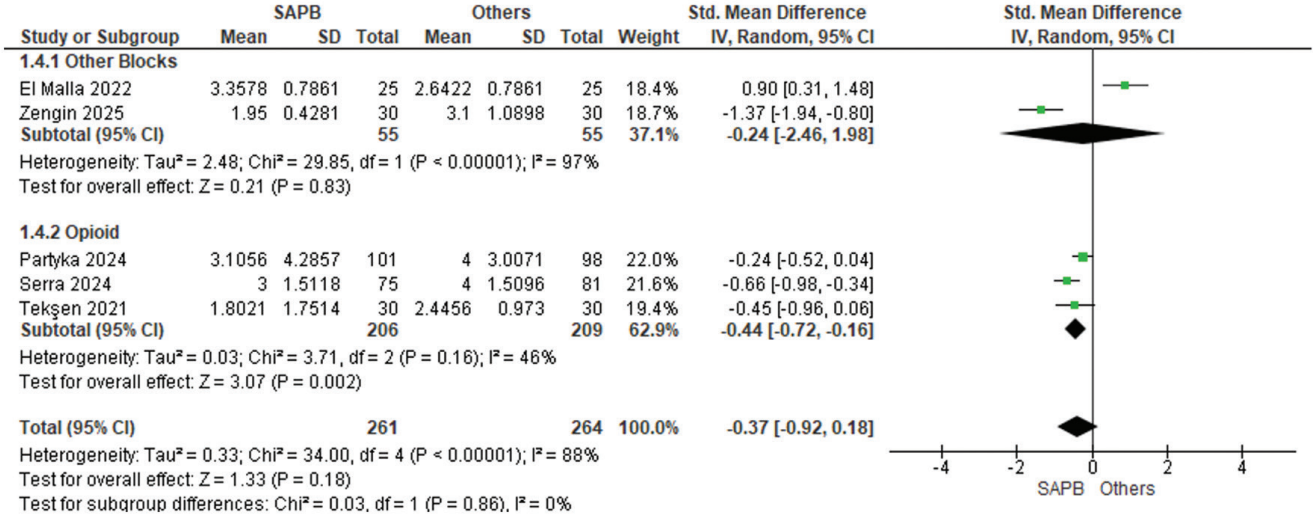


Figure 5. Mean pain intensity between SAPB and comparators at 12 hours

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

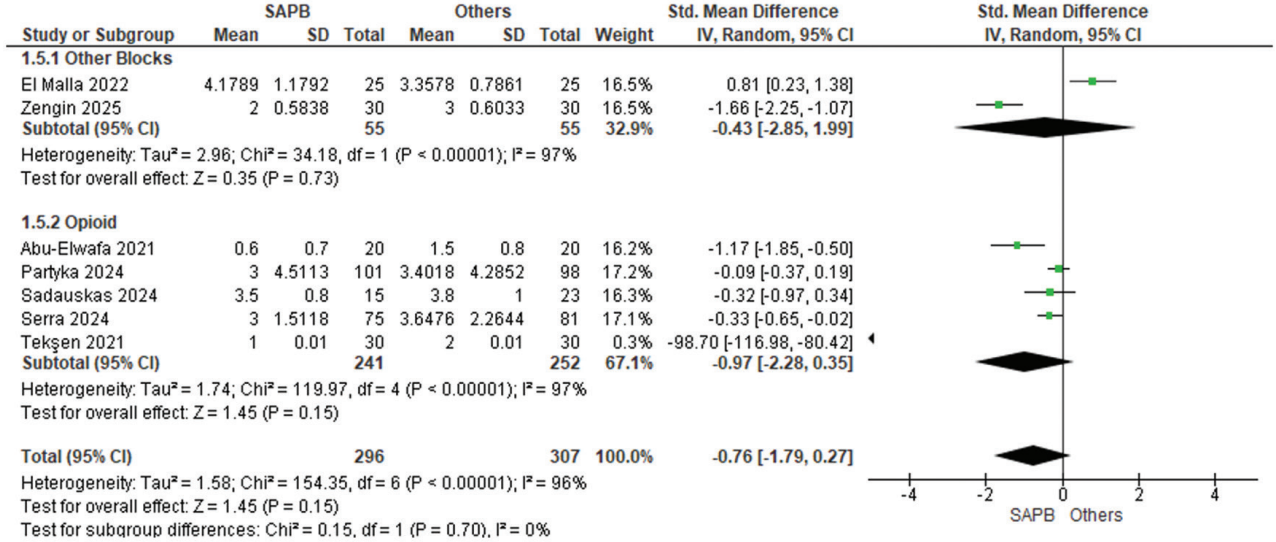


Figure 6. Mean pain intensity between SAPB and comparators at 24 hours

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

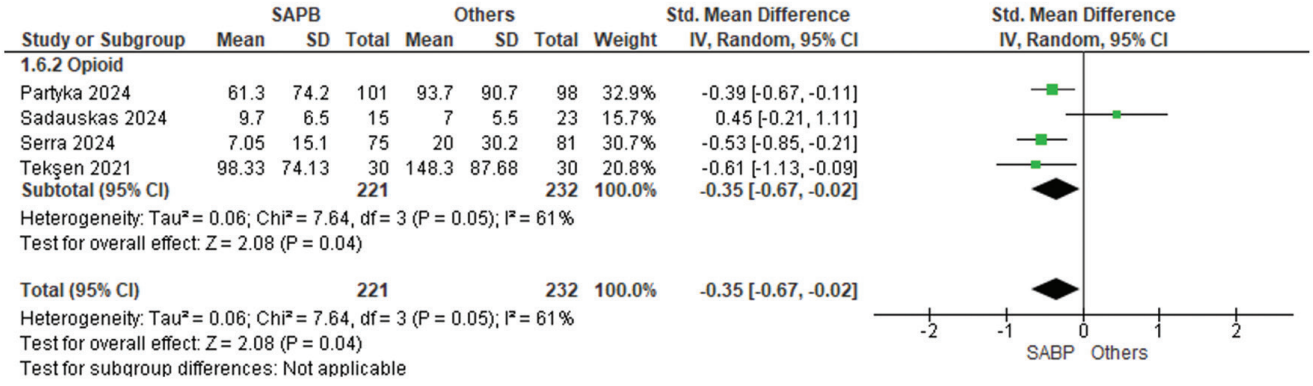


Figure 7. Total opioid consumption

SAPB: serratus anterior plane block, SD: standard deviation, SMD: standardized mean difference, IV: inverse variance, CI: confidence interval, df: degrees of freedom

controls, SAPB was associated with a significant reduction in opioid requirements (pooled SMD: –0.35; 95% CI –0.67 to –0.02; $P = 0.04$; $I^2 = 61\%$), which indicates a moderate opioid-sparing effect, although this substantial statistical heterogeneity and the small number of contributing studies warrant cautious interpretation (Figure 7).

Risk-of-Bias Assessment and Quality of Evidence

Risk-of-Bias Assessment in Randomized Studies

The risk of bias assessment of the randomized studies indicated that most domains were judged to be at low risk of bias. El Malla et al.[20] were assessed as having a low risk of bias across all domains, except for outcome measurement (D4), which was rated as having "some concerns." Zengin et al.[14] demonstrated a low risk of bias in most domains; however, concerns were identified in the domain of deviations from the intended interventions (D2). Similarly, Tekşen et al.[11] showed a low risk of bias in the domains of randomization, missing outcome data, and selection of the reported results, while concerns were noted in D2 and outcome measurement (D4). Partyka et al.[12] demonstrated a low risk of bias in D1 (randomization process), D3 (missing outcome data), and D5 (selection of the reported result), with some concerns in D2 and D4. Overall, the randomized studies included in this review were judged to have a low to moderate risk of bias, with particular concerns related to deviations from intended interventions and outcome measurement methods (Supplementary Figure 4).

Risk-of-Bias Assessment in Non-randomized Studies

The risk-of-bias assessment for non-randomized studies demonstrated greater variability than that for randomized studies. Serra et al.[22] exhibited a serious risk of bias, particularly in the domains of confounding (D1) and selection of the reported results (D7). Sadauskas et al.[23] showed a serious risk of bias related to confounding (D1) and a moderate risk of bias in participant selection (D2). Overall, non-randomized studies included in this review tended to have a higher risk of bias, primarily attributable to confounding, deviations from interventions, and outcome selection and measurement issues (Supplementary Figure 5).

Quality of Evidence

Using the GRADE framework, the certainty of evidence for pain-related outcomes ranged from very low to low. Evidence for baseline pain intensity was rated low certainty, primarily due to moderate risk of bias and substantial heterogeneity ($I^2 = 77\%$), despite the presence of direct comparisons and adequate precision. Evidence for pain intensity at 3 hours was of very low certainty, driven by a high risk of bias and considerable inconsistency ($I^2 = 67\%$). For pain outcomes at 6, 12, and 24 hours, the certainty of evidence was consistently low; the downgrading was mainly attributable to moderate risk of bias and high inconsistency (I^2 ranging from 88% to 96%). At these time points, the overall pooled estimates did not reach statistical significance, further limiting the strength of any conclusion. Indirectness, imprecision, and other factors were not considered serious concerns (Supplementary Table 1).

DISCUSSION

The SAPB has been increasingly utilized as an analgesic technique for patients with rib fractures. Multiple studies have demonstrated that SAPB provides rapid analgesia, is relatively easy to perform under ultrasound guidance, and has a favorable safety profile; no serious complications, such as pneumothorax or hematoma, have been reported.[8,11,24] In addition to pain control, SAPB has been shown to improve respiratory function, as evidenced by increased diaphragmatic excursion,[14] stabilization of the SpO_2/FiO_2 ratio,[24] and reduced supplemental oxygen requirements in several studies.[25] Collectively, these findings suggest that SAPB not only alleviates pain but also contributes to the preservation of pulmonary function, which is critical in preventing respiratory complications in patients with rib fractures.

Our findings suggest that SAPB may provide more consistent and sustained analgesia than other analgesic modalities. Baseline pain scores were broadly comparable between groups, with no statistically significant difference overall (baseline SMD: 0.18; $P = 0.25$) or within the opioid or other-block subgroups, indicating that the groups were reasonably balanced before intervention. An early analgesic effect of SAPB relative to opioids was evident at 3 hours (SMD: −0.40; $P = 0.04$). This rapid early effect may be explained by the mechanism of the

blockade: deposition of local anesthetic in the plane of the serratus anterior muscle produces relatively rapid blockade of the lateral cutaneous branches of the intercostal nerves (T2-T9), thereby providing analgesia to the anterolateral thoracic region.[26] In the opioid subgroup, this association remained statistically significant at 12 hours (SMD: −0.44; $P = 0.002$). However, the overall pooled estimates at 6, 12, and 24 hours did not reach statistical significance and were accompanied by wide CIs and very high between-study heterogeneity (I^2 up to 96%), leading to uncertainty about the persistence of analgesic efficacy beyond the early period.

One possible explanation for the transient attenuation of the observed effect is the limited duration of analgesia associated with single-injection SAPB. Variations among studies in local anesthetic type, concentration, volume, and delivery technique (single-shot and continuous catheter) may have influenced both the temporal pattern of analgesic efficacy and the substantial between-study heterogeneity observed (I^2 up to 96%). Direct evidence comparing single-shot and continuous SAPB remains limited. While the present meta-analysis examined only single-shot SAPB for rib fracture analgesia, continuous SAPB administered via a PCA device has also demonstrated effectiveness in managing acute pain and is frequently recommended when extended analgesic coverage is required.[27] A trial by Er et al.[28] evaluated single-shot SAPB, continuous SAPB, and PCA. The study found that continuous SAPB was associated with better recovery outcomes and fewer postoperative complications compared with the single-shot approach. However, patients receiving continuous SAPB reported higher pain scores during activity. Additional well-designed studies are needed to establish the comparative advantages of single-shot versus continuous SAPB.[28]

One possible explanation for the 6-hour dip followed by recovery is the pharmacokinetic profile of a single-shot block: as the initial local anesthetic bolus is redistributed and metabolized, analgesia may wane before the next scheduled assessment, whereas continuous catheter infusion or the use of larger volumes and higher concentrations of longer-acting agents such as bupivacaine or ropivacaine, would be expected to provide more sustained coverage. Differences between studies in the choice, concentration, and volume of local anesthetic, and in single-shot versus catheter techniques, are therefore plausible contributors both to the time-dependent pattern of effect and to the high between-study heterogeneity (I^2 up to 96%).

Compared with other regional analgesic techniques, SAPB demonstrated time-dependent effectiveness. In the early phase (≤6 hours), some studies reported that traditional regional blocks, such as thoracic epidural or PVBs, provided superior analgesia.[9] Beyond the early hours, the comparison between SAPB and other regional blocks was inconclusive: the pooled estimates at 12 and 24 hours did not reach statistical significance and were accompanied by very high heterogeneity; therefore, no firm conclusion about relative efficacy at later time points can be drawn. Nonetheless, the potential advantages of SAPB include its technical simplicity, a favorable safety profile in patients with coagulopathy, and its potential for continuous administration via catheter placement, making it a viable alternative when conventional techniques are contraindicated or technically challenging.[29] Overall, the available data do not allow a firm conclusion about the relative duration of the effect of SAPB versus that of other regional techniques within the first 24 hours.

At 6 hours, SAPB was associated with higher pain scores than other regional blocks, whereas comparisons at 12 and 24 hours were not statistically significant. These differing point estimates may reflect differences in the onset and duration profiles of the comparator techniques rather than a true reversal of effect; however, because the comparator group pooled several diverse techniques (TEA, PVB, ICNB, and ESPB) with distinct pharmacodynamics, and because the later estimates were imprecise and highly heterogeneous, any time-dependent pattern should be regarded as hypothesis-generating rather than definitive.

Compared with systemic opioid analgesia, SAPB was associated with lower pain scores in the pooled subgroup analyses. This association reached statistical significance at 3 hours and, within the opioid subgroup, at 12 hours, although the wide CIs, substantial heterogeneity, and non-significant overall estimates at later time points warrant caution.[11] This finding is clinically relevant given the well-recognized limitations of opioid therapy, including the risks of respiratory depression, sedation, constipation, and delirium, particularly in elderly patients.[21] Therefore, SAPB may provide more effective analgesia than systemic opioids while also reducing patient exposure to opioid-related adverse effects. The opioid-sparing effect observed in the pooled analysis (SMD: −0.35; $P = 0.04$) is clinically meaningful because lowering cumulative opioid exposure is expected to reduce the incidence of respiratory depression, nausea and vomiting, ileus, and delirium in the predominantly elderly rib-fracture population. By providing targeted regional analgesia, SAPB can serve as the regional component of a multimodal strategy, allowing opioids to be reserved for breakthrough pain rather than serving as the mainstay analgesic.

The opioid-sparing effect of SAPB further reinforces its role within multimodal analgesia strategies. Evidence indicates that patients receiving SAPB require significantly less supplemental opioid analgesia, which in turn reduces the incidence of opioid-associated nausea and vomiting.[11] Abu-Elwafa et al.[21] similarly reported that SAPB was comparable to intravenous morphine infusion in reducing pain scores, while avoiding the risk of respiratory compromise. These findings are consistent with case series demonstrating that SAPB can serve as an effective strategy to reduce opioid dependence in patients with multiple rib fractures.[8,10]

Despite the demonstrated benefits of SAPB for analgesia and respiratory function, evidence regarding its impact on hospital LOS remains heterogeneous. Serra et al.[22] reported a shorter duration of hospitalization in the SAPB group compared with controls [median 4 (3–6) vs. 5 (4–6) days]. Similar results were observed by Partyka et al.[12] with a median LOS of 4.2 (2.2–7.7) days in the SAPB group versus 5 (3–7.3) days in the control group. In contrast, Sadauskas et al.[23] found no significant difference in LOS between SAPB and non-SAPB cohorts. These discrepancies suggest that although SAPB may shorten hospitalization through optimized analgesia and improved

respiratory mechanics, its effect on LOS is not consistently observed across patient populations, underscoring the need for large-scale RCTs to clarify this association.

These findings must be interpreted in light of the risk of bias and GRADE assessments. Under the GRADE framework, the certainty of evidence for the pain outcomes was low to very low at all time points, downgraded primarily for serious inconsistency (I^2, ranging from approximately 67% to 96%) and for risk of bias. The risk-of-bias evaluation identified recurring concerns in the randomized trials regarding deviations from intended interventions (D2) and outcome measurement (D4), which is especially relevant because pain is a subjective outcome and several studies were not blinded, thereby raising the possibility of outcome-measurement bias. In the non-randomized studies, confounding (D1) was judged to be serious in more than one study. Taken together, the low certainty of the evidence and these specific bias domains mean that the pooled estimates should be regarded as preliminary, and any clinical recommendation derived from them must be interpreted with caution.

Study Limitations

This study has several important limitations. First, the included studies were heterogeneous in design, combining RCTs with prospective and retrospective observational studies. Pooling randomized and non-randomized data increases the risk of bias and statistical heterogeneity; the heterogeneity was substantial across nearly all time points (I^2 approximately 67–96%). To mitigate this, we used a random-effects model, conducted subgroup analyses (opioid comparators and other regional blocks), and performed sensitivity analyses, but these steps could not fully overcome the underlying design heterogeneity. The number of studies included was small, and several pooled estimates rested on as few as three studies, limiting statistical power and making the estimates sensitive to the influence of any single study. The risk of bias was serious in several studies, with concerns regarding outcome measurement (a subjective pain outcome assessed largely without blinding) and confounding in the non-randomized studies. The included studies used different pain scales (NRS 0–10 and VAS 0–100). Although this was addressed by pooling SMDs, combining instruments introduces additional uncertainty. Although baseline pain scores did not differ significantly between groups in the pooled analysis, small sample sizes limited the precision of this comparison. Furthermore, the number and anatomical location of fractured ribs and the type, concentration, and volume of local anesthetic were inconsistently reported and could not be pooled, despite their potential influence on block efficacy. Finally, the certainty of evidence was low to very low; long-term outcomes and mortality data were largely unavailable; and the potential for publication and language bias cannot be excluded. These limitations should be weighed when interpreting the findings, and should underscore the need for adequately powered, well-designed RCTs.

CONCLUSION

Although the certainty of evidence remains low, SAPB may provide effective early analgesia and an opioid-sparing effect in patients with rib fractures; however, its comparative efficacy against other regional techniques remains uncertain and does not reach statistical significance in pooled analyses beyond the early hours. Given its favorable safety profile, technical simplicity, and potential opioid-sparing effects, SAPB may be a useful component of multimodal analgesia. Because the available studies were few, heterogeneous, and at substantial risk of bias, these findings should be interpreted with caution and confirmed in high-quality, well-designed RCTs before clinical recommendations can be made.

Ethics

Ethics Committee Approval: Not applicable.

Informed Consent: Not applicable.

Footnotes

Authorship Contributions

Concept: C.A., S.F.S., S.A.'A., P.P.M.E., Design: C.A., S.F.S., S.A.'A., P.P.M.E., Data Collection or Processing: C.A., S.F.S., S.A.'A., Analysis or Interpretation: C.A., S.F.S., S.A.'A., P.P.M.E., Literature Search: C.A., S.F.S., Writing: C.A., S.F.S., S.A.'A., P.P.M.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Tables Link: https://d2v96fxpocvxx.cloudfront.net/beb8919b-f013-4ea1-b1c8-40332e840fe1/content-images/452a3e4c-6ee5-4817-824d-140f985ad1e0.pdf

Supplementary Figures Link: https://d2v96fxpocvxx.cloudfront.net/beb8919b-f013-4ea1-b1c8-40332e840fe1/content-images/93968981-2e75-44ad-9bcc-337e6fb1147b.pdf

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Review

Artificial Stone Silicosis: New Face of an Old Disease

Heng Sieh Yen Samantha[1], Tan Kian Wei Alvin[2], Koh Soo Quee David[2,3]

[1]National University Health System, Singapore
[2]Department of Occupational and Environmental Medicine, Singapore General Hospital, Singapore
[3]Saw Swee Hock School of Public Health, National University of Singapore, Singapore; University of Occupational and Environmental Health, Japan

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ABSTRACT

Artificial stone (AS) silicosis has emerged as a major global occupational health concern, challenging the perception of silicosis as a disease of the past. Driven by the fabrication of AS products containing high concentrations of crystalline silica (>90%), this rapidly progressive form disproportionately affects younger workers and develops after a much shorter exposure duration (median 7–19 years) than in classic silicosis. As cases continue to emerge worldwide, clinicians and occupational health practitioners are increasingly likely to encounter affected workers in clinical practice. This review provides a clinically focused synthesis of the current evidence on the epidemiology, pathophysiology, clinical manifestations, diagnosis, and management of AS silicosis. Compared with traditional silicosis, the unique physicochemical properties of AS dust may amplify lung toxicity and promote a self-perpetuating inflammatory response. This frequently results in rapid development of progressive massive fibrosis, with disease progression often continuing after exposure cessation. Diagnosis is often delayed because of overlapping clinical features and the limited sensitivity of conventional screening tools, highlighting the importance of early clinical recognition, detailed occupational history-taking, and the use of high-resolution computed tomography where appropriate. Lung transplantation remains the only definitive treatment for advanced disease, underscoring the importance of prevention. Effective prevention requires strong workplace controls, systematic medical surveillance, and appropriate regulatory measures. Clinicians play a key role in early detection, patient education, and mandatory disease reporting. Coordinated action across clinical, occupational, and policy domains is essential to improve recognition, strengthen preventive measures, and avert further cases of this highly preventable occupational disease.

KEYWORDS: Silicosis, dust, occupational diseases, silicon dioxide

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INTRODUCTION

Silicosis is caused by the inhalation of respirable crystalline silica (RCS), which refers to the fraction of silica dust small enough to penetrate beyond the upper airways and deposit in the lower respiratory tract. It is one of the oldest recognised occupational fibrotic lung diseases.[1]

Historically, silicosis was closely associated with industries that dominated early industrial economies such as mining, quarrying, tunnelling, and sandblasting.[2] Occupational silicosis became a major concern globally in the 1900s, exemplified by the Hawk's Nest Tunnel disaster in the United States (US) during the 1930s, in which over 700 tunnel workers died from exposure to large amounts of silica dust.[2] However, improved industrial hygiene practices, medical surveillance, and regulatory controls in many high-income countries over the past decades have led to a substantial reduction in the incidence of silicosis.[1] This led to a widespread perception of silicosis as a "disease of the past" in modern industrialised societies.

Three main clinical forms of silicosis have been described, largely corresponding to the intensity and duration of RCS exposure. Chronic (or classic) silicosis is the most common form and arises after long-term exposure to relatively low concentrations, whereas accelerated silicosis develops over a shorter latency following higher-intensity exposure.[1] Acute

Corresponding author: Heng Sieh Yen Samantha, MBBCh, e-mail: hs.yen28@gmail.com

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silicosis (also known as silicoproteinosis), the least common but most severe form, results from intense exposure to RCS during a brief period and may manifest within weeks to years.[1,2]

Emergence of Artificial Stone in the Built Environment

Unlike naturally occurring silica-containing materials, historically encountered in the industries described earlier, artificial stone (AS) is a relatively new, manufactured composite introduced commercially in the 1980s.[2,3] AS, also known as engineered stone, reconstituted stone, quartz conglomerate or agglomerated stone, is manufactured by combining finely crushed stone with polymer resins, pigments, and other additives, which are then moulded and cured to produce a dense, non-porous surface.[2,4] A defining feature of AS is its exceptionally high crystalline silica content, often exceeding 90% by weight, which is markedly higher than the silica content of natural stones such as marble (which contains minimal silica) or granite.[4,5] This distinctive composition differentiates AS from traditional silica-containing materials and has important implications for RCS generation during fabrication and finishing.

A New Face of a Preventable Disease

AS has become increasingly used for kitchen and bathroom countertop fabrication because of its durability, appearance, and cost-effectiveness.[4,6] Correspondingly, there has been a re-emergence of silicosis in a more aggressive and rapidly progressive form.[2,7] Since the 2010s, silicosis linked to AS fabrication has been reported in multiple regions, including Israel, Europe, the United Kingdom, the US, China, Australia, and Türkiye.[3,8-11] These cases have highlighted a paradox in which a well-characterised, preventable historical occupational disease has resurfaced in modern economies because of contemporary materials and work practices. This marks a shift in the epidemiology and clinical presentation of silicosis, and has prompted renewed scrutiny of existing exposure controls, surveillance systems, and regulatory frameworks. The extent of recognition of AS silicosis as an emerging disease of concern is also reflected in the rapidly growing body of clinical research and literature, with publications increasing substantially since 2014 and accelerating markedly over the past decade (Figure 1).

This review aims to synthesise the current evidence on AS silicosis, with a particular focus on lessons for clinicians, occupational health practitioners, and policymakers.

Main Points

- Artificial stone (AS) silicosis is a rapidly progressive form of silicosis, characterised by a shorter latency period and more aggressive clinical course than traditional silicosis.
- The high crystalline silica content of AS, together with the generation of fine respirable dust during fabrication, are likely the principal drivers of disease development and severity. Disease progression may continue despite cessation of AS dust exposure.
- Clinicians, particularly those in occupational health, play a critical role in the early detection of AS silicosis through comprehensive occupational history-taking, timely diagnosis, and targeted health surveillance of exposed workers.
- Prevention relies on eliminating or minimising respirable crystalline silica exposure through effective controls such as avoidance of dry processing, regular health surveillance, and appropriate respiratory protection.

Occupational Context of AS Silicosis

Manufacturing and Fabrication Processes of AS

The currently widely used AS manufacturing system was first developed in the 1970s,[2] and involves vibro-compression under vacuum, whereby finely crushed stone, predominantly crystalline silica, is combined with polymeric resin binders, pigments, and additives to form dense, uniform slabs.[2,12]

High-risk exposures occur during fabrication and installation. Fabrication processes include cutting, grinding, drilling, polishing, and edge finishing to customise slabs for kitchen and bathroom benchtops.[2,7] Compared with natural stone fabrication, AS processing generates substantially higher RCS exposures because AS has a higher silica content. Dust generated during dry-cutting of AS typically contains more than 80% crystalline silica, whereas dust from natural stone contains substantially lower proportions of crystalline silica, averaging 1–4% in marble and 30–50% in granite.[8,13,14]

Exposure assessments have shown that dry cutting can generate RCS concentrations exceeding 40 mg/m^3, exceeding various legislative occupational limits of 0.05 mg/m^3.[2,4] Wet cutting substantially reduces exposure, but does not eliminate the risk. Furthermore, brief dry tasks frequently occur during finishing and on-site installation, where water suppression may be unavailable.[4]

Occupational Context and High-risk Work Settings

AS fabrication is commonly undertaken in smaller enterprises with fewer than 10 workers.[10,15] AS workers tend to use small, handheld power tools without integrated water-delivery systems, such as angle grinders, because of their lower cost and greater flexibility.[2,4] Additional workplace risk factors that exacerbate exposure to RCS for both AS workers and bystanders include inadequate local exhaust ventilation, poor general ventilation and limited segregation of dusty tasks,[4,7,15,16] and non-compliance or incorrect use of respiratory protective equipment (RPE). This, coupled with productivity pressures, a lack of comprehensive occupational safety programmes and weak regulatory oversight,[15,17,18] substantially increases RCS exposure risk.

Processing of AS could also release volatile organic compounds (VOCs), such as styrene and other aromatic hydrocarbons, which may contribute to inflammatory and obstructive airway disease observed in exposed workers.[2,4]

Epidemiology

Global Burden of AS Silicosis

Estimates from the Global Burden of Disease Study 2021 indicated that the age-standardised incidence, mortality,

and disability-adjusted life years attributable to silicosis have declined since 1990,[19] with a greater burden observed in medium and medium-high sociodemographic indices regions.[19] However, these estimates do not distinguish between occupational exposure sources and cases attributable to AS. The American Thoracic Society Workshop Report, released in 2026, estimated that at least 6,351 cases of AS silicosis had been identified worldwide as of December 2025, based on available data from 12 countries across the Americas, Europe, the Middle East, Asia, and the Pacific region.[20] However, as acknowledged in the report, this figure was likely underestimated because many countries lack systematic medical screening, disease surveillance, and universal access to healthcare, leading to undetected or unreported cases.[20] As a result, the true global burden of AS silicosis remains unknown.

Clinical Epidemiology of AS Silicosis

AS silicosis represents a distinct epidemiological pattern compared with classic silicosis. Affected AS workers are typically relatively young, commonly diagnosed in the mid-40s, and often present after a markedly shorter exposure duration (median 7–19 years), with rapid disease progression.[2,10,21] These features contrast sharply with classic silicosis, which typically manifests after decades of low-level exposure and in older individuals.[1,7,16,21] Progression to progressive massive fibrosis (PMF) may continue even after cessation of exposure.[10]

Pathophysiology of AS Silicosis

Mechanism of Lung Injury

The pathogenesis of AS silicosis shares core pathways with traditional silicosis (Figure 2), but appears to be amplified by the distinctive physico-chemical properties of AS dust that may contribute to AS's toxicity and accelerate disease progression.

In addition to its high crystalline silica content, AS typically contains 8–20% polymeric resin used to bind crushed stones.[13] This resin coating on silica particles may stabilise surface radicals produced during cutting, influence their reactive pathways, and thereby amplify oxidative stress and injury.[13,23]

AS dust also contains transition metals (e.g., cobalt, copper, aluminium, titanium) derived from pigments and resins[13,24] which have been associated with increased macrophage cytotoxicity and inflammatory responses independent of silica concentration.[25] This further promotes reactive oxygen species generation and activation of pro-fibrotic inflammatory pathways, thereby acting as an adjuvant that intensifies the fibrogenic response to silica exposure.[13,25] The cumulative oxidative stress and cytokine release lead to macrophage death, releasing the indigestible RCS particles back into the alveolar space. They are again re-phagocytosed by newly recruited macrophages, establishing a self-perpetuating "vicious cycle" of inflammation that continues even after workplace exposure has ceased.[1,26] This persistent inflammatory cycle drives fibrogenesis through growth factors from alveolar macrophages and epithelial cells [e.g., transforming growth factor-β (TGF-β) and platelet-derived growth factor], resulting in progressive parenchymal fibrosis.[11,26]

Individual genetic susceptibility appears to affect disease risk and severity. Polymorphisms in cytokines and inflammasome genes such as TNF-α, interleukin-1 (IL-1), TGF-β-1, and FASLG have been associated with susceptibility to silicosis and disease severity, albeit inconsistently across different populations.[4]

Histopathological Patterns and Unique Features of AS Silicosis

AS silicosis frequently presents as a complex "mixed" phenotype, instead of neatly fitting into the distinct classical forms.

In early disease, lung biopsies demonstrate inflammatory nodules composed predominantly of histiocytic cells and fibroblasts, without central hyalinisation.[5] Birefringent dust particles consistent with silica may be identified by polarised

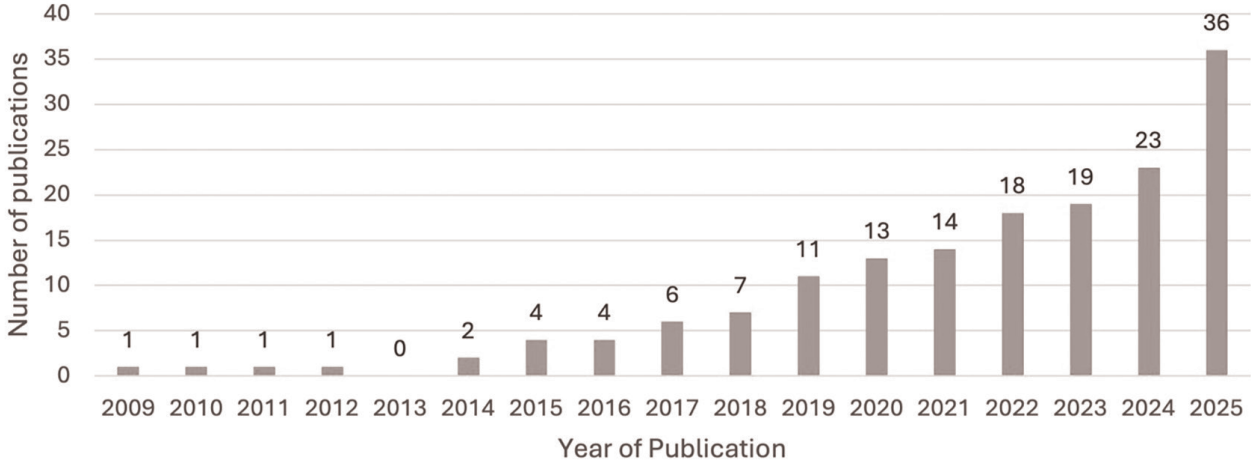


Figure 1. Trend of the publication on artificial stone (AS) silicosis found in the PubMed Database from 2009 to 2025. A simple search strategy was used on the PubMed database to identify English-language publications on AS silicosis; the search employed the keywords (silicosis[All Fields] OR "silicosis" [MeSH Terms] OR "silica dust" [All Fields]) AND ("artificial stone" OR "engineered stone" OR "quartz conglomerate*" OR "agglomerated stone" OR "reconstituted stone" OR "artificial silica"), covered the period 1 Jan 2009 to 31 Dec 2025, and its results were retrieved on 25 June 2026. A detailed list of the retrieved publications can be found in Supplementary Material 1

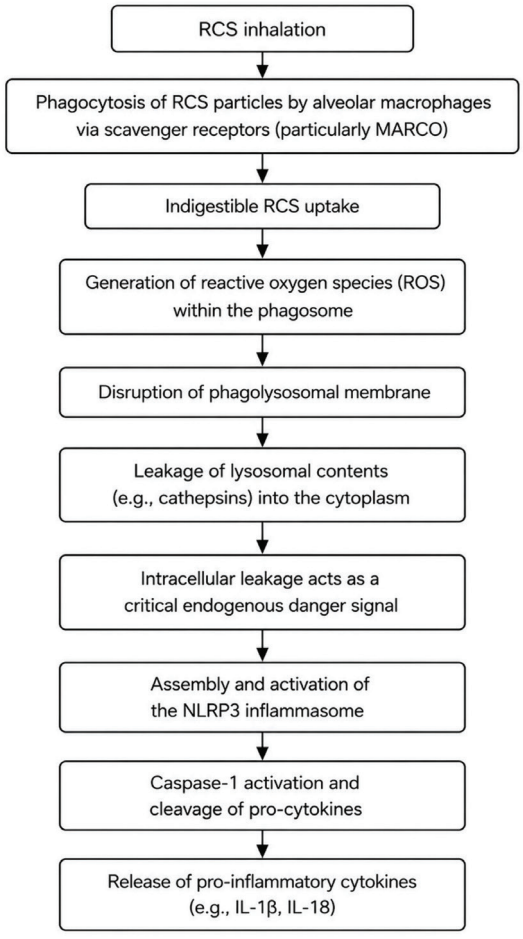


Figure 2. Simplified pathogenesis of silicosis.[5,11,22] Inhaled respirable crystalline silica (RCS) particles are phagocytosed by alveolar macrophages via scavenger receptors, particularly the macrophage receptor with collagenous structure (MARCO). Because RCS is indigestible, its uptake generates ROS and disrupts phagolysosomal membranes, resulting in leakage of lysosomal contents into the cytoplasm. This intracellular danger signal triggers assembly and activation of the NLRP3 inflammasome, leading to caspase-1-mediated cleavage of pro-cytokines and release of pro-inflammatory cytokines, such as interleukin (IL)-1β and IL-18

light microscopy, which provides an important diagnostic clue.[27] In advanced disease, coalescence of silicotic nodules into large fibrotic masses with marked distortion of lung parenchyma[27] results in PMF. A pathologically distinctive feature of AS silicosis is the coexistence of dense hyalinised fibrosis (chronic silicosis) and proteinaceous material within alveolar spaces (silicoproteinosis/acute silicosis;[27] see Figure 3), reflecting the extremely high intensity of RCS exposure in AS fabrication.[2]

Elemental analysis of AS-exposed lung tissue has further demonstrated high concentrations of aluminium and silicon at the centre of silicotic nodules, a mineralogical pattern that differentiates AS silicosis from natural stone silicosis.[5,25]

Without particulate identification under polarised light microscopy, the cellular aggregations seen in early silicosis mimic the non-caseating granulomas commonly seen in classical sarcoidosis, which is usually idiopathic.[20,28] Hence, early-stage AS silicosis is frequently misdiagnosed as sarcoidosis due to their histopathological and clinical overlap, making histopathological characterisation of the condition challenging.[23] In addition, transition metals present in AS dust, including aluminium, titanium, and zirconium, may also induce sarcoid-like granulomatosis, making the diagnosis more challenging.[29]

To reflect the expanding histopathological spectrum of AS silicosis, evolving terminology with descriptive indicators such as "silica-induced sarcoidosis", "sarcoid-like granulomatosis induced by silica", "sarcoid-like granulomatous lung disease" has been introduced in the scientific literature.[30] To unify these similarly overlap conditions that appear to exist along a continuum, silicosarcoidosis is an increasingly commonly used term to refer to a recognised entity characterised by the concurrent histological presence of silicotic nodules and epithelioid granulomas.[31] However, consensus on these entities remains unclear. Histopathological differentiation of these entities from AS silicosis remains clinically and radiologically challenging and requires integration of occupational history and clinical trajectory.

Underdiagnosis and Surveillance Gaps

Despite increasing recognition, AS silicosis remains underdiagnosed in many countries. Surveillance systems for occupational lung disease are often fragmented, passive, or absent, especially in small-scale enterprises that dominate the AS industry.[32] Diagnostic delays are frequent, with many cases initially misdiagnosed as infection, sarcoidosis, or autoimmune disease,[8,16,21] especially in the absence of a detailed occupational history.[7,8] Evidence from jurisdictions that have implemented systematic screening suggests that a substantial proportion of AS workers would remain undetected without active surveillance. Screening programmes in Australia identified silicosis in approximately 23–28% of screened workers,[32] with many AS workers asymptomatic at the time of diagnosis, underscoring the limitations of symptom-based case finding.[32]

These gaps underscore the need for improved occupational health surveillance, clinician awareness, and regulatory oversight in industries involving AS fabrication.

Regulatory Landscape of AS

The rise in AS cases has prompted regulatory responses in several jurisdictions (Table 1).

Clinical Manifestations

Symptomology

AS silicosis predominantly manifests as accelerated disease with mixed features, though acute and chronic patterns may also occur depending on exposure intensity and duration. Typically, symptoms in AS workers often appear after a much shorter latency period (ranging 4–10 years) due to the high intensity of exposure,[2,7] unlike traditional chronic silicosis (Table 2).

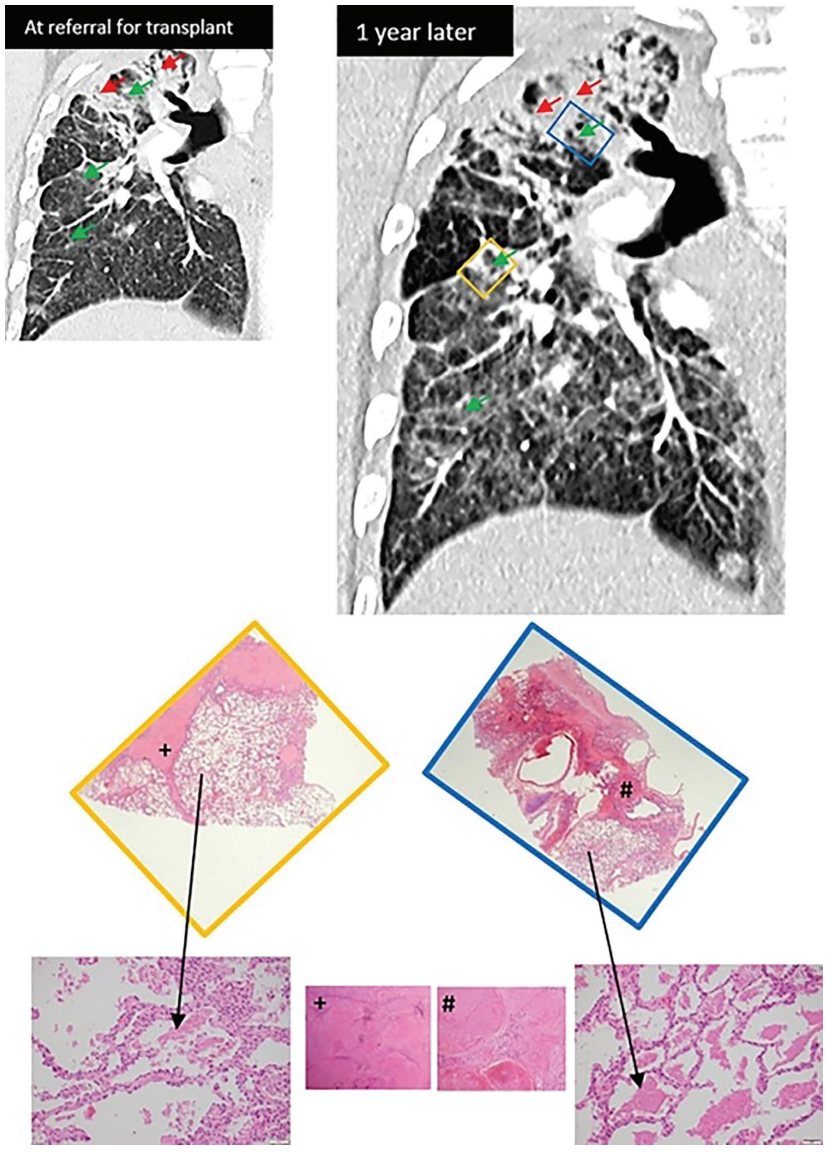


Figure 3. Radiological and histopathologic findings of an artificial stone worker with silicosis at referral for transplant and 1 year later. Conspicuous areas of alveolar proteinosis (black arrows) corresponding with areas of ground glass changes on computed tomography chest imaging (green arrows). Adjacent parenchyma shows dense fibrosis, silicotic nodules, and progressive massive fibrosis (PMF) (indicated by '+' and '#'). Red arrows indicate upper lobe confluent opacities, traction bronchiectasis, hilar retraction, and volume loss, consistent with PMF. Reproduced from Levin et al.,[27] with permission from John Wiley and Sons

The clinical presentation of AS silicosis can range from asymptomatic disease in early stages, which may not correlate with radiological severity, to severe and debilitating respiratory failure with complications, including pulmonary hypertension and right heart failure.[2,3,21] Patients may present with non-specific respiratory and constitutional symptoms, contributing to diagnostic confusion with infectious or inflammatory diseases.

Other Associated Conditions

Beyond classic silicosis, RCS exposure has been associated with a broader spectrum of interstitial lung diseases (ILDs). Notably, it is an independent risk factor for idiopathic pulmonary fibrosis (IPF), with an estimated 4% of IPF cases attributable to RCS exposure.[2] Although 9–10% of workers with known occupational silica exposure have been reported to exhibit radiological features of usual interstitial pneumonia (UIP), including lower-zone predominant abnormalities and honeycombing, without findings of classic silicosis, a UIP pattern has not yet been described in published case series involving AS workers.[2]

Other pulmonary conditions commonly associated with AS silicosis include work-related asthma; chronic obstructive pulmonary disease (COPD), including emphysema, arising from polymer resins and VOCs; and lung cancer, given that RCS is classified as a Group 1 carcinogen by the International Agency for Research on Cancer.[2,13] Silica-induced impairment of alveolar macrophage function also confers a markedly increased susceptibility to mycobacterial infections, including silicotuberculosis and non-tuberculous mycobacterial disease, particularly *Mycobacterium kansasii*.[2]

Table 1. Key regulatory responses in the US, Australia, and the UK

Jurisdiction	Key response
US	US federal regulation of AS nationally remains anchored to the Occupational Safety and Health Administration respirable crystalline silica standard. However, across the different states, varying regulatory standards specific to AS have been imposed. Arising from the California silicosis epidemic in AS workers in 2025, California adopted a permanent silica standard to enhance worker protection during high-exposure trigger tasks involving AS containing more than 0.1% crystalline silica or natural stone containing more than 10% crystalline silica.[33] As of June 2025, silicosis also became a reportable disease in California.[33] In May 2026, the California Occupational Safety and Health Standards Board approved a petition to commence the process for prohibiting the fabrication and installation of AS products containing more than 1% crystalline silica.[34]
Australia	Since July 2024, the use, supply, and manufacture of AS benchtops, panels and slabs are banned across Australia while the importation of these products has been banned since January 2025.[35] Australia remains the first and only country thus far to implement a nationwide AS ban as of May 2026. Under the model Work Health and Safety Regulations, AS is defined as "an artificial product that: (1) contains at least 1% crystalline silica as a weight/weight concentration, and (2) is created by combining natural stone materials with other chemical constituents (such as water, resins, or pigments), and (3) becomes hardened".[35]
UK	In May 2026, the Health and Safety Executive published the first Control of Substances Hazardous to Health guidance sheet for AS workers, following concerns arising from silicosis deaths among young workers. The guidance outlines the controls that should be in place when working with the material, which effectively rules out dry-cutting, unless businesses can demonstrate an equally effective or better control is in place.[36]

AS: artificial stone, US: United States, UK: United Kingdom

Table 2. Disease spectrum and relevance in AS silicosis[2,27,32,37]

Disease spectrum	Characteristics	Relevance in AS silicosis
Acute silicosis	May manifest within weeks to a few years (typically less than 5 years) of first exposure. Rapidly progressive respiratory and constitutional symptoms, often resulting in respiratory failure and high mortality. Radiological descriptions may include diffuse centrilobular nodules, ground-glass opacities, and patchy bilateral consolidation on HRCT imaging.	Less common as a standalone entity but its features have been reported following exceptionally high-intensity RCS exposures. Both radiological and histopathological findings consistent with silicoproteinosis have been identified in a subset of AS workers.
Accelerated silicosis	Typically develops within 2 to 10 years of initial exposure. Rapid clinical, radiological, and functional progression, with overlapping features of both acute and chronic disease. Early disease may be radiographically occult on plain chest radiography, with abnormalities detectable only on HRCT, underscoring the limitations of conventional screening modalities. As disease progresses, imaging findings may include silicotic nodules, interstitial fibrosis, ground-glass opacities, and early conglomeration.	Predominant disease pattern observed in AS silicosis, reflecting the high silica content of AS and the frequent occurrence of high-intensity exposure during fabrication tasks. Carries a high-risk of progression to PMF in AS workers, often over a relatively short time frame and despite cessation of exposure.
Chronic silicosis	Classified into simple silicosis and complicated silicosis or PMF. Simple silicosis is characterised by small (less than 1 cm), upper lobe-predominant nodules and may be asymptomatic, often detected through surveillance imaging. These nodules may enlarge and coalesce into conglomerate masses consistent with PMF, accompanied by parenchymal distortion, lymphadenopathy, and emphysematous change.	Less frequently observed on its own in AS workers compared with traditional silica-exposed industries but remains relevant, particularly among individuals with longer employment duration and lower-intensity exposure.

AS: artificial stone, HRCT: high resolution computed tomography, PMF: progressive massive fibrosis, RCS: respirable crystalline silica

High-intensity exposure to RCS in AS is strongly associated with autoimmune diseases such as systemic sclerosis, rheumatoid arthritis, and systemic lupus erythematosus.[9,38] This occurs alongside recognised syndromes, including Erasmus syndrome (systemic sclerosis with silica exposure) and Caplan's syndrome (rheumatoid arthritis with lung nodules).[39] Silica has also been associated with immune dysregulation, manifested by elevated autoantibody levels (e.g., anti-nuclear antibodies), circulating immune complexes, and increased immunoglobulin production, even in the absence of autoimmune disease.[39]

Silica exposure has also been linked to renal diseases such as chronic kidney disease and glomerulonephritis, potentially through both direct nephrotoxicity from silica particle deposition and indirect immune-mediated mechanisms.[2,11]

Disease Progression After Exposure Cessation

A clinically striking feature of AS silicosis is the potential for continued rapid radiological and functional deterioration even after exposure has ceased.[10] Studies have shown that up to 56% of AS workers exhibited radiological progression of two or more International Labour Organization (ILO) subcategories, and 37% developed PMF (Figure 4) following a mean follow-up of only four years.[10] The decline in lung function, with mean annual reductions in forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) of approximately 87 mL and 83 mL, respectively, was observed, with 25% of patients experiencing even greater losses, exceeding 150 mL per year in FVC and 133 mL per year in FEV_1.[10]

This distinguishes it from chronic silicosis, which tends to stabilise or progress slowly after cessation of exposure.[3,10] This is consistent with the self-perpetuating inflammatory cycle described earlier.

Effect of Smoking

Tobacco smoking acts synergistically with RCS exposure to exacerbate pulmonary toxicity.[40] Critically, smoking substantially amplifies the risk of comorbid conditions in RCS-exposed workers, including lung cancer, COPD, tuberculosis, and autoimmune diseases, underscoring its contribution to overall morbidity and mortality in this population.[11,38,41]

A greater loss of lung function, with reductions in diffusing capacity of the lungs for carbon monoxide (DLCO), FVC, and FEV_1, was observed in AS workers who were current or former smokers compared with non-smokers.[42] However, current evidence suggests that smoking may not be the primary driver of radiological disease progression to PMF in AS workers.[10,42]

Diagnostic Approach for AS Silicosis

History Taking and Physical Examination

Occupational history is key to diagnosing AS silicosis, but it requires specific, targeted questioning, as workers may not recognise the term "engineered/artificial stone", may misclassify the material as "marble" or "granite", or may face language barriers, thereby concealing the true nature of the exposure.[2,8,15] Therefore, clinicians must explicitly ask about the fabrication of AS, including the duration of work, specific tasks performed (e.g., cutting vs. installing), and the use of dry cutting or grinding methods.[2] Given the shorter latency observed in AS silicosis, even relatively brief exposure histories are clinically relevant.[2,13]

Physical examination findings are frequently unremarkable with limited sensitivity and are generally unreliable for screening or diagnosis of AS silicosis.

Clinical Investigations

Pulmonary function testing (PFT) provides complementary information, but it has limited sensitivity in early-stage disease.[1] Restrictive, obstructive or mixed patterns with reduced DLCO have been observed in AS silicosis,[1,7] but can be normal despite radiologically confirmed silicosis.[2] Therefore, normal spirometry and gas transfer do not exclude the diagnosis and should not delay further evaluation in AS-exposed individuals.

Radiological classification of silicosis with plain chest radiographs is conventionally based on the ILO International Classification of Radiographs of Pneumoconioses,[43] but has limited sensitivity for AS silicosis, with up to 39.6% false negative rates.[32] High-resolution computed tomography (HRCT) with the International Classification of HRCT for Occupational and Environmental Respiratory Diseases (ICOERD)[44] is therefore increasingly preferred, albeit not a universally accepted CT-based classification system. In some areas, such as Western Australia, low-dose HRCT with modified ICOERD is mandated for screening and diagnosis.[2,45] HRCT commonly demonstrates mixed features, including bilateral upper-lobe fibrosis, small centrilobular or perilymphatic nodules, ground-glass opacities, and PMF.[7]

Invasive investigations, including bronchoscopy or lung biopsy, are not routinely required when the exposure history and

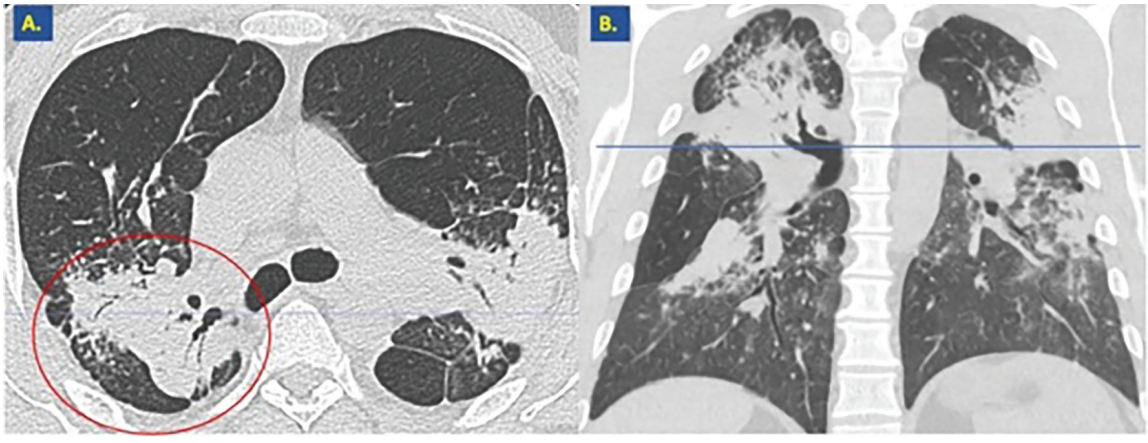


Figure 4. Complicated silicosis/progressive massive fibrosis. A 44-year-old man who worked in the engineered-stone countertop manufacturing industry presented with dyspnoea. Chest computed tomography (A, axial; B, coronal) revealed large bilateral masses predominantly in the posterior upper lungs with partially sharp margins, hilar and pulmonary distortion, bronchiectasis, and mild para-cicatricial emphysema (red circle), consistent with PMF. The blue horizontal line in the coronal view (B) corresponds to the level of the axial CT image (A).Reproduced from Fazio et al.,[2] with permission from Springer Nature

imaging findings are compatible. They may be considered when radiological features are atypical or when infection, malignancy, or sarcoidosis cannot be excluded.[2,5] When a biopsy is performed, histopathology typically demonstrates silicotic nodules, often with features of alveolar proteinosis in acute or accelerated forms of the disease.[7] Mineralogical analysis to identify metals may, in selected cases, assist by supporting attribution of metals to AS exposure.[5]

Laboratory investigations are non-specific and primarily serve to identify comorbidities and exclude alternative diagnoses. Elevated serum angiotensin-converting enzyme levels may be observed, but they are non-specific and occur in conditions including sarcoidosis, contributing to diagnostic confusion.[2,46]

Overall, AS silicosis is diagnosed by comprehensive occupational history-taking, radiological evaluation, and exclusion of alternative diagnoses.

Clinical Management and Treatment

Clinical management is primarily supportive and focuses on symptom control, the prevention and treatment of complications, and the optimisation of functional status.[2] Pharmacological therapies are limited and largely directed at associated conditions or secondary complications.[1,2]

Lung transplantation remains the only definitive treatment for AS silicosis.[2,7] However, access to transplantation may be constrained by socioeconomic barriers such as a lack of necessary medical insurance or financial means.[3] Among those who underwent transplantation, short- to medium-term survival appeared comparable to that for other indications, such as IPF, despite recipients being significantly younger at the time of transplantation.[7] Nevertheless, long-term prognosis remains guarded, as median post-transplant survival is limited (reported to be approximately seven years), thereby exposing younger recipients to the risk of premature mortality.[11]

However, specific interventions are being explored for AS silicosis. For patients presenting with silicoproteinosis, whole-lung lavage (WLL) has been used to clear proteinaceous material and dust burden from the alveoli.[47] While some studies have shown radiological improvement and symptomatic relief following WLL, evidence regarding improvement in lung function (spirometry and DLCO) has been mixed or statistically non-significant, and long-term survival benefits remain unclear.[47] Additionally, antifibrotic agents (e.g., nintedanib, pirfenidone, tetrandrine) are currently being evaluated for silicosis.[48,49]

Occupational Management

Prevention and Control Measures

Occupational management should be initiated promptly following diagnosis. The primary recommendation following diagnosis is removal from further exposure to RCS. However, removal does not guarantee disease stabilisation.[10]

If complete withdrawal from the industry is not immediately feasible, strict work restrictions and redeployment to a dust-free environment should be implemented.[1] Return to a silica-related workplace should only be considered after a formal medical assessment confirms fitness for work and after verification that effective workplace controls have been established.[50] Given that AS silicosis frequently affects relatively young workers with substantial functional impairment, disability assessment and workers' compensation form an important part of management.[1] In practice, navigating compensation systems can be challenging. Clinicians can facilitate access to appropriate medical, occupational, and compensation pathways.

Workplace Management

The prevention of AS silicosis relies heavily on the Hierarchy of Controls, summarised in Table 3.

Workplace Hygiene Monitoring

Regular workplace environmental monitoring is essential to ensure that workers' exposure to RCS remains below stipulated exposure limits and to verify that control measures are functioning effectively.

Personal exposure monitoring is typically conducted by placing respirable cyclones in the worker's breathing zone during specific tasks or for a full shift to collect dust for gravimetric analysis.[15,17,52] Workplace monitoring programmes should also encompass support staff who are exposed to RCS as bystanders.

Training and Education

Administrative controls and personal protective equipment (PPE) rely heavily on worker compliance, underscoring the importance of adequate training and education.[4] Employers must ensure that workers understand the serious health hazards associated with RCS exposure and can identify high-exposure tasks. Training should cover the correct implementation of controls, good housekeeping practices, and the proper use, fit, and maintenance of RPE.[33,51]

Medical Surveillance

Medical surveillance is an important secondary prevention strategy aimed at detecting silicosis in its early stages. Surveillance programmes should begin with a baseline medical assessment before, or shortly after, the commencement of silica-exposed work, followed by periodic evaluations.

Challenges and Gaps

Incomplete Understanding of AS Silicosis

The exact mechanism driving the accelerated and severe nature of AS silicosis remains poorly understood, although it has been postulated to result from the unique physicochemical properties of AS dust.[13] While the exceptionally high silica content is a primary factor, researchers hypothesise that other components of AS, specifically transition metal ions and polymer resins, significantly modify and amplify silica toxicity.[5,7,13,25]

Table 3. Hierarchy of controls in AS silicosis at the workplace	
Elimination	The most effective strategy to protect workers is to eliminate the hazard from the workplace entirely. A prime example of elimination is Australia's world-first regulatory action to completely ban the use, supply, and manufacture of engineered stone containing respirable crystalline silica, which took effect in July 2024.[35]
Substitution	Where complete elimination is not practical, substitution involves replacing high-silica engineered stone with lower-silica or silica-free alternatives.[4,6] While substitution reduces silica exposure, ongoing evaluation is required to ensure these new materials do not introduce alternative respiratory hazards.[4]
Engineering controls	Automated Machinery: The use of computer numerical control machines, robotic arm saws, and automated edge-shaping machines isolates the worker from the dust source, significantly reducing their exposure compared to using hand-held tools. [2,4,50] Wet Cutting: Processing AS with integrated water delivery systems (water-fed tools or sheet-flow wetting) should be used to suppress dust generation.[2] However, wet methods alone are often insufficient to reduce RCS below permissible exposure limits.[4] Dust Extraction: To further reduce RCS levels, wet cutting can be combined with LEV or on-tool dust extraction systems, which capture the dust directly at the point of generation before it enters the worker's breathing zone.[4] Further dust reduction can be achieved using extraction wall booths, suction benches, or waterfall curtain ventilation systems that use both air circulation and water to pull dust out of the environment.[2,17]
Administrative controls	Workshop Layout and Job Rotation: Workspaces should be designed to physically isolate dust-generating tasks, protecting support employee or nearby workers from bystander exposure. Employers can also implement shift or job rotations to minimise the total hours an individual worker spends performing high-exposure activities. Routine Housekeeping: Meticulous housekeeping prevents secondary exposure from settled dust becoming airborne again. Workplaces should prohibit dry sweeping or the use of compressed air for cleaning. Instead, they should utilise wet mopping, floor drainage systems, or industrial vacuums fitted with the appropriate high-efficiency particulate air filters.[2,17] Hygiene and Laundering: To prevent contamination outside the dusty work area, employers should provide separate designated changing and eating areas, and an industrial laundering service to clean dusty workwear.[51] Equipment Maintenance: There should be regular inspection, cleaning, storage, and maintenance of all machinery, ventilation systems, and personal protective equipment.
PPE	RPE should only be used as a supplementary measure in conjunction with robust engineering and administrative controls. AS workers must be provided with respirators appropriate to the level of RCS exposure and the tasks performed. International guidance generally recommends selecting respirators with an APF sufficient to reduce worker exposure below applicable occupational exposure limits.[52,53] In practice, filtering facepiece respirators (such as N95 or P2 masks) and elastomeric half-mask respirators typically provide an APF of 10 while full-face respirators provide an APF of 50, and PAPRs offer varying levels of protection depending on their configuration (e.g., loose-fitting hood PAPRs provide an APF of 25, half-face PAPRs an APF of 50, and tight-fitting full-face or helmet/hood PAPRs provide an APF of 1000).[33,52] However, N95 and P2 filtering facepiece respirators do not protect against VOCs emitted during AS fabrication. This should therefore be considered when selecting appropriate RPE, particularly where combined exposures to dust and chemical vapours may occur, and respirators with suitable chemical filter cartridges may be required.[2] In addition, workers who are not directly involved in fabrication tasks, such as forklift drivers, cleaners, and quality assurance staff, may still experience exposure to RCS due to ambient dust and poor housekeeping practices. These workers should therefore also be included within workplace respiratory protection programmes.[53]

AS: artificial stone, LEV: local exhaust ventilation, RCS: respirable crystalline silica, RPE: respiratory protective equipment, VOC: volatile organic compound, APF: assigned protection factor, PAPR: powered air-purifying respirator, PPE: personal protective equipment

Diagnostic Uncertainty and Inaccuracy

Diagnosing AS silicosis can be challenging because its radiological and clinical features overlap with those of other diseases such as sarcoidosis, respiratory bronchiolitis, hypersensitivity pneumonitis, and lung cancer, which can lead to misdiagnosis and delayed management.[23] This diagnostic uncertainty is compounded by a lack of validated, specific biomarkers for early diagnosis and prognostication, as no biomarker has yet demonstrated sufficient specificity or diagnostic accuracy for routine clinical use in silicosis.[54]

Limited Treatment Modalities

Currently, there is no curative therapy for silicosis; lung transplantation is the only definitive treatment for end-stage disease.[2] While drugs approved for IPF have shown promise in reducing silica-induced lung inflammation, collagen deposition, and fibrotic progression in mice, robust human clinical trials are still needed.[26,48]

There is emerging research on the use of mesenchymal stem cell therapy to reduce inflammation, and nanotechnology is being explored to create nanocarriers that enhance targeted

drug delivery and retention in the lungs while minimising systemic toxicity,[22,26] but they continue to remain experimental.

There is a growing interest in immunomodulatory approaches targeting early inflammatory pathways in silicosis. For example, inhalation of anti-NLRP3 molecules targeting the NLRP3 pathway or IL-1 pathway antagonists such as anakinra may provide more targeted delivery of the drug and limit systemic toxicity.[38]

Suboptimal Medical Surveillance Strategy and Implementation

Current surveillance strategies rely heavily on chest radiographs and PFT, but there is a growing consensus that these tools are inadequate. Although HRCT is more sensitive in detecting early pathological changes, it is often associated with higher costs and radiation exposure, which complicate its use for frequent, lifelong screening.[46]

Artificial intelligence (AI) is increasingly being explored as a potential tool to address limitations in screening, diagnosis, and staging of pneumoconiosis, including AS silicosis. Recent advances in AI, including deep learning and convolutional neural networks, show promise for improving screening sensitivity and staging accuracy, with reported diagnostic accuracies exceeding 90% in preliminary studies.[55,56] However, differentiation from similar ILDs remains challenging, and clinical integration requires further validation and interpretability tools.[23,55,56]

Even with an ideal medical surveillance and screening tool, the implementation of surveillance for silicosis remains inconsistent despite legal requirements, particularly in small fabrication workshops.[6,16,18]

Lack of Low-silica and Silica-free Alternatives

Australia's world-first ban on AS has accelerated the adoption of next-generation low-silica or silica-free alternative materials, but their long-term health effects remain uncertain. The toxicological profile of replacement materials is not yet fully characterised.

Early evidence raised concerns about the composition and toxicity of dust generated during the processing of low-silica and zero-silica products. They are highly heterogeneous and commonly incorporate recycled glass, aluminosilicates such as feldspars, aluminium trihydrate, and polymeric resins.[4] During machining, these materials can generate respirable dust containing alternative metals and VOCs, which may result in health effects similar to those of AS.[4]

Continued longitudinal evaluation is required to ensure that these alternatives do not introduce unintended health risks.

Role of the Clinician and Call to Action

Maintain High Index of Suspicion

AS silicosis shifted the demographic of occupational lung disease. A high index of suspicion among medical professionals is necessary when evaluating relatively young workers presenting with symptoms of ILD and a short latency period.[9] Occupational history remains key, with a low threshold for further workup in exposed workers.

Provide Patient Education

For diagnosed or suspected cases, clinicians must clearly communicate the severe risks of continued exposure to RCS, including accelerated decline in lung function, and strongly advise immediate removal from the exposure source to reduce disease severity.[6] There is also a need for transparent discussions about the natural progression and prognosis of silicosis, potentially leading to PMF, respiratory failure, and the need for lung transplantation, even after workplace exposure has ceased.[10]

Clinicians must educate patients on the warning signs of disease complications and other associated conditions, and consider implementing routine screening for complications.

For workers who are starting work or continuing to work in the industry, education and training regarding workplace safety measures are vital. Clinicians should emphasise the importance of the hierarchy of controls, explaining to workers and employers that they should not rely solely on PPE; these must be used in conjunction with other control measures. As the AS industry often employs migrant workers, educational programmes should account for language and demographic factors.[15] Hazard communication through translated materials, audiovisual resources, and safety signage is important to ensure comprehension and to reinforce safe work practices.

Reporting and Surveillance

The medical professional's role extends beyond individual patient care. Clinicians must also comply with mandatory reporting requirements for silicosis, which vary by jurisdiction but generally require notification of occupational lung diseases to public health authorities or occupational safety regulators.

These public health notifications are critical because they serve as sentinel health events, signalling hazardous occupational exposures and triggering workplace investigations by regulatory agencies, including worksite inspections, enforcement of silica exposure standards, and medical screening of similarly exposed, potentially asymptomatic co-workers.[6,16]

Notification also contributes to disease registries, facilitating the collection of critical epidemiological data, improving the understanding of the natural history of silicosis, identifying emerging sources of silica exposure, and informing prevention strategies and therapeutic research.[9]

CONCLUSION

AS silicosis represents a preventable resurgence of severe silica-related lung disease and an emerging public health crisis. Unlike classic silicosis, it affects younger workers exposed to high-intensity RCS and leads to a more aggressive and rapidly progressive disease. This reflects not only the potentially hazardous properties of materials but also gaps in workplace controls, surveillance, and early detection.

Effective prevention requires a combined approach. Regulations must be paired with strong controls and systematic medical surveillance. Clinician awareness and timely reporting are equally critical to enable early detection and interventions.

Global responses remain uneven, with many jurisdictions relying on conventional silica standards that may be inadequate for AS exposures. There is a clear need for greater international harmonisation of regulations, exposure limits, and surveillance systems, alongside targeted protection for vulnerable workers, particularly those in small enterprises and among migrant populations.

AS silicosis is a sentinel warning of the consequences of delayed implementation of occupational health safeguards. Coordinated action across clinical, occupational, and policy domains is essential to halt the resurgence of this preventable disease in modern workplaces.

Footnotes

Authorship Contributions

Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: All authors contributed equally to all sections.

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Declaration Regarding the Use of AI and AI-assisted Technologies: During the preparation of this work, the authors utilised Claude v 4.6 Sonnet solely to assist with language editing to improve linguistic clarity, and OpenAI's ChatGPT v 5.6 Luna, based on scientific content created by the author(s), for the visual formatting and conceptual layout of "Figure 2. Simplified Pathogenesis of Silicosis.". The final schematic was verified against established pathophysiological pathways to ensure scientific accuracy. After carefully reviewing and editing the content as necessary, the authors take full responsibility for the publication's content. This incorporation of AI tools primarily affected the visual formatting and conceptual design of Figure 2.

Supplementary Material Link: https://d2v96fxpocvxx.cloudfront.net/25021570-dd5c-48cc-b052-771af43e75cc/content-images/929bef3f-12a6-4394-8a59-2fa4fc594bfd.pdf

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Letter to the Editor

Reply: Comparative Clinical Outcomes of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Five-Year Real-Life Study

Ayça Yanalak, Onur Yazıcı

Department of Chest Diseases, Aydın Adnan Menderes University Faculty of Medicine, Aydın, Türkiye

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DEAR EDITOR,

We sincerely thank the authors for their thoughtful comments and their interest in our article entitled "Comparative Long-term Effects of Nintedanib and Pirfenidone in Idiopathic Pulmonary Fibrosis: A Real-life Study with Five-year Follow-up."[1] We appreciate their constructive remarks[2] and the opportunity to further clarify several methodological aspects of our study.

We fully agree that baseline disease severity should be carefully considered when interpreting survival outcomes in idiopathic pulmonary fibrosis (IPF). As noted by the authors, patients in the pirfenidone group had significantly higher Gender–Age–Physiology scores and more extensive radiological involvement at baseline. These findings were explicitly reported in the Results section and further discussed in both the Discussion and Limitations sections of our manuscript. Accordingly, we acknowledged that these baseline differences may have contributed to the observed mortality differences and that our findings should be interpreted with caution, rather than considered definitive evidence of treatment superiority.

We also appreciate the authors' comments regarding treatment switching during follow-up. Treatment switching is an inherent feature of real-world clinical practice and commonly occurs because of adverse events, disease progression, or individual patient characteristics. In our study, treatment-switching rates were transparently reported. To avoid attributing outcomes that occurred after treatment crossover to the initial antifibrotic therapy, patients who switched treatments were excluded from subsequent treatment-specific longitudinal analyses, including the overall mortality comparison presented in Table 5 of our original article.[1] We agree that future studies using time-dependent survival models may further strengthen the evaluation of long-term treatment effects in real-world cohorts.

We are also grateful for the authors' suggestions regarding more advanced survival analyses. Kaplan-Meier survival curves, log-rank testing, multivariable Cox proportional hazards regression models, and propensity score-based approaches are valuable statistical methods for evaluating survival outcomes in observational studies. Our primary objective was to describe long-term real-world clinical outcomes associated with antifibrotic therapy in a retrospective cohort. Considering the retrospective design of our study, baseline heterogeneity between treatment groups, treatment switching during follow-up, and incomplete longitudinal follow-up for some secondary outcomes, we presented direct comparative analyses and

Corresponding author: Assoc. Prof. Onur Yazıcı, MD, e-mail: onur.yazici@adu.edu.tr

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explicitly acknowledged these methodological limitations in our manuscript. We agree that prospective studies that include larger, more homogeneous patient populations and incorporate advanced survival analyses will provide further insight into the comparative effectiveness of antifibrotic therapies.

Finally, we appreciate the authors' recognition of our study's contribution to the limited body of long-term real-world evidence in IPF. We share their view that future multicenter prospective studies with balanced baseline characteristics and robust survival methodologies will further clarify the comparative effectiveness of nintedanib and pirfenidone.

We thank again the authors for their valuable comments and the editor for providing us with the opportunity to respond.

Footnotes

Authorship Contributions

Concept: A.Y., O.Y., Design: A.Y., O.Y., Data Collection or Processing: A.Y., O.Y., Analysis or Interpretation: O.Y., Literature Search: A.Y., O.Y., Writing: A.Y., O.Y.

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Erratum

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Following the publication of the article titled "Evaluation of COVID-19 Patients Followed in Intensive Care Units During the Second Year of the Pandemic: A Multicenter Point Prevalence Study" (Güngör S, Ediboğlu Ö, Moçin ÖY, Adıgüzel N, Tuncay E, İşcanlı İGE. *Thorac Res Pract.* 202322;25(1):11-16. doi: 10.5152/ThoracResPract.2023.23024. Erratum in: *Thorac Res Pract.* 2024;25(2):99), a request was submitted to correct the name of one of the authors, Ümit Karatepe, which had been incorrectly listed as "Umut" due to an inadvertent error. This correction has been implemented. The specific sections where the corrections have been applied are indicated below:

Published on page 11;

Sinem Güngör[1], Özlem Ediboğlu[2], Özlem Yazıcıoğlu Moçin[1], Nalan Adıgüzel[1], Eylem Tunçay[3], İnşa Gül Ekiz İşcanlı[1], Berrin Er[4], Zuhal Karakurt[1], Sema Turan[4], Behiye Deniz Kosovalı[5], Nevzat Mehmet Mutlu[6], Duygu Kayar[4], Şerife Gökbulut Bektaş[7], Elmas Uysal[4], Fatih Seğmen[4], Gürayalp Alp[8], Deniz Erdem[8], Nazan Has Selmi[4], Pınar Güven[9], Zerrin Özçelik[9], Merve Ocakcıoğlu[3], Canan Yazıcı Özgür[10], Rabia Yılmaz[11], Deniz Bilgi Özel[12], Halil Cebeci[12], Bahar Güler[11], Canan Cansever[13], Mehmet Çakırca[14], Hansa İnceöz[15], İlker Solmaz[15], Fatma Özkan Sipahioğlu[16], Eda Macit Aydın[16], Hakan Dayanır[17], Sait Fatih Öner[18], Umut Karatepe[18], Serkan Özen[18], Maruf Boran[19], Dursun Fırat Ergül[19], Umut Sabri Kasapoğlu[20], Leman Acun Delen[21], Erol Toy[22], Koray Altun[23], Tuna Albayrak[24], Hülya Yanal[25], Gizem Zaim[26], Volkan Yarar[27], Gökhan Kılınç[27], Mustafa Deniz[28], Esra Özdemir[29], Veysel Garani Soylu[30], Ayşe Yılmaz[31], Saba Mukaddes Saygılı[2], Ejder Kamil Öztürk[32], Begüm Ergan[32], Selin Eyüpoğlu[33], Yiğit Şahin[34], Beyza Yüksel[33], Azime Bulut[33], Aykut Sarıtaş[35], Hicret Yeniay[35], Mürşide Genç[36], Feyza Kargın[37], Osman Özcan[38], Ebru Karakoç[38], Ümran Karaca[39], Didem Sözütek[40], Sema Sarı[41], Nimet Şenoğlu[42], Hakan Aygün[42], Arzu Ceren Yiğit[43], Nilgün Kavrut Öztürk[44], Çağdaş Alp Uzan[45], Murat Bıçakcıoğlu[46], Serkan Solak[47], Hatice Kutbay Özçelik[48], Kamuran Uluç[49], İlker Yıldırım[50], Makbule Cavidan Arar[50], İsmail Demirel[51], Soner Umut Küver[52], Eylem Sercan Özgür[53], Kutlay Aydın[54], Gül Erdal Dönmez[55], Gülbin Aygencel[56], Aliye Esmaoğlu[57], Berrak Sebil Aydın[58], Murat Emre Tokur[59], Pervin Korkmaz Ekren[60], Yusuf Aydemir[61], Başak Çakır Güney[62], Ömer Yavuz Erdil[63], Abdurrahman Tünay[64], Türkan Bahadır[65], Serkan Uçkun[66], Nazan Kocaoğlu[66], Hüseyin Ulaş Pınar[67], Nurcan Kutluer Karaca[68], Hamza Gültekin[69], Pınar Ayvat[70], Ayşe Belin Özer[71], Ahmet Eroğlu[72], Ufuk Kuyrukluyıldız[73], Çağdaş Baytar[74], Hilal Ayoğlu[74], Serpil Mızrakçı[75], Hatice Metin[76], Özgecan Pırıl Zanbak Mutlu[77], Hakan Yılmaz[78], Filiz Tüzüner[78]

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Sinem Güngör[1], Özlem Ediboğlu[2], Özlem Yazıcıoğlu Moçin[1], Nalan Adıgüzel[1], Eylem Tunçay[3], İnşa Gül Ekiz İşcanlı[1], Berrin Er[4], Zuhal Karakurt[1], Sema Turan[4], Behiye Deniz Kosovalı[5], Nevzat Mehmet Mutlu[6], Duygu Kayar[4], Şerife Gökbulut Bektaş[7], Elmas Uysal[4], Fatih Seğmen[4], Gürayalp Alp[8], Deniz Erdem[8], Nazan Has Selmi[4], Pınar Güven[9], Zerrin Özçelik[9], Merve Ocakcıoğlu[3], Canan Yazıcı Özgür[10], Rabia Yılmaz[11], Deniz Bilgi Özel[12], Halil Cebeci[12], Bahar Güler[11], Canan Cansever[13], Mehmet Çakırca[14], Hansa İnceöz[15], İlker Solmaz[15], Fatma Özkan Sipahioğlu[16], Eda Macit Aydın[16], Hakan Dayanır[17], Sait Fatih Öner[18], **Ümit** Karatepe[18], Serkan Özen[18], Maruf Boran[19], Dursun Fırat Ergül[19], Umut Sabri Kasapoğlu[20], Leman Acun Delen[21], Erol Toy[22], Koray Altun[23], Tuna Albayrak[24], Hülya Yanal[25], Gizem Zaim[26], Volkan Yarar[27], Gökhan Kılınç[27], Mustafa Deniz[28], Esra Özdemir[29], Veysel Garani Soylu[30], Ayşe Yılmaz[31], Saba Mukaddes Saygılı[2], Ejder Kamil Öztürk[32], Begüm Ergan[32], Selin Eyüpoğlu[33], Yiğit Şahin[34], Beyza Yüksel[33], Azime Bulut[33], Aykut Sarıtaş[35], Hicret Yeniay[35], Mürşide Genç[36], Feyza Kargın[37], Osman Özcan[38], Ebru Karakoç[38], Ümran Karaca[39], Didem Sözütek[40], Sema Sarı[41], Nimet Şenoğlu[42], Hakan Aygün[42], Arzu Ceren Yiğit[43], Nilgün Kavrut Öztürk[44], Çağdaş Alp Uzan[45], Murat Bıçakcıoğlu[46], Serkan Solak[47], Hatice Kutbay Özçelik[48], Kamuran Uluç[49], İlker Yıldırım[50], Makbule Cavidan Arar[50], İsmail Demirel[51], Soner Umut Küver[52], Eylem Sercan Özgür[53], Kutlay Aydın[54], Gül Erdal Dönmez[55], Gülbin Aygencel[56], Aliye Esmaoğlu[57], Berrak Sebil Aydın[58], Murat Emre Tokur[59], Pervin Korkmaz Ekren[60], Yusuf Aydemir[61], Başak Çakır Güney[62], Ömer Yavuz Erdil[63], Abdurrahman Tünay[64], Türkan Bahadır[65], Serkan Uçkun[66], Nazan Kocaoğlu[66], Hüseyin Ulaş Pınar[67], Nurcan Kutluer Karaca[68], Hamza Gültekin[69], Pınar Ayvat[70], Ayşe Belin Özer[71], Ahmet Eroğlu[72], Ufuk Kuyrukluyıldız[73], Çağdaş Baytar[74], Hilal Ayoğlu[74], Serpil Mızrakçı[75], Hatice Metin[76], Özgecan Pırıl Zanbak Mutlu[77], Hakan Yılmaz[78], Filiz Tüzüner[78]

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Author Contributions

Concept – S.G., Ö.E.; Design – Ö.E., Ö.Y.M.; Supervision – N.A., E.T.; Resources – İ.G.E.İ., B.E.; Materials – S.G., E.T.; Data collection and/or Processing – S.T., B.D.K., N.M.M., D.K., Ş.G.B., E.U., F.S., G.A., D.E., N.H.S., P.Ö., Z.Ö., M.O., C.Y.Ö., R.Y., D.Ö.B., H.C., B.G., C.C., M.G., H.İ., İ.S., F.Ö.S., E.M.A., H.D., S.F.Ö., Ü.K., S.Ö., M.B., D.F.E., U.S.K., L.A.D., E.T., K.A., T.A., H.Y., G.Z., V.Y., G.K., M.D., E.Ö., B.E., S.E., Y.Ş., B.Y., A.B., A.S., M.G., F.K., O.Ö.A., E.K., Ü.K., D.S.A., S.S., N.Ş., H.A., A.C.Y., N.K.Ö., Ç.A.U., M.B., S.S., H.K.Ö., K.U., İ.Y., M.C.A., İ.D., S.U.K., E.S.Ö., K.A., G.E.D., G.A., A.E., B.S.A., M.E.T., P.K., Y.A., B.Ç.G., Ö.Y.E., A.T., T.B., S.U., N.K., H.U.P., N.K.K., H.G., P.A., A.B.Ö., A.E., U.K., Ç.B., H.A., S.M., H.M., O.P.Z.M., H.Y., F.T.; Analysis and/or interpretation – Z.K., S.G.; Literature Search – Ö.Y.M., B.E.; Writing – S.G., Ö.E., E.T.; Critical Review – S.G., Ö.E., N.A.

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Author Contributions

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