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IN THIS ISSUE

About PJCD

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The **PJCD** is published by the PCCP two times a year (June and December).

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As 2024 comes to a close, the Philippine College of Chest Physicians is delighted to share the final issue of the Philippine Journal of Chest Diseases for this year.

This issue highlights the remarkable scientific work of our members. Publishing in the PJCD is an opportunity to contribute to the growing body of scientific literature originating from the Philippines. This helps position the Filipino pulmonologist as an active contributor to the global scientific community. We thank everyone who shared their researches in this issue.

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Albert B. Albay Jr., MD, FPCCP
Head, Publications Committee, Philippine College of Chest Physicians

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Original Article

Factors Associated with Adherence to the 2022 Pre-Employment Algorithm for Asymptomatic Patients with Suspected Pulmonary Tuberculosis Among Pulmonologists in the Lung Center of the Philippines

Anthea Grace B. Esver, MD,[1] Precious Mae A. Gomez, MD,[1] Pamela Joy V. Dionisio, MD,[2] Eileen G. Aniceto, MD[3]

ABSTRACT

Background: Pulmonary tuberculosis is a global health concern and a leading cause of death from infectious diseases. Screening is crucial in high prevalence TB areas such as the Philippines, particularly among asymptomatic patients. This study explores factors influencing pulmonologists' adherence to the 2022 Pre-Employment Algorithm at the Health and Fitness Assessment Office (HFAO) of the Lung Center of the Philippines.

Methodology: Using a sequential explanatory mixed-methods design, the study conducted a quantitative survey of 16 HFAO pulmonologists, followed by a qualitative focused group discussion (FGD) with 12 participants. Thematic analysis of FGD transcripts provided insights into factors influencing adherence to the algorithm.

Results: The quantitative phase revealed varying awareness and compliance levels among pulmonologists that directly affected adherence to the algorithm. The FGD identified these specific factors influencing adherence: limited awareness resulting in inconsistent application of the guidelines; personal beliefs and patient-related factors influencing individualized decision-making; institutional challenges (i.e., resource constraints) hindering the implementation process; and perceived algorithm inefficacy, coupled with communication barriers among healthcare professionals, further reducing adherence rates.

Conclusions: Knowledge gaps, resource limitations, and personal decision-making significantly affected adherence to the 2022 Pre-Employment Algorithm. Addressing these issues through targeted training, clearer guidelines, and improved resource management can improve adherence and enhance TB screening outcomes

Keywords: pre-employment clearance, tuberculosis, fit to work, FGD, awareness

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INTRODUCTION

Pulmonary tuberculosis (PTB) remains a major global health issue and is the second-leading cause of death from infectious diseases globally.[1] In areas with a high TB prevalence such as the Philippines, screening is crucial as missed diagnosis remains notably significant, especially among asymptomatic patients.[2] As the National Apex Center for Lung and Chest Diseases, the Lung Center of the Philippines (LCP) receives a high volume of referrals for the assessment of work applicants before local and overseas employment since most PTB-affected Filipinos are amongst individuals aged ≥15 years, potentially posing an infectious risk to others in their work environments.[3] In 2005, the Department of Labor and Employment released implementation guidelines that mandate employers to implement TB prevention and control policies to alleviate the spread of disease in the workplace.[4] Since the mandate's release, employers have required job applicants to pass the Pre-Employment Medical Examination which included a TB screening protocol based on national guidelines. Pulmonologists at LCP evaluate the TB status of applicants referred for pulmonary clearance prior to local or international employment through its Health and Fitness Assessment Office (HFAO). HFAO, which is part of the LCP Outpatient Department, is tasked to provide comprehensive, quality, and timely diagnostic services to individuals with health risks at a reasonable price. It caters to clients seeking pre-employment TB clearance, outpatient executive check-ups, pre-flight assessments, and outpatient COVID home care services. HFAO recommends using the LCP Pre-Employment PTB Clearance Algorithm (Supplementary Material 1) based on existing National Tuberculosis Program guidelines. The LCP algorithm on diagnosis and management of pre-employment applicants suspected of PTB was first released in 2015 and revised last November 2022.

METHODOLOGY

Research design

The research adopted a sequential explanatory mixed-methods (quanti→QUALI) design, incorporating an initial quantitative survey followed by a qualitative focused group discussion (FGD), with the overarching objective of thoroughly investigating factors influencing adherence to the 2022 Pre-Employment Algorithm. Adherence to the algorithm was categorized as complete when pulmonologists consistently followed all guidelines, partial when they selectively applied the algorithm based on individual cases, and non-adherence when they used a personal or alternative algorithm instead of the recommended guidelines.

Following ethical approval from the review board, the quantitative phase of the study commenced; the researchers distributed a semi-structured questionnaire via Google Forms to 19 pulmonologists practicing in the HFAO of the Lung Center of the Philippines. Preliminary analysis of the survey results

revealed factors influencing adherence that exhibited the highest variation. These gave way to the qualitative phase (FGD) of this research. Purposive sampling involving 19 pulmonologists was employed. Informed consent was sought; 16 consented and completed the questionnaire, but only 12 participated in the FGD. Eligible participants were HFAO pulmonologists who gave consent. Participants were notified seven days before the FGD and received reminders 24 hours prior. A trained moderator facilitated the three-hour discussion in a conducive and private setting at the Lung Center of the Philippines.

Participants

A total enumeration approach was employed for the quantitative component, encompassing 19 pulmonologists practicing in the HFAO. The researchers excluded two co-authors, both pulmonologists, and another who did not consent, resulting in 16 study participants. In the FGD, the researchers included a minimum of 12 participants.

Instrumentation and data collection

For the quantitative phase, a semi-structured questionnaire delivered using Google Forms was used for data collection. The questionnaire, which was launched on December 7, 2023 included questions about pulmonologists' awareness of the 2022 Pre-Employment Algorithm, compliance levels, and factors influencing adherence to the guidelines (Supplementary Material 2). The Focus Group Discussion (FGD) was conducted on December 19, 2023. The questionnaire was developed to capture comprehensive quantitative insights related to the study objectives.

For the qualitative phase, a semi-structured discussion guide was developed based on the survey responses to facilitate the FGD (Supplementary Materials 2, 3). The guide was designed to facilitate an in-depth exploration of participants' understanding of the algorithm, challenges with adherence, perceived barriers and recommendations for improvement. Purposive sampling ensured a diverse representation of perspectives among eligible participants. The FGD employed audio recording and detailed note-taking to ensure accurate data capture; visual recording was not done. An observer documented non-verbal cues and group dynamics through careful note-taking. This approach was chosen to address ethical considerations and foster a more natural and unrestrained discussion environment.

Procedure

The FGD provided a platform for participants to discuss variations in decision-making in pre-employment assessments. For the study, the key steps were: defining objectives, inviting participants, explaining the FGD's purpose, and obtaining consent.

Logistics including venue and equipment were arranged. Participants were welcomed, and the study purpose and ground rules were explained. The FGD followed the facilitator's guide, using probing questions to generate insights (Supplementary Material 3). Audio recording and note-taking captured data accurately. Data were transcribed and analyzed for themes, and key findings were identified. Member checking was done to validate the data. The technique involved discussing findings with participants while the researchers reviewed the methodological and analytic procedures.

The study explored the following areas of discussion: participants' understanding of the algorithm, challenges with adherence, perceived barriers and recommendations for improvement.

Data analysis

The FGD transcripts were transcribed verbatim, followed by thematic analysis of data. The researchers familiarized themselves with the data and assigned preliminary codes to text segments based on recurring themes. These codes were grouped into broader themes and subthemes to identify critical factors related to algorithm adherence. Preliminary findings were shared with participants for validation. Qualitative findings were integrated with quantitative results to provide a comprehensive understanding of factors associated with adherence to the 2022 Pre-Employment Algorithm, using data triangulation to enhance insight.

Further analysis led to Level III codes (themes), with constant comparisons between transcribed narratives.

Validity and reliability

Content validity ensured that the survey and FGD guide aligned with the study objectives. Construct validity confirmed that the methods accurately assessed factors influencing adherence. Internal validity was boosted through the mixed-methods design. External validity was enhanced by including a diverse group of pulmonologists from LCP HFAO to ensure broader applicability. Reliability was ensured by evaluating the test-retest reliability of the survey and inter-rater reliability of the FGD, with standardized data collection procedures for consistency.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki, National Ethical Guidelines for Research Involving Human Participants 2022, and the Data Privacy Act of 2012. The study was approved by the LCP Institutional Ethics and Review Board (LCP-IERB code: LCP-PF-028-2023). Informed consent was obtained in compliance with ethical guidelines. Thorough explanations were provided to participants' questions, ensuring their understanding of the procedure. Results were disclosed to participants when the results were scientifically valid, confirmed, and had significant positive implications for patients.

RESULTS

Sixteen pulmonologists from HFAO comprised the study sample, with 12 participating in the FGD. All were board-certified by the Philippine College of Chest Physicians and engaged in private practice at LCP. None of the participants were directly involved in formulating the 2022 Pre-Employment Algorithm. Twelve out of 16 participants had been using the pre-employment algorithm before the 2022 version, highlighting a mix of experience levels in applying previous and updated guidelines. Out of the 16 participants who gave consent, only 12 attended the scheduled FGD due to time constraints.

Awareness of the algorithm was initially assessed through binary survey responses (yes/no) while compliance level was categorized into "always," "often," "sometimes," "rarely," and "never." Responses were further explored qualitatively. Based on the results of the survey and FGD, participants' awareness of the algorithm was "moderate to high" (high awareness: n = 13, partial awareness: n = 3) while compliance was variable (consistent compliance: n = 14, selective compliance: n = 2).

Table 1. Integration of quantitative and qualitative data

Thematic areas	Codes	Key findings
Awareness and understanding of the algorithm	A1: Knowledge gaps A2: Misconceptions A3: Clarity about the algorithm	- Varying adherence levels to the algorithm - Influencing factors include patient and system-related, and country-specific considerations
Personal factors influencing adherence	B1: Individual beliefs B2: Attitudes B3: Experiences affecting adherence	- Impact of personal experiences and beliefs on adherence - Differences in X-ray interpretation lead to individualized decisions
Patient-related factors	C1: Patient characteristics C2: Communication challenges C3: Perceived patient preferences	- Influence of each codes on decision-making
Facility/institutional factors	D1: Resource constraints D2: Organizational policies D3: Administrative support	- Limited awareness of central order and challenges in disseminating the protocol within the institution - Variability in institutional adherence due to resource availability and organizational policies
Challenges in algorithm implementation	E1: Practical difficulties E2: Time constraints E3: Workflow issues	- Challenges in implementation, including test availability and time constraints - Discrepancies in interpreting chest X-ray findings pose practical difficulties
Perceived effectiveness of the algorithm	F1: Opinions on efficacy F2: Perceived benefits	- Concerns about the algorithm's effectiveness in certain scenarios - Suggestions for improvement, such as clarifications on abnormal X-ray classifications
Feedback and suggestions for Improvement	G1: Modifications to the algorithm G2: Enhancing training G3: Improving implementation	- Proposals for algorithm modifications, such as subdividing abnormal X-ray findings - Calls for standardization and continuous training to address challenges
Communication and collaboration	H1: Interaction with healthcare professionals H2: Interaction with patients	- Collaboration and communication challenges exist, particularly in cases referred from other agencies - Suggestions include conducting workshops and lectures to improve awareness and understanding

Among pulmonologists who consistently complied, occasional deviations may happen due to case complexity, resource availability, and patient preferences. Significant variation arose from knowledge gaps, resource constraints, communication challenges, and institutional issues. Barriers like limited IGRA (interferon gamma release assay) availability, X-ray classification confusion, and personal decision-making further impacted adherence.

Participants also answered open-ended questions like "How familiar are you with the 2022 Pre-Employment Algorithm?" and "How comfortable are you applying the algorithm in practice?" High familiarity was assigned to participants who expressed confidence in their knowledge and indicated consistent algorithm use, while participants who reported partial awareness or uncertainty about specific components were assigned low familiarity, indicating areas where more understanding was needed.. High familiarity was noted in 14 participants, and low familiarity in two. Compliance was grouped into high, moderate, and low. High compliance, defined as always or often followed the algorithm, was reported by 14 participants, while low compliance, defined as sometimes or rarely followed the algorithm, was noted by two.

Reasons cited for low adherence included varying interpretations of abnormal X-rays, lack of awareness or familiarity with the algorithm, and institutional challenges such as outdated or unclear protocols, as highlighted in Table 1 under Challenges in algorithm implementation (E1, E2).

To address these issues, the participants recommended refining the algorithm to provide clearer guidelines on X-ray classifications, enhancing training programs to improve knowledge and application consistency, and ensuring resource availability to support the standardized protocol, as noted in Table 1 under Feedback and suggestions for improvement (G1, G2). Implementing these recommendations could reduce variability and improve adherence rates among pulmonologists.

Conversely, areas of high adherence were noted in routine screening processes where guidelines were well-established and supported by institutional protocols. Participants who frequently adhered to the algorithm cited clear guidance, consistent training, and the availability of necessary resources as key drivers of compliance. These factors drove high adherence (Table 1 under Facility/institutional factors; D1), emphasizing the importance of continuous education and standardized practices. These areas demonstrate how clear and well-supported protocols can enhance adherence and effectiveness in clinical settings.

The participants' recommendations for algorithm improvement are presented in Table 2. Participants recommended modifying the algorithm, enhancing training, and improving overall implementation. Proposals included subdividing abnormal X-ray findings, standardizing procedures, and offering continuous training to address challenges. Discussion occurred on the interaction between

Table 2. Recommendations for algorithm improvement

Recommendations
Provide clarity on local versus international application
Address individualized decision-making based on beliefs and attitudes
Enhance communication and patient understanding
Improve resource allocation and institutional support
Streamline algorithm implementation challenges
Clarify abnormal X-ray classifications and efficacy concerns
Standardize and continuously train pulmonologists
Facilitate workshops and lectures for better collaboration

Table 3. Recommendations for algorithm improvement with key issues addressed

Recommendations	Key Issues Addressed
Modify the algorithm	- Clarity - Individualized decision-making
Enhance training	- Continuous training
Improve implementation strategies	- Communication - Resource allocation

pulmonologists, other healthcare professionals, and patients in the algorithm context. Collaboration and communication issues, especially with cases referred from other agencies, were discussed. Suggestions included workshops and lectures to improve awareness and understanding. These recommendations addressed issues like clarity, individualized decision-making, communication, resource allocation, and continuous training (Table 3).

DISCUSSION

Pulmonary tuberculosis stands as a formidable global health concern, particularly in regions of high prevalence like the Philippines. The LCP plays a key role in evaluating job applicants to prevent workplace transmission, with missed diagnoses, particularly in asymptomatic patients, posing significant risks. This study explores the factors influencing pulmonologists' adherence to the 2022 Pre-Employment Algorithm.

The research used a sequential explanatory mixed-methods design which involved quantitative surveys of 16 HFAO pulmonologists, followed by an FGD with 10 participants. The survey showed varying levels of awareness and compliance with the algorithm, while the subsequent FGD unearthed thematic areas influencing adherence such as awareness, personal/patient-related and facility/institutional factors, implementation challenges, and perceived effectiveness, feedback, suggestions for improvement, and communication issues (Table 1, Supplementary Material 4). Knowledge gaps, misconceptions, and clarity issues about the algorithm were identified and showed that while participants were generally aware of the algorithm, they demonstrated varying adherence levels. Factors influencing adherence encompassed patient and system-related, and country-specific considerations. Clarity was needed regarding the algorithm's application in local versus international employment. We identified individual beliefs, attitudes, and experiences affecting adherence. Personal experiences and beliefs, including perceptions of patient risk, impacted adherence. Differences in interpreting X-ray findings contributed to individualized decisions.

Decision-making was influenced by patient characteristics, communication challenges, and perceived patient preferences. Patient understanding, compliance, and preferences influenced the process, while challenges in obtaining sputum samples contributed to treatment delays. Adherence was impacted by resource constraints, organizational policies, and administrative support. Limited awareness of the central order and challenges in disseminating the protocol within the institution were noted. Institutional adherence varied due to differences in resources and policies.

Challenges in algorithm implementation included practical difficulties, time constraints, and workflow issues such as test availability, time constraints, and discrepancies in interpreting chest X-ray findings. The participants expressed their opinions on the algorithm's efficacy and perceived benefits. Its effectiveness in specific scenarios was raised and the participants suggested improvements including clarification of abnormal X-ray classifications.

The integrated data analysis provided key insights and recommendations, addressing concerns such as clarity in application, individualized decision-making, communication improvement, streamlined implementation, abnormal X-ray classification, and ongoing training and standardization. The study's findings have implications for policy-making, training, and continuous improvements in healthcare, highlighting the need to address limitations and advocate further research to enhance generalizability. The study's design contributed significantly to understanding factors influencing pulmonologists' adherence to the 2022 Pre-Employment Algorithm, offering insights for better disease prevention and control in employment settings.

A SWOT analysis highlighted critical factors that influence adherence to the 2022 Pre-Employment Algorithm (Supplementary Material 5). Strengths included provision of standardized guidance for TB screening, support for consistent decision-making, prevention of TB in workplaces, and implementation in a tertiary healthcare institution, all of which enhance the algorithm's credibility. Weaknesses included inconsistent adherence, knowledge gaps regarding the algorithm, perceived effectiveness issues, and limited training and standardization efforts. Opportunities involved refining the algorithm based on feedback, enhancement of training programs, standardization of practices across institutions, and improvement of stakeholder communication and collaboration. Threats included resource constraints, limited test availability, miscommunication among healthcare professionals, varying international TB screening requirements, and resistance to change in established practices.

The study has limitations inherent to the qualitative design. While the exchange of ideas during the FGD can elicit new insights, it may also unintentionally silence participants who are hesitant to voice dissenting opinions or feel pressured to

conform. To address this, a trained moderator managed the FGD, ensuring that no individual dominates the discussion that less vocal participants can share their views.

CONCLUSION

Knowledge gaps, resource limitations, and personal decision-making significantly affected adherence to the 2022 Pre-Employment Algorithm. Addressing these issues through targeted training, clearer guidelines, and improved resource management can improve adherence and enhance TB screening outcomes. The study provided an understanding of factors that influence adherence to the algorithm and offered valuable insights for policy-making, training initiatives, and continuous improvement efforts in similar healthcare settings.

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Dr. Racquel Ibanez: Conceptualization, Supervision, Methodology; **Dr. Gerald Tejada:** Project Administration, Investigation; **Dr. Ma. Lalaine Gumiran-Cheng:** Formal Analysis, Resources

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Authors' Disclosure

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References

1. World Health Organization. WHO policy on collaborative TB/HIV activities: guidelines for national programs and other stakeholders. Geneva: World Health Organization; 2012. Accessed October 26, 2024. Available from: https://www.who.int
2. Department of Health, Government of the Philippines. Comprehensive and Unified Policy for TB Control in the Philippines (C.U.P. 2004). 2004
3. Lansang MAD, Alejandria MM, Law I, et al; Philippine NTPS 2016 Group. High TB burden and low notification rates in the Philippines: The 2016 national TB prevalence survey. *PLoS One*. 2021;16(6). https://doi.org/10.1371/journal.pone.0252240
4. Department Order No. 73-05. Guidelines for the Implementation of Policy and Program in Tuberculosis. Accessed October 26, 2024. Available from: https://www.dole.gov.ph/php_assets/uploads/2005/03/DO-73-05.pdf
5. Monera OM, Delos Reyes V. Knowledge and Practices among Pulmonologists of the Lung Center of the Philippines in Giving Pre-Employment Clearance in Asymptomatic Patients with Findings Suggestive of Tuberculosis in the Common Diagnostic Examinations. 2020
6. World Health Organization. WHO consolidated guidelines on tuberculosis: Module 2: screening – systematic screening for tuberculosis disease [Internet]. Geneva: World Health Organization; 2021. Accessed October 26, 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK569336/
7. World Health Organization. Global Tuberculosis Report. 2022. Accessed March 21, 2020
8. Republic of the Philippines. Executive Order No. 187: Instituting a Comprehensive and Unified Policy for the Tuberculosis Control in the Philippines. Manila, Philippines: Republic of the Philippines; 2003:1-2
9. Department of Health, Manila, Philippines. Manual of Procedures for the National TB Control Program. 5th ed. 2013
10. Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. *PLoS Med*. 2007;4(7). https://doi.org/10.1371/journal.pmed.0040238
11. Gebreweld FH, Kifle MM, Gebremicheal FE, et al. Factors influencing adherence to tuberculosis treatment in Asmara, Eritrea: a qualitative study. *J Health Popul Nutr*. 2018;37(1):1. https://doi.org/10.1186/s41043-017-0132-y
12. Department of Health. Review report. 2019 Philippines TB Joint Program Review; October 3-14, 2019:56,74
13. Arreola A, Obusan J, Gonong JR, Balanag V. Clinical profile and outcome of job applicants with chest X-ray findings suspicious of PTB seen in the Lung Center of the Philippines. 2017
14. Creswell JW. Qualitative Inquiry and Research Designs: Choosing Among Five Approaches. 2nd ed. California: Sage Publication, Inc.; 2007
15. Daniel WW, Cross CL. Biostatistics: A Foundation for Analysis in the Health Sciences. 10th ed. Wiley & Sons, Inc.; 2013
16. Al-Med A, Abbas B, Al-Ubaidi B. The radiological diagnosis of pulmonary tuberculosis (TB) in primary care. *J Fam Med Dis Prev*. 2018;4. https://doi.org/10.23937/2469-5793/1510073
17. Onwuegbuzie AJ, et al. A qualitative framework for collecting and analyzing data in focus group research. *Int J Qual Methods*. 2009;8(3). https://doi.org/10.1177/160940690900800301

Original Article

Association of Increasing Body Mass Index with Obstructive Ventilatory Defect Among Adult Patients in Perpetual Help Medical Center

Sherry Mae T. Dominguez, MD[1] and Jose Edzel V. Tamayo, MD[1]

ABSTRACT

Background: Various studies show an association between obesity and obstructive ventilatory defects. The changing diet of the population plays an important role in public health thus it is important to assess the association of increased body mass index (BMI) with lung ventilatory defects to be able to formulate health programs that will reduce the risk of obesity.

Methodology: This cross-sectional study included adult patients subjected to pulmonary function testing at Perpetual Help Medical Center, Las Piñas. A review of records was performed to gather data on demographics, pulmonary function test, and BMI.

Results: A total of 459 patients were included. Seventy (15.3%) had normal spirometry values, 79 (17.2%) had restrictive ventilatory defect, 306 (66.7%) had obstructive ventilatory defect, and 4 (0.9%) had mixed defects. The mean age was highest among those with obstructive ventilatory defect (59.5 ±16.6 years; p <0.001). The proportion of obstructive ventilatory defect was significantly higher among males than females (76.0% vs 53.2%; p = 0.001). Height, weight, and BMI did not vary significantly between the groups. Majority of patients were either overweight (39.6%) or normal (37.2%). The prevalence of abnormal spirometry did not vary across BMI classifications (p = 0.068). Significant correlations with BMI were observed only with post-bronchodilator FEV_1 % predicted (r = 0.09; p = 0.044), post-bronchodilator FEV_1/FVC (r = 0.11; p = 0.015), and post-bronchodilator $FEF_{25-75\%}$ (r = 0.09; p = 0.047). After adjustment, obesity was not associated with obstructive ventilatory defect (OR 0.9, 95% CI 0.5 to 1.8; p = 0.601) and post-bronchodilator FEV_1 (OR 0.9, 95% CI 0.5 to 1.7; p = 0.940).

Conclusions: BMI is not correlated with spirometric parameters, and obesity is not associated with obstructive ventilatory defect or post-bronchodilator FEV_1. Although some correlations are observed with BMI and post-bronchodilator spirometric parameters, the observed correlations are weak. Further studies are needed to determine the effect of other measures of body mass on obstructive ventilatory defect.

Keywords: BMI, obstructive ventilatory defect, spirometry, pulmonary function test

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INTRODUCTION

Obstructive lung diseases include chronic obstructive pulmonary disease (COPD), emphysema, and asthma. In these conditions, less air flows in and out of the alveoli, leading to reduced gas exchange. This is debilitating to patients and requires proper medical attention.[1] COPD affects nearly 210 million people worldwide, with a local prevalence rate of 14% in Metro Manila and 20% in rural areas.[2] Asthma has affected an estimated 339.[4] million people worldwide, with a slightly higher prevalence rate in rural areas than in urban areas (15.3% vs 13.3%).[3-4] Spirometry is commonly used to assess lung function and it provides a more accurate diagnosis of bronchial asthma and COPD by measuring the volume of air an individual can expel from the lungs after maximal inspiration.[5] The method enables detection of airway obstruction, making a definitive diagnosis of an obstructive lung disease.[6]

Obesity, a chronic medical condition that is characterized by excessive fat accumulation on human body, is measured by the body mass index (BMI), which reflects weight in relation to height. The WHO classification is as follows: BMI of 18 to 24.9 kg/m^2 is normal weight, BMI of 25.0 to 29.9 kg/m^2 is overweight, and BMI of 30 kg/m^2 or higher is obese.[7]

Obesity has been a global problem because of its significant contribution to mortality and morbidity. Studies have reported an association between body mass index (BMI) and asthma, with asthma prevalence being shown to increase with obesity.[8] One study observed that a BMI of 28 and above increased the risk of asthma, but with the relationship being significant only among women.[9] Similar findings of increasing asthma prevalence with obesity have been reported in several other studies, with the association seen to be stronger in women and non-smokers.[10-16] However, there are also studies that show no association between obstructive lung disease and obesity.[17-18] One study explained that an elevated BMI might have a protective impact on lung function in chronic obstructive pulmonary disease with GOLD grades 3 to 4, while dietary status significantly influences lung function in later stages.[19,20]

In the Philippines, there is a paucity of published literature regarding BMI and prevalence of obstructive ventilatory defects. Chua et al. described the body composition of Filipinos with chronic obstructive ventilatory defect and concluded in their study that underweight individuals with low fat-free mass indices were correlated with reduced lung function.[21] Variations in BMI are multifactorial and are influenced by environmental factors such as lifestyle, physical activity, and emotional factors. Las Piñas has become more populated over the last decade, with the changing diet of the population playing an important role in public health. As such, this study has a big contribution in this area as there are no local studies addressing the association between BMI and pulmonary defects. This study aimed to establish this association so

corrective steps can be taken to address obesity risk factors in Las Piñas, such as diet and lifestyle, given obesity's effects on respiratory health.

METHODOLOGY

The study was a cross-sectional, analytic study that involved a review of records of adult patients subjected to pulmonary function test at Perpetual Help Medical Center, Las Piñas from January 2019 to December 2023. Excluded in the study were pregnant patients, those who did not complete the procedure, and spirometry results that did not meet the American Thoracic Society—European Respiratory Society 2019 guidelines. Records were obtained and reviewed, clinico-demographic data and spirometric values from pulmonary function tests were extracted, and data was tabulated and coded in an SPSS (Statistical Product and Service Solutions) spreadsheet.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and standard deviation for normally distributed continuous variables. Independent samples t-test, Mann-Whitney U test, and Fisher's exact test/chi-square test were used to determine the difference in mean, rank, and frequency, respectively, between patients with and without obstructive ventilatory defects. Pearson's correlation was used to determine the correlation between BMI and spirometric parameters. Univariable and multivariable logistic regression analyses were employed to determine the association between BMI categories (specifically obese and non-obese) and obstructive ventilatory defects. Missing values were neither replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis.

Operational definition of terms

Body mass index (BMI) refers to an individual's weight in kilograms divided by their height in meters squared. It is a measure of body size categorized into four groups, according to the conventional WHO classification: underweight (less than 18.5 kg/m^2), normal weight (18.5 to 24.9 kg/m^2), overweight (25 to 29.9 kg/m^2), and obese (30 kg/m^2 and above).[7]

Obstructive ventilatory defect refers to a disproportionate decrease in maximal airflow from the lungs (forced expiratory volume in 1 second; FEV_1) relative to the maximal volume that can be displaced from the lungs (forced vital capacity; FVC), and is characterized by an FEV_1/FVC of less than 70%.[22]

Restrictive ventilatory defect is characterized by a normal FEV_1/FVC (more than 0.70) and a reduction in total lung capacity (TLC) below the fifth percentile, or 80% of the predicted value.[22]

Mixed ventilatory defect is characterized by obstructive and restrictive defects, diagnosed when both FEV_1/FVC and TLC are below the fifth percentile of their predicted values; or when FEV_1/FVC is less than 0.70 and TLC is less than 80% of the predicted value.[22]

Forced expiratory volume 1 (FEV_1) refers to the volume of air that can be forced out in one second after full inspiration. FEV_1 is used to categorize the severity of any spirometric abnormality.

Forced vital capacity (FVC) refers to the total amount of air exhaled during the FEV test. The normal value is 80% and above.[23]

FEV/FVC ratio, also called the Tiffeneau-Pinelli index, is a spirometric parameter that represents the proportion of a patient's vital capacity that is expired in the first second of forced expiration. The normal value is 0.70 and above.[24]

$FEF_{25-75\%}$ refers to the average forced expiratory flow rate at 25% to 75% of the vital capacity and is expressed as a percentage of the predicted value (% predicted $FEF_{25-75\%}$). The normal value is 65% and above.[25]

Computation of sample size

The study examined all spirometries done from January 2019 to December 2023. A minimum of 190 patients were needed based on 95% confidence interval, 80% power, a 29% prevalence of obstructive ventilatory defects among non-obese individuals, and a reported odds ratio of 2.4 for the association between obstructive ventilatory defects and obesity.[4] This was computed using OpenEpi calculator.

Ethical considerations

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the International Conference on Harmonization—Good Clinical Practice and upon the approval of the Technical and Institutional Ethics Review Board (IERB) of the Perpetual Help Medical Center—Las Piñas (UPHS-IERB 2023-020 RP). A waiver of informed consent was approved by the ethical review board and was given to the hospital where the study was conducted. The waiver assured the hospital that strict confidentiality was maintained, that the study employed pure records review, and that the patients will be anonymous. Patient identities were replaced by codes on data collection forms and data encoding sheets. There were no anticipated ethical issues on the conduct of this study. The study carried minimal risk, bringing no harm and discomfort to its subjects, as it was purely a chart review.

RESULTS

Table 1 shows the characteristics of the study population, classifying patients into those with and without obstructive ventilatory defect. A total of 459 patients were included in the study. Of these, 70 (15.3%) had normal spirometry values, 79 (17.2%) had restrictive ventilatory defects, 306 (66.7%) had obstructive ventilatory defects, and 4 (0.9%) had mixed ventilatory defects. The mean age was highest among those with obstructive ventilatory defect (59.5 ± 16.6; p <0.001). The proportion of obstructive ventilatory defect was significantly higher among males than females (76.0% vs 53.2%; p = 0.001). Mean height (161.4 ± 10.5 cm), mean weight (67.8 ± 16.1 kg), and mean BMI (26.0 ± 3.7 kg/m^2) did not vary significantly between the groups. Majority of patients were either overweight (39.6%) or with normal BMI (37.2%). The prevalence of abnormal spirometry did not vary across BMI classifications (p = 0.068).

Table 2 shows significant correlations between BMI and post-bronchodilator FEV_1 % predicted, (r = 0.09; p = 0.044), post-bronchodilator FEV_1/FVC (r = 0.11, p=0.015), and post-bronchodilator $FEF_{25-75\%}$ (r= 0.09; p = 0.047). These observed correlations, however, were weak (r <0.1).

As seen in Table 3, obesity was not significantly associated with obstructive ventilatory defect in the univariable analysis (odds

Table 1. Characteristics of the study participants

	With obstructive ventilatory defect	Without obstructive ventilatory defect			Overall	p-value
		Normal	Restrictive	Mixed		
Total number of participants, n	306 (66.7)	70 (15.3)	79 (17.2)	4 (0.9)	459	
Age, years	59.5 ± 16.6	43.9 ± 16.9	42.7 ± 14.2	48.2 ± 15.1	54.1 ± 16.6	<0.001
Sex						
Male	206 (76.0)	28 (10.3)	36 (13.3)	1 (0.4)	271 (59.0)	0.001
Female	100 (53.2)	42 (22.3)	43 (22.9)	3 (1.6)	188 (41.0)	
Height, cm	162.1 ± 10.5	159.3 ± 10.3	160.5 ± 10.8	159 ± 10.2	161.4 ± 10.5	0.069
Weight, kg	67.3 ± 16.6	67.1 ± 12.7	68.2 ± 17.2	109.1 ± 21.2	67.8 ± 16.1	0.712
Smoking history						
Non-smoker	110 (50.5)	52 (23.8)	53 (24.3)	3 (1.4)	218 (47.5)	<0.001
Smoker	61 (78.2)	8 (10.3)	9 (11.5)	0 (0.0)	78 (17.0)	
Previous smoker	135 (82.8)	10 (6.1)	17 (10.4)	1 (0.6)	163 (35.5)	
BMI, kg/m^2	25.6 ± 5.9	26.3 ± 3.9	26.4 ± 4.9	43.2 ± 2.5	26.0 ± 3.7	0.642
BMI classification						
Underweight	19 (65.5)	2 (6.9)	8 (27.6)	0 (0.0)	29 (6.4)	0.068
Normal	121 (71.2)	19 (11.2)	30 (17.6)	0 (0.0)	170 (37.2)	
Overweight	115 (64.5)	39 (21.5)	27 (14.9)	0 (0.0)	181 (39.6)	
Obese	50 (64.9)	10 (13.0)	13 (16.9)	4 (5.2)	77 (16.8)	

Data presented as mean (SD) and frequency (percentages); across-column percentages were computed
BMI: body mass index

Table 2. Correlation of different spirometric parameters with BMI

	Mean ± SD	Pearson's correlation	p-value
Pre-bronchodilator tests			
FVC, L	3.0 ± 4.1	0.03	0.492
% predicted	77.3 ± 17.4	0.03	0.531
FEV_1, L	2.1 ± 3.0	0.02	0.672
% predicted	71.9 ± 20.9	0.01	0.715
FEV_1/FVC, %	69.3 ± 18.5	0.04	0.361
% predicted	70.6 ± 15.5	0.08	0.110
$FEF_{25–75\%}$, L/s	1.6 ± 1.6	0.08	0.083
% predicted	52.6 ± 32.1	0.04	0.390
Post-bronchodilator tests			
FVC, L	2.8 ± 0.8	0.003	0.946
% predicted	79.7 ± 16.6	0.05	0.288
FEV_1, L	2.2 ± 4.0	0.04	0.358
% predicted	77.2 ± 9.9	0.09	0.044
FEV_1/FVC, %	71.8 ± 15.2	0.11	0.015
% predicted	73.3 ± 16.0	0.08	0.241
$FEF_{25–75\%}$, L/s	1.8 ± 1.2	0.09	0.047
% predicted	61.6 ± 35.5	0.08	0.051

BMI: body mass index; FVC: forced vital capacity; FEV_1: forced expiratory volume in the 1st second; FEV_1/FVC: ratio of FEV_1 to FVC; $FEF_{25-75\%}$: forced expiratory flow rate at 25% to 75% of the vital capacity

ratio [OR] 0.8, 95% confidence interval [CI] 0.4 to 1.7; p = 0.534) and multivariable analysis (OR 0.9, 95% CI 0.5 to 1.8; p = 0.601). Table 4 shows that obesity was not significantly associated with post-bronchodilator FEV1 in the univariable analysis (OR 1.0, 95%CI 0.6 to 1.7; p = 0.989) and multivariable analysis (OR 0.9, 95% CI 0.5 to 1.7; p = 0.940).

DISCUSSION

The relationship between obstructive ventilatory defects and obesity remains a topic of debate. Various studies have shown both positive and negative relationships between increased

Table 3. Association of obesity with obstructive ventilatory defect, before and after adjusting for sex, age, and smoking status

	OR (unadjusted)	p-value	OR (adjusted)	p-value
Non-obese	1.2 (0.6 to 2.5)	0.534	1.1 (0.5 to 2.0)	0.601
Obese	0.8 (0.4 to 1.7)		0.9 (0.5 to 1.8)	

OR: odds ratio

Table 4. Association of obesity with post-bronchodilator FEV_1 before and after adjusting for sex, age, and smoking status

	OR (unadjusted)	p-value	OR (adjusted)	p-value
Non-obese	1.0 (0.5 to 1.8)	0.989	1.0 (0.6 to 2.0)	0.940
Obese	1.0 (0.6 to 1.7)		0.9 (0.5 to 1.7)	

OR: odds ratio

BMI and FEV_1/FVC.[26-29] Weight gain and increased BMI are associated with decreased lung volumes, as reflected by a more restrictive ventilatory pattern on spirometry.[30] However, obesity is also being recognized as being linked to obstructive lung diseases such as asthma.[31]

The result of this study revealed that obesity did not significantly affect the odds of having an obstructive ventilatory defect. This agrees with the study of Schachter et al which showed that even with reduced FEV_1 and FVC in obese subjects, they did not show any evidence of obstruction nor was there an increase in airway responsiveness.[32] This is in contrast with Liu et al which showed an increased prevalence of obesity on obstructive lung diseases.[33]

In the study of Tang et al, individuals with obstructive lung disease and moderate to very severe COPD were shown to have

significantly greater FEV_1/FVC in the overweight/obese group compared to the normal BMI group.[29] According to Jing Zhu et al, elevated BMI had a protective impact on lung function in COPD GOLD grades 3 to 4.[19] The protective effect of BMI was more compelling in patients with severe COPD, as dietary status significantly influences lung function in later-stage patients.[20] Such protective impact was not seen in the current study. The protection afforded by obesity may be explained by several factors. For example, individuals with obstructive lung disease or COPD may benefit from increased respiratory muscle mass to manage elevated airway resistance and airflow blockage.[34] Obese COPD patients are also shown to benefit from an increased fat-free mass, a proxy for skeletal muscle mass, accounting for the protective effect.[35] Additionally, the expiratory reserve capacity and end-expiratory lung volume are less in obese COPD patients.[36] There is also a decrease in hyperinflation as a result of weight-related restrictions that counterbalance obstructive lung defects.[37] Ultimately, the processes underpinning the "obesity paradox" need to be further investigated and clarified.

By increasing the position of the diaphragm in the thoracic cavity as a person gains weight, obesity impairs lung function and increases the effort required to breathe. It also prevents the thoracic cage from moving freely because of direct resistance and/or abnormal functioning of the intercostal muscles brought on by fat accumulation in the chest wall. Therefore, obesity is typically associated with lung volume abnormalities, and not airway obstruction.[38] The findings of Wang et al support this wherein FVC was found to be decreased in obese people, but not the FEV_1, FEV_1/FVC, peak expiratory flow, and FEF_{25-75}.[38] Similarly, Al Ghobain et al did not find a significant correlation between BMI and post-bronchodilator FEV_1, FEV_1/FVC, and $FEF_{25-75\%}$[17] However, in the present study, a weak correlation was seen.

The difference in the results of this study with previous studies may be attributed to the difference in the population used. Based on research, body fat distribution and BMI vary among populations. Asians have a greater body fat percentage and a lower average BMI than Americans and Europeans.[39] The different cut-off scores used to classify obesity (e.g., WHO 30 kg/m^2, Asian 25 kg/m^2, and Chinese 28 kg/m^2) may have also affected the finding[40]

In terms of the association between BMI and spirometric parameters, the study did not find a significant correlation with most parameters. For those parameters with significant correlation, these were found to be weak. The results are in contrast with the study of Salahuddin et al which showed a decreasing trend of bronchodilator response with increasing BMI.[41]

The study has a number of limitations. As a cross-sectional study, it cannot establish causation. Despite an adequate sample size, the estimated accuracy may be limited by the comparatively lower sample sizes in a number of subgroups. Because of the observational, records-based design of the study, the outcomes could have been biased by unmeasured or unknown confounders. There may not be enough standardization of the procedure performed in terms of the technician's role in performing the pulmonary function test in which the attitude of a well-motivated and enthusiastic technician is vital for its successful performance.[42] The study also did not account for the type of test performed (e.g., simple or complete spirometry, with or without DLCO [diffusing capacity for carbon monoxide]) and severity of obstruction. Further, this study did not mention the comorbid conditions of the subjects, and adjustment for the presence of asthma and COPD was not done. It is recommended that prospective studies with equal sample sizes of subgroups be done in the future, with inclusion of other demographic data such as comorbid conditions (e.g., asthma, COPD) which may affect the actual relationship between BMI and airway obstruction. Likewise, as fat accumulation greatly affects lung functions, future studies may also take into account other body measurements such as chest circumference, abdomen circumference, and hip circumference, or their ratios.

CONCLUSION

This study observed that BMI is not correlated with spirometric parameters, and obesity is not associated with obstructive ventilatory defect or post-bronchodilator FEV_1. Although some correlations are observed with BMI and post-bronchodilator spirometric parameters, the observed correlations are weak. Further studies are needed to determine the effect of other measures of body mass on obstructive ventilatory defect.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Authors' Disclosure

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References

1. Bousquet J, Dahl R, Khaltaev N. Global Alliance against Chronic Respiratory Diseases. *Allergy*. 2007;62(3):216-223. https://doi.org/10.1111/j.1398-9995.2007.01307
2. Nicolas J. Study aims to look at COPD prevalence in PHL. BusinessWorld Online. Published October 26, 2017. Accessed November 2024. https://www.bworldonline.com/health/2017/10/27/67658/study-aims-look-copd-prevalence-phl/
3. The Global Asthma Report 2018. globalasthmareport.org. Accessed November 2023. http://globalasthmareport.org/2018/burden/burden.php
4. Varona LL, HA A, Jovilia Abong, Kwong SL. Varona LL, Alava HA, Abong J, Castor MR, De Leon JC, Kwong SL for the 2008 NNHeS group. Prevalence of asthma among Filipino adults based on the National Nutrition and Health Survey (NNHeS). *Philippine Journal of Internal Medicine*. 2014;52(4):1-7. Accessed November 2023. https://www.researchgate.net/publication/301363443_Varona_LL_Alava_HA_Abong_J_Castor_MR_De_Leon_JC_Kwong_SL_for_the_2008_NNHeS_group_Prevalence_of_asthma_among_Filipino_adults_based_on_the_National_Nutrition_and_Health_Survey_NNHeS_Phil_J_Int_Med_2014
5. Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *American Journal of Respiratory and Critical Care Medicine*. 2013;187(4):347-365. https://doi.org/10.1164/rccm.201204-0596PP
6. Pelegrino NRG, Faganello MM, Sanchez FF, Padovani CR, de Godoy I. Relationship between body mass index and asthma severity in adults. *J Bras Pneumol.* 2007;33(6):641-646. Accessed November 2023. https://repositorio.unesp.br/server/api/core/bitstreams/71aa96f1-f473-43da-8073-fe221de49d00/content
7. WHO Consultation on Obesity (1999): Geneva S, Organization

WHO. *Obesity : Preventing and Managing the Global Epidemic: Report of a WHO Consultation*. World Health Organization; 2000. Accessed November 2023. https://iris.who.int/handle/10665/42330
8. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma. *American Journal of Respiratory and Critical Care Medicine*. 2007;175(7):661-666. https://doi.org/10.1164/rccm.200611-1717oc
9. Guerra S, Sherrill DL, Bobadilla A, Martinez FD, Barbee RA. The Relation of Body Mass Index to Asthma, Chronic Bronchitis, and Emphysema. *Chest*. 2002;122(4):1256-1263. https://doi.org/10.1378/chest.122.4.1256
10. Ford E. The epidemiology of obesity and asthma. *Journal of Allergy and Clinical Immunology*. 2005;115(5):897-909. https://doi.org/10.1016/j.jaci.2004.11.050
11. Camargo CA, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Archives of Internal Medicine*. 1999;159(21):2582-2588. https://doi.org/10.1001/archinte.159.21.2582
12. Banerjee J. Association of body mass index (BMI) with lung function parameters in non-asthmatics identified by spirometric protocols. *Journal of Clinical and Diagnostic Research*. 2014;8(2). https://doi.org/10.7860/jcdr/2014/7306.3993
13. Chen Y, Rennie D, Cormier Y, Dosman J. Sex Specificity of asthma associated With objectively measured body mass index and waist circumference. *Chest*. 2005;128(4):3048-3054. https://doi.org/10.1378/chest.128.4.3048
14. Davis A, Lipsett M, Milet M, Etherton M, Kreutzer R. An Association between asthma and BMI in adolescents: Results from the California Healthy Kids Survey. *Journal of Asthma*. 2007;44(10):873-879. https://doi.org/10.1080/02770900701752656
15. Coogan PF, Palmer JR, O'Connor GT, Rosenberg L. Body mass index and asthma incidence in the Black Women's Health Study. *The Journal of Allergy and Clinical Immunology*. 2009;123(1):89-95. https://doi.org/10.1016/j.jaci.2008.09.040
16. Hjellvik V, Tverdal A, Furu K. Body mass index as predictor for asthma: a cohort study of 118,723 males and females. *European Respiratory Journal*. 2010;35(6):1235-1242. https://doi.org/10.1183/09031936.00192408
17. Al Ghobain M. The effect of obesity on spirometry tests among healthy non-smoking adults. *BMC Pulmonary Medicine*. 2012;12(1). https://doi.org/10.1186/1471-2466-12-10
18. Hancox RJ, Milne BJ, Poulton R, et al. Sex differences in the relation between body mass index and asthma and atopy in a birth cohort. *American Journal of Respiratory and Critical Care Medicine*. 2005;171(5):440-445. https://doi.org/10.1164/rccm.200405-623oc
19. Zhu J, Zhao Z, Wu B, et al. Effect of body mass index on lung function in Chinese patients with chronic obstructive pulmonary disease: A multicenter cross-sectional study. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2477-2486. https://doi:10.2147/COPD.S265676
20. Landbo C, Prescott E, Lange P, Vestbo J, Almdal Thomas P. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 1999;160(6):1856-1861. https://doi.org/10.1164/ajrccm.160.6.9902115
21. Chua JR, Albay Jr AB, Tee ML. Body composition of Filipino chronic obstructive pulmonary disease (COPD) patients in relation to their lung function, exercise capacity and quality of life. *International Journal of Chronic Obstructive Pulmonary Disease*. 2019;14:2759-2765. https://doi.org/10.2147/copd.s222809
22. Mc P, S S. Pulmonary Function Tests. PubMed. Published 2023. Accessed November 2023. https://pubmed.ncbi.nlm.nih.gov/29493964/
23. David S, Edwards CW. Forced expiratory volume. PubMed. Published August 8, 2022. Accessed November 2023. https://www.ncbi.nlm.nih.gov/books/NBK540970/
24. Weerakkody Y. Restrictive lung disease | Radiology Reference Article | Radiopaedia.org. Radiopaedia. Accessed November 2023. https://radiopaedia.org/articles/restrictive-lung-disease
25. Ronish BE, Couper DJ, Barjaktarevic IZ, et al. Forced expiratory Flow at 25%-75% links COPD physiology to emphysema and disease severity in the SPIROMICS cohort. *Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation*. 2022;9(2):111-121. https://doi.org/10.15326/jcopdf.2021.0241
26. Grigsby MR, Siddharthan T, Pollard SL, et al. Low body mass index is associated with higher odds of COPD and lower lung function in low- and middle-income countries. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2019;16(1):58-65. https://doi.org/10.1080/15412555.2019.1589443
27. Svartengren M, Cai GH, Malinovschi A, et al. The impact of body mass index, central obesity and physical activity on lung function: results of the EpiHealth study. *ERJ Open Research*. 2020;6(4):00214-2020. https://doi.org/10.1183/23120541.00214-2020
28. Molani Gol R, Rafraf M. Association between abdominal obesity and pulmonary function in apparently healthy adults: A systematic review. *Obesity Research & Clinical Practice*. Published online July 2021. https://doi.org/10.1016/j.orcp.2021.06.011
29. Tang X, Lei J, Li W, et al. The relationship between BMI and lung function in populations with different characteristics: A cross-sectional study based on the Enjoying Breathing Program in China. *International Journal of Chronic Obstructive Pulmonary Disease*. 2022;17:2677-2692. https://doi.org/10.2147/copd.s378247
30. Makker H. Obesity and respiratory diseases. *International Journal of General Medicine*. 2010;3:335. https://doi.org/10.2147/ijgm.s11926
31. Mohanan S, Tapp H, McWilliams A, Dulin M. Obesity and asthma: Pathophysiology and implications for diagnosis and management in primary care. *Experimental Biology and Medicine*. 2014;239(11):1531-1540. https://doi.org/10.1177/1535370214525302
32. Schachter LM. Obesity is a risk for asthma and wheeze but not airway hyperresponsiveness. *Thorax*. 2001;56(1):4-8. https://doi.org/10.1136/thorax.56.1.4
33. Liu Y, Pleasants RA, Croft JB, et al. Body mass index, respiratory conditions, asthma, and chronic obstructive pulmonary disease. *Respiratory Medicine*. 2015;109(7):851-859. https://doi.org/10.1016/j.rmed.2015.05.006
34. Gea J, Pascual S, Casadevall C, Orozco-Levi M, Barreiro E. Muscle dysfunction in chronic obstructive pulmonary disease: update on causes and biological findings. *J Thorac Dis*. 2015;7(10):E418-E438. https://doi.org/10.3978/j.issn.2072-1439.2015.08.04
35. Park CH, Yi Y, Do JG, Lee YT, Yoon KJ. Relationship between skeletal muscle mass and lung function in Korean adults without clinically apparent lung disease. *Medicine (Baltimore)*. 2018;97(37):e12281. https://doi.org/10.1097/MD.0000000000012281
36. Guenette JA, Jensen D, O'Donnell DE. Respiratory function and the obesity paradox. *Current Opinion in Clinical Nutrition & Metabolic Care*. 2010;13(6):618-624. https://doi.org/10.1097/MCO.0b013e32833e3453
37. Schaeffer MR, Kumar DS, Assayag D, et al. Association of BMI with pulmonary function, functional capacity, symptoms, and quality of life in ILD. *Respiratory Medicine*. 2022;195:106792. https://doi.org/10.1016/j.rmed.2022.106792
38. Wang S, Sun X, Hsia TC, Lin X, Li M. The effects of body mass index on spirometry tests among adults in Xi'an, China. *Medicine (Baltimore)*. 2017;96(15):e6596. https://doi.org/10.1097/MD.0000000000006596

39. Oh SW, Shin SA, Yun YH, Yoo T, Huh BY. Cut-off point of BMI and obesity-related comorbidities and mortality in middle-aged Koreans. *Obes Res*. 2004;12(12):2031-2040. https://doi.org/10.1038/oby.2004.254
40. Zhang X, Chen H, Gu K, Chen J, Jiang X. Association of body mass index with risk of chronic obstructive pulmonary disease: A systematic review and meta-analysis. *COPD*. 2021;18(1):101-113. https://doi.org/10.1080/15412555.2021.1884213
41. Salahuddin M, Vasudevan A, Rodriguez M, Mora J. The effect of obesity on bronchodilator responsiveness in asthma patients. *Chest*. 2016;150(4):846A. https://doi.org/https://

Original Article

Relationship Between White Blood Cell, Neutrophil-to-Lymphocyte Ratio, Procalcitonin, and Severe Community-Acquired Pneumonia in a Private Tertiary Hospital

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ABSTRACT

Background: Studies have tried to determine the diagnostic value of serum inflammatory biomarkers in patients with community-acquired pneumonia (CAP) to help guide clinical decision making. This study aimed to determine the relationship between white blood cell (WBC), neutrophil-to-lymphocyte ratio (NLR), procalcitonin (PCT), and severe CAP.

Methodology: This study reviewed records of patients aged 18 years and above diagnosed with CAP from January 2022 to January 2024 at Perpetual Help Medical Center—Las Piñas. Data collected were demographics, WBC and neutrophil and lymphocyte counts, procalcitonin, and CURB-65 scores. Receiver operating characteristic (ROC) curve analysis was done to determine the best cut-off for WBC, NLR, and procalcitonin in diagnosing severe CAP (CURB-65 score 3 to 5). Pearson correlation test was used to determine pairwise correlations between WBC, NLR, and procalcitonin.

Results: A total of 120 patients were included. The mean WBC count and mean NLR were higher among patients with elevated PCT than those with normal PCT (15.2 ± 5.8 vs 10.7 ± 3.7; p <0.001 and 18.6 ± 17.9 vs 8.6 ± 7.9; p = 0.005, respectively). The prevalence of severe pneumonia was higher in patients with elevated PCT than those with normal PCT (65.8% vs 12.8%; p <0.001). Procalcitonin level at a threshold of 0.5 ng/mL showed the highest sensitivity (90%, 95% confidence interval [CI] 0.77 to 0.97) and best test performance (area under the ROC 0.79, 95% CI 0.72 to 0.86) in diagnosing severe pneumonia. The mean NLR was weakly correlated with WBC (r = 0.300; p = 0.002). The mean PCT was moderately correlated with WBC (r = 0.637, p = 0.04) and NLR (r = 0.750, p = 0.03).

Conclusions: Procalcitonin shows acceptable performance in diagnosing severe pneumonia. This study also suggests a significant correlation between WBC, NLR, and PCT. Multicenter studies are recommended to better generalize the results to the larger population.

Keywords: pneumonia, neutrophil/lymphocyte ratio, procalcitonin, CURB-65

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INTRODUCTION

Community-acquired pneumonia is a leading cause of mortality and morbidity worldwide.[1] The incidence of CAP in the Philippines is 4,205 patients per 100,000 discharges.[2] CAP, a type of lower respiratory tract infection (LRTI), is diagnosed by the presence of infiltrates on chest imaging in patients with fever, dyspnea, cough, and sputum.[1] Clinical signs and symptoms of bacterial and viral LRTIs are often indistinguishable. Microbiologic testing is helpful but often takes days until a pathogen is identified.[3] Nowadays, biomarkers combined with clinical risk scores are used to identify specific patients at risk, assess the severity of illness and prognosticate patients, and guide antibiotic therapy.[4]

Researchers have explored the prognostic value of serum inflammatory biomarkers like white blood cell (WBC) and procalcitonin (PCT) in CAP patients.[5,6,7] The WBC subpopulation is of note in the systemic inflammatory response to infection, with neutrophilia and lymphocytopenia recognized as possible markers in infectious disease management.[4] The neutrophil-to-lymphocyte ratio (NLR), a ratio between neutrophil and lymphocyte counts, is a biomarker which relates the innate and adaptive immune response supported by neutrophils and lymphocytes, respectively.[8] An increased NLR is associated with a high CURB-65 score, intensive care unit admission, and mortality.[4]

Procalcitonin, another serum biomarker, helps differentiate bacterial infection from other causes of infection or inflammation and is widely used to guide antibiotic therapy in LRTI patients. It is generally used to determine the need to continue antibiotic therapy.[1] Non-infectious conditions may also elevate PCT levels. These conditions include trauma, burn, medullary C-cell carcinoma, small cell carcinoma of the lung and bronchial carcinoid, immunomodulatory therapy, cardiogenic shock, during peritoneal dialysis, and in some patients with cirrhosis or chronic kidney disease. Clinicians must take note of the above conditions that might affect PCT levels.[9]

Several studies have tried to determine the relationship of NLR and PCT to CAP, separately, with promising results.[6,7] However, there are also studies on both NLR and procalcitonin showing no significant relationship with CAP.[5] This study aimed to determine the correlation between WBC, NLR, PCT, and severe CAP in patients admitted in Perpetual Help Medical Center – Las Piñas. Further, optimal cut-off values for WBC, NLR and PCT to diagnose severe CAP were determined. CURB-65 (confusion, uremia, respiratory rate, BP, age ≥65 years) was used to classify pneumonia as severe. Capelastegui et al. reported that patients with CURB-65 score of more than two are high risk for mortality and should be managed as having severe pneumonia.[10] No local data has yet examined the relationship between WBC, NLR and PCT in severe CAP.

METHODOLOGY

Research design
The study used a cross-sectional, records-based design.

Study site
Perpetual Help Medical Center – Las Piñas is a tertiary hospital which caters to patients with CAP.

Target population
The research included patients aged 18 years old and above who were admitted in Perpetual Help Medical Center – Las Piñas, with a diagnosis of CAP from January 2022 to January 2024.

Inclusion/exclusion criteria
Cases of CAP were identified based on the diagnosis of the treating physicians as reflected in the medical record. Excluded from this study were patients with a history of tumors, burns, trauma, surgery, kidney disease, inflammatory diseases, immunosuppression, extrapulmonary infections, or CAP but with no procalcitonin results upon admission. Likewise, patients who were diagnosed with COVID-19 and pulmonary tuberculosis were excluded.

Study procedure
The investigator obtained permission to access medical records of adult patients who were diagnosed with CAP in Perpetual Help Medical Center – Las Piñas. Simple random sampling was done. Each eligible patient was assigned a number and a table of random numbers was used to select participants for the study.

The researcher reviewed medical records to fill-up the data collection tool. Data on patient demographics, neutrophil and lymphocyte counts, and PCT levels on the first day of admission were collected. NLR was measured by dividing the number of neutrophils by the number of lymphocytes. CURB-65 scores were computed using data upon admission. Severe CAP was identified in patients with a CURB-65 score of greater than two.

Patients were divided into two groups: those with normal PCT levels and those with elevated PCT levels.

Sample size calculation
To answer the primary objective of determining the correlation between WBC, NLR, and PCT, the minimum sample size for a two-tailed correlational analysis was calculated. Based on 95% confidence interval, mean effect size of 0.25,5 with 80% power, at least 120 patients were needed. This was also sufficient to detect a medium effect size of 0.5 in an independent t-test with 80% power and 95% confidence interval. Calculations were done using G*Power software v3.1.9.7. Based on patient census, the study site had enough number of patients to meet the sample size for the study.

Data processing and encoding
Data was encoded in a tabulated form using SPSS for Windows version 20.

Data analysis
Data was analyzed using IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as means ± standard deviations and counts (percentages). Chi-square test was used to compare categorical data. Independent Student's t-test was used to compare mean WBC, neutrophil, lymphocyte, and NLR by PCT level. Analysis of the area under the receiver operating characteristic (AUROC) curves was used to determine the best cut-off value for WBC, NLR, and PCT to diagnose severe CAP. The optimal cut-off was defined as the point where sensitivity and specificity values were the closest to the value of the area under the ROC, with minimal difference between them. Pearson correlation test was used to determine pairwise correlations between WBC, NLR and PCT. A p value of <0.05 was considered statistically significant.

Ethical Considerations
This research adhered to the Declaration of Helsinki and was approved by the University of Perpetual Help System—Jonelta Institutional Ethics Review Board (UPHS-IERB 2023-022 RP).

A waiver of written and verbal informed consent was requested from the IERB. The protocol was eligible for waiver or alteration of all required elements of informed consent.

RESULTS
A total of 120 patients with CAP were included, with 60.8% showing elevated PCT. The mean age was 68.2 ± 15.5 years among those with elevated PCT and 68.7 ± 16.4 years among those with normal PCT (p = 0.921). A comparison of patients' demographics and blood parameters in those with normal and elevated PCT are detailed in Table 1.

Among those with elevated PCT, 54.8% were male compared to 42.5% in the normal PCT group (p = 0.152). The mean WBC count was significantly higher among those with elevated PCT than those with normal PCT (15.2 ± 5.8 vs 10.7 ± 3.7; p <0.001). The mean neutrophil count was significantly higher among those with elevated PCT than those with normal PCT (84.0 ± 8.7 vs 75.2 ± 11.9; p <0.001). The mean lymphocyte count was significantly lower among those with elevated PCT than those with normal PCT (8.6 ± 7.0 vs 14.7 ± 9.7; p = 0.001) . The mean NLR was significantly higher among those with elevated PCT than those with normal PCT (18.6 ± 17.9 vs 8.6 ± 7.9; p = 0.005). The prevalence of severe CAP (CURB-65 score 3 to 5) was significantly higher in those with elevated PCT than those with normal PCT (65.8% vs 12.8%; p <0.001).

Table 1. Demographic data and blood parameters of patients diagnosed with CAP, with normal and elevated PCT levels

	Procalcitonin ≤0.5 ng/mL (normal)	Procalcitonin >0.5 ng/mL (elevated)	p-value
Total number of participants	47 (39.2)	73 (60.8)	
Age	68.7 ± 16.4	68.2 ± 15.5	0.921
Sex			
Male	20 (42.5)	40 (54.8)	0.152
Female	27 (57.5)	33 (45.2)	
WBC count, x $10^3/mm^3$	10.7 ± 3.7	15.2 ± 5.8	<0.001
Neutrophil count, %	75.2 ± 11.9	84.0 ± 8.7	<0.001
Lymphocyte count, %	14.7 ± 9.7	8.6 ± 7.0	0.001
NLR	8.6 ± 7.9	18.6 ± 17.9	0.005
CURB-65			
Less than 3	41 (87.2)	33 (45.2)	<0.001
3 to 5	6 (12.8)	40 (65.8)	

WBC, white blood cell; CURB-65, confusion, uremia, respiratory rate, blood pressure, age ≥65 years

Table 2. AUROC curve analysis for the prediction of severe CAP (CURB-65 score 3 to 5)

	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
WBC count, x $10^3/mm^3$	13.5	0.64 (0.54 to 0.74)	0.71 (0.61 to 0.81)	0.68 (0.54 to 0.81)
NLR	10.7	0.51 (0.45 to 0.57)	0.59 (0.53 to 0.65)	0.55 (0.45 to 0.65)
PCT, ng/ml	0.5	0.90 (0.77 to 0.97)	0.55 (0.43 to 0.67)	0.79 (0.72 to 0.86)

AUROC, area under the receiver operating characteristic curve; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio, PCT, procalcitonin

Table 3. Correlation between WBC, NLR, and PCT

	WBC	NLR	PCT
WBC	…	…	…
NLR	r = 0.300 p-value = 0.002	…	…
PCT	r = 0.637 p-value = 0.04	r = 0.750 p-value = 0.03	…

WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio, PCT, procalcitonin

In the AUROC analysis (Table 2) for diagnosing severe CAP, the WBC cut-off value was 13.5 x 103/mm3 (AUC 0.68, 95% CI 0.54 to 0.81), the NLR cut-off value was 10.7 (AUC 0.55, 95% CI 0.45 to 0.65), and the PCT cut-off value was 0.5 ng/mL (AUC 0.79, 95% CI 0.72 to 0.86). Procalcitonin showed the highest sensitivity (90%, 95% CI 0.77 to 0.97) and best test performance (AUC 0.79, 95% CI 0.72 to 0.86) in diagnosing severe CAP. However, its specificity was lowest (55%, 95% CI 0.43 to 0.67).

In Table 3, the mean NLR was significantly but weakly correlated with WBC (r = 0.300, p = 0.002). The mean PCT was significantly and moderately correlated with WBC (r = 0.637, p = 0.04) and NLR (r = 0.750, p = 0.03).

DISCUSSION

Community-acquired pneumonia is an acute infection of the pulmonary parenchyma.[2] Clinical features of bacterial and viral LRTIs are similar and cannot be solely distinguished by features alone.[1] Viral pathogens are increasingly being recognized as common causes of CAP, sometimes surpassing bacterial cases with the aid of modern diagnostic panels.[7] However, these tests are costly. In our institution, the cost of PCT testing is five times more than CBC. It also takes time before the clinician gets the results. This is probably why antibiotic therapy is essentially empirical in most cases of pneumonia.[8] Studies have been done to determine the use of biologic markers in predicting the severity of illness, for prognostication in patients with CAP. and to guide antibiotic therapy.[4,5] In this retrospective cross-sectional study, WBC, neutrophil, NLR, and CURB-65 scores were found to be significantly higher in patients with elevated procalcitonin, while lymphocyte count was significantly lower in those with elevated procalcitonin. In a study done by Cil et al., WBC, neutrophil, and NLR were also found to be significantly higher in patients with elevated procalcitonin.[5]

Our study showed a weak correlation between NLR and WBC. PCT was significantly and moderately correlated with WBC and NLR. This is supported by previous studies done by Beyaz et al. and Huang et al.,[6,7] wherein a positive correlation was found between PCT and NLR. However, this study finding differs from a study done by Cil et al. wherein no significant correlation was found between PCT and NLR.[5]

The WBC cut-off value was determined to be 13.5 x $10^3/mm^3$ (AUC 0.68), NLR cut-off 10.7 (AUC 0.55), and PCT cut-off 0.5 ng/ml (AUC 0.79) in this study. Procalcitonin showed the highest sensitivity (90%) and best test performance (AUC 0.79) in diagnosing severe pneumonia, while Cil et al. found the highest AUC with neutrophil counts.[5]

Findings on the correlation of PCT with NLR and WBC were different among different studies. In a study by Beyaz et al.[6] PCT and NLR were observed to be correlated in pneumonia patients. However, Cil et al. found no correlation between PCT and NLR.[5] Our study found significant correlations between WBC, NLR, and PCT suggesting that these markers could reflect the magnitude of inflammatory response in CAP patients, with PCT showing the highest sensitivity and best test performance in diagnosing severe CAP. These biomarkers may be used with PCT instead of PCT alone. However, in our country where most patients have budget constraints, because of the correlations seen between NLR, WBC, and PCT, NLR may be used since it is cheaper than serum procalcitonin.[12]

There are a few limitations to the study. Because data was secondarily obtained from records, the quality of data cannot be fully assured. The study does not differentiate between viral and bacterial pneumonia since culture studies and viral panel results were not collected. Patients with viral pneumonia who were classified as severe CAP might have distorted the results. The use of CURB-65 to determine pneumonia severity might have caused misclassification bias. Patients with higher-risk CAP without requested procalcitonin were excluded from the study, hence, possibly affecting the generalizability of results.

Despite these limitations, this study still provides valuable insights on the relationship between WBC, NLR, PCT, and severe CAP. To the best of our knowledge, there is no previous research in the Philippines with regard to their relationship. Further studies can be done in a multicenter approach to better generalize the results to a larger population. We recommend that WBC, NLR, PCT be used as an adjunct to CURB-65 in determining pneumonia severity. Other scoring systems may be utilized to further support the diagnosis of severe pneumonia.

CONCLUSION

Evaluating PCT and complete blood count parameters particularly WBC and NLR may assist clinicians in diagnosing and managing patients with severe CAP. With the significant correlations of the biomarkers and the high cost of PCT, WBC and NLR may be cheaper alternatives in some clinical settings. The high sensitivity of PCT may assist the clinician to consider the severity of patient's infection but complete assessment is best due to its low specificity.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Authors' Disclosure
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References

1. Ramirez, J. A. (n.d.). Overview of community-acquired pneumonia in adults. UpToDate. Accessed April 23, 2023. https://www.uptodate.com/contents/overview-of-community-acquired-pneumonia-in-adults
2. Shirley Paz B, B., Joel, S., & Adolf, L.-T. Prevalence, demographic, clinical characteristics and outcomes of elderly patients with community acquired pneumonia admitted in a tertiary medical center: A retrospective cohort study. *Journal of Geriatric Medicine and Gerontology*. 2021;*7*(3). https://doi.org/10.23937/2469-5858/1510117
3. Rhee, C., & Mansour, M. K. (n.d.). Procalcitonin use in lower respiratory tract infections. UpToDate. Accessed April 23, 2023. https://www.uptodate.com/contents/procalcitonin-use-in-lower-respiratory-tract-infections
4. de Jager, C. P., Wever, P. C., Gemen, E. F., Kusters, R., van Gageldonk-Lafeber, A. B., van der Poll, T., & Laheij, R. J. The Neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia. *PLoS ONE*. 2012;*7*(10). https://doi.org/10.1371/journal.pone.0046561
5. Çil E, Karadeniz G, Yenigün S, Çoraplı G. Evaluation of the relationships between procalcitonin and neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients with pneumonia. *Eur Rev Med Pharmacol Sci*. 2022;26(9):3200-3205. https://doi.org/10.26355/eurrev_202205_28738. PMID: 35587071
6. Beyaz A, Atilla N, Arpağ H, Bozkuş F, Kahraman H, Uğuz FA. The effect of C-reactive protein, procalcytonine, neutrophil/lymphocyte levels on mortality and duration of hospital stay in pneumonia. *Anatolian Curr Med J*. 2021;3(1):15-19. https://doi.org/10.38053/acmj.1023590
7. Huang Y, Liu A, Liang L, et al. Diagnostic value of blood parameters for community-acquired pneumonia. *Int Immunopharmacol*. 2018;64:10-15. https://doi.org/ 10.1016/j.intimp.2018.08.022. Epub 2018 Aug 23. PMID: 30144639
8. Buonacera, A., Stancanelli, B., Colaci, M., & Malatino, L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. *International Journal of Molecular Sciences*. 2022;*23*(7):3636. https://doi.org/10.3390/ijms23073636
9. Cleland DA, Eranki AP. Procalcitonin. [Updated 2023 Apr 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. https://www.ncbi.nlm.nih.gov/books/NBK539794/
10. Capelastegui A, España PP, Quintana JM, et al. Validation of a predictive rule for the management of community-acquired pneumonia. *European Respiratory Journal*. 2006;27(1):151-157. https://doi.org/10.1183/09031936.06.00062505
11. Waterer G. W. Diagnosing Viral and Atypical Pathogens in the Setting of Community-Acquired Pneumonia. *Clinics in Chest Medicine*. 2017;*38*(1):21–28. https://doi.org/10.1016/j.ccm.2016.11.004
12. Najm, R. A., AL-dujaili, A. N. G., & Hashim, J. M. Study of Procalcitonin and neutrophil/ lymphocyte count ratio in children infected with Community-acquired pneumonia. *International Journal of Health Sciences*. 2022;6(S1):4218–4232. https://doi.org/10.53730/ijhs.v6nS1.5845
13. Aryani IGAD, Mayangsari ASM, Gunawijaya E, et al. Agreement between neutrophil/lymphocyte ratio and procalcitonin for determining severe community acquired pneumonia in children. *Sri Lanka Journal of Child Health*. 2022;51(4):547. https://doi.org /10.4038/sljch.v51i4.10368

Due to a technical error, the manuscript underwent single-anonymous rather than double-anonymous review. The reviewers confirmed that their review of the manuscript was unbiased and they had no conflicts of interest in reviewing the article.

Case Report

Emergence of *Candida famata* Fungemia in an Immunocompromised Patient: A Case Report Highlighting Clinical Presentation, Diagnosis, and Therapeutic Strategy

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ABSTRACT

Candida famata, once regarded as benign, is now being recognized as an opportunistic pathogen. This case presents an 88-year-old male with multiple comorbidities who developed *C. famata* bloodstream infection during treatment for healthcare-associated pneumonia complicated by prolonged central catheter use and hospital stay. Antifungal therapy with voriconazole led to clinical improvement and eventual discharge of the patient in stable condition. The rarity of *C. famata* infection presents diagnostic and therapeutic challenges. This case highlights the importance of timely antifungal therapy and a multidisciplinary approach in managing invasive candidiasis, particularly in immunocompromised patients. Further research is needed to optimize treatment.

Keywords: *Candida famata* fungemia, immunocompromised host, voriconazole, invasive candidiasis, case report

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INTRODUCTION

Candida famata, formerly recognized as *Debaryomyces hansenii* and *Torulopsis candida* and historically regarded as a benign commensal yeast, has recently emerged as an opportunistic pathogen in human infections.[1] Initially isolated from dairy products, marine environments, and animals, its pathogenic potential was underestimated until the early 2000s.[2-4] Although *C. famata* accounts for 0.2 to 2% of *Candida* bloodstream infections, its clinical significance is growing due to its reduced susceptibility to antifungal agents such as fluconazole and echinocandins.[6]

The rise in *C. famata* infections emphasizes the need for heightened clinical vigilance, especially in patients with predisposing risk factors such as prolonged hospitalizations, invasive procedures, or prior antimicrobial use. This case report presents the diagnostic and therapeutic challenges of *C. famata* fungemia in an elderly, immunocompromised patient, stressing the importance of early recognition and prompt antifungal therapy. This report adds to the growing literature on rare fungal pathogens and their management in modern healthcare.

CASE PRESENTATION

We present the case of an 88-year-old Filipino male with chronic obstructive pulmonary disease, type 2 diabetes mellitus (non-insulin requiring), coronary artery disease, chronic kidney disease stage IV, and hypertension. The patient had recurrent hospitalizations due to various medical conditions such as sepsis, pneumonia, and post-Guillain-Barré syndrome. He also completed steroid therapy and received multiple antibiotics.

One month prior to admission, the patient experienced progressive loss of appetite and generalized body weakness without other symptoms. Six days before admission, he developed an undocumented fever and occasional dry cough. Progressive symptoms prompted the visit to the emergency department (ED). Upon arrival at the ED, the patient was bradycardic (pulse rate 30 to 40 beats per minute), tachypneic (respiratory rate 22 to 28 cycles per minute), and had oxygen saturation of 96% at room air. Physical examination revealed pale conjunctivae, dry lips, generalized crackles, occasional wheezing, and whitish plaques on the tongue, palate, and buccal mucosa. A chest X-ray revealed pneumonic infiltrates in the right paracardiac area and ipsilateral pleural effusion (Figure 1A). The patient was diagnosed with healthcare-associated pneumonia with right parapneumonic pleural effusion, atrial fibrillation with slow ventricular response, and congestive heart failure.

Cefepime was initially started but, on the seventh hospital day, the patient developed high-grade fever, tachycardia, tachypnea, and hypotension. He produced copious yellowish sputum and became progressively drowsier. Repeat laboratory investigations revealed leukocytosis with predominant neutrophilic response. A repeat chest X-ray revealed progression of basal pneumonia. Cefepime was shifted to meropenem.

On the same day, a peripherally inserted central catheter (PICC) was placed at the R basilic vein. Blood cultures were drawn from two peripheral sites which grew *Candida famata* (Figure 2) in one site and *Staphylococcus hemolyticus* in another. Based on these results, vancomycin and voriconazole 200 mg IV once daily were added.

On the 12th day, the patient developed red man syndrome from vancomycin, prompting the switch to linezolid. The right PICC line was removed and replaced with a new one in the left arm. Despite these measures, the patient remained febrile and developed respiratory failure, requiring high-flow oxygen and methylprednisolone. Meropenem was shifted to imipenem.

By the 15th hospital day, the patient appeared more comfortable and was clinically stable. High-flow oxygen was

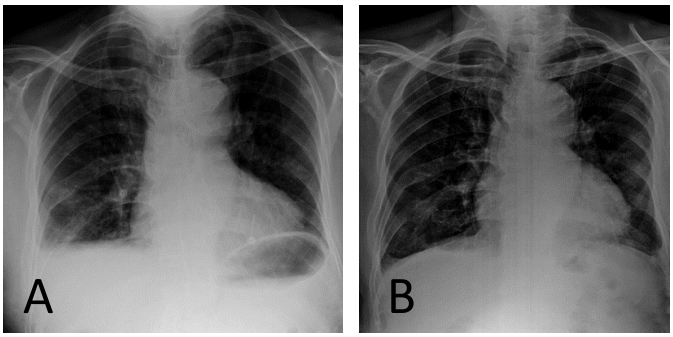

Figure 1. Chest radiographs on admission and upon discharge. Pneumonic infiltrates in the right paracardiac area and right-sided pleural effusion were noted during admission (A). There was regression of findings in the discharge chest X-ray (B).

gradually titrated down until weaned off. Repeat blood culture indicated persistent fungemia, with sensitivity to voriconazole. The dose of voriconazole was increased to 200 mg IV every 12 hours (weight-adjusted). The left PICC line was removed.

By the 17th hospital day, the patient showed marked improvement, without recurrence of fever, and with resolution of pneumonia on chest X-ray (Figure 1B). Repeat blood cultures from two sites showed no growth which confirmed resolution of the infection. After three weeks of voriconazole, two weeks of imipenem, and two weeks of linezolid, the patient was discharged in an improved condition.

DISCUSSION

Managing *Candida famata* bloodstream infections presents significant challenges, especially in immunocompromised patients with multiple comorbidities. Once considered non-pathogenic, *C. famata* has emerged as an opportunistic pathogen, particularly in individuals with weakened immune systems.[11,12,13] The rarity of *C. famata* infection, accounting for only 0.08 to 0.5% of invasive candidiasis cases, complicates diagnosis and treatment. Its reduced susceptibility to common antifungals such as fluconazole and echinocandins adds complexity to the management. [14,15]

In this case, voriconazole was chosen for its broad-spectrum activity and susceptibility profile on blood culture. A second-generation triazole, voriconazole is effective against a variety of fungi, well-tolerated, and distributes widely in body fluids, making it an effective agent in systemic fungal infections.[16] It is also available in both oral and intravenous formulations, making it suitable for patients requiring prolonged antifungal therapy.

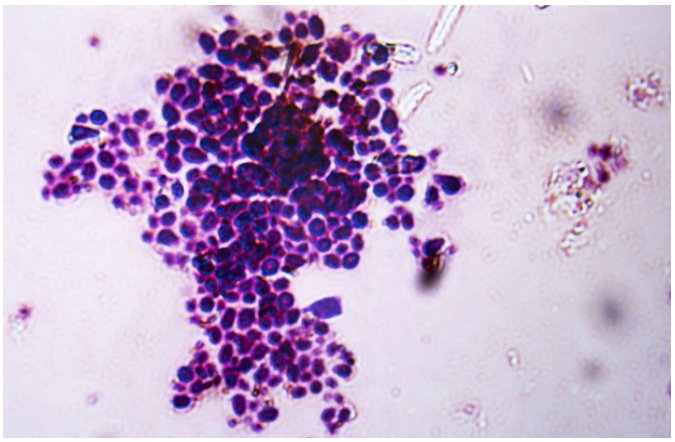

Figure 2. *Candida famata* seen under light microscope at 40x using Gram stain. The specimen was grown in blood culture using VITEC 2 technology and YST card or identification.

After dose adjustment of voriconazole following clinical guidelines and with removal of catheter, the patient's condition improved with prolonged three-week voriconazole therapy.[16] Studies have demonstrated voriconazole's similar efficacy to amphotericin B, and better safety profile especially in patients with renal impairment, because of fewer nephrotoxic effects.[17]

The rarity of *C. famata* infection makes standardized treatment protocols challenging. As highlighted in the case, prompt antifungal therapy and central venous catheter removal are critical to effective management.

The management of *C. famata* bloodstream infections requires close collaboration among infectious disease specialists, microbiologists, and intensivists to optimize therapeutic strategies and patient outcomes. While more extensive studies are needed to establish standardized treatment protocols, our experience suggests that voriconazole remains an effective therapeutic agent, especially in patients without prior antifungal exposure. Timely recognition, appropriate antifungal susceptibility testing, and individualized therapeutic adjustments are key to managing these rare infections effectively.

CONCLUSION

This case emphasizes the emerging importance of *Candida famata* as an opportunistic pathogen, especially in immunocompromised patients with central venous catheters. Its reduced susceptibility to common antifungals like fluconazole and echinocandins poses therapeutic challenges.

Voriconazole proved effective in this case, particularly given the patient's lack of prior antifungal exposure. Despite initial complications like persistent fungemia, adjustments in antifungal therapy, catheter removal, and close monitoring led to the patient's clinical improvement.

Early recognition and timely, targeted antifungal therapy are crucial for managing invasive candidiasis. A multidisciplinary approach is key to optimizing care, and further research is needed to refine treatment strategies and improve outcomes for vulnerable populations.

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Ethical Consideration

The authors declared that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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References

1. Voronovsky AY, Abbas CA, Dmytruk KV, et al. *Candida famata* (Debaryomyces hansenii) DNA sequences containing genes involved in riboflavin synthesis. *Yeast*. 2004;21(15):1307-1316. https://doi.org/10.1002/yea.1173
2. Desnos-Ollivier M, Ragon M, Robert V, Raoux D, Gantier J-C, Dromer F. *Debaryomyces hansenii* (*Candida famata*), a rare human fungal pathogen often misidentified as *Pichia guilliermondii* (*Candida guilliermondii*). *J Clin Microbiol*. 2008;46(10):3237-3242. https://doi.org/10.1128/JCM.00855-08
3. Jang YH, Lee SJ, Lee JH, Chae HS, Kim SH, Choe NH. Prevalence of yeast-like fungi and evaluation of several virulence factors from feral pigeons in Seoul, Korea. *Lett Appl Microbiol*. 2011;52(4):367-371. https://doi.org/10.1111/j.1472-765X.2011.03002.x
4. Nawange SR, Singh K, Naidu J, Singh SM. Naturally acquired systemic dual infection caused by *Candida famata* (Debaryomyces hansenii) and *Candida catenulata* in albino rats bred for sale in the market at Jabalpur (Madhya Pradesh), India. *Mycoses*. 2010;53 (2):173-175. https://doi.org/10.1111/j.1439-0507.2009.01777.x
5. Al-Hedaithy SS. The yeast species causing fungemia at a university hospital in Riyadh, Saudi Arabia, during a 10-year period. *Mycoses*. 2003;46(8):293-298. https://doi.org/10.1046/j.1439-0507.2003.00893.x
6. Beyda ND, Chuang SH, Alam MJ, et al. Treatment of *Candida famata* bloodstream infections: case series and review of the literature. *J Antimicrob Chemother*. 2013;68(2):438-443. https://doi.org/10.1093/jac/dks390
7. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for CYP2C19 and Voriconazole Therapy. Clinical Pharmacogenetics Implementation Consortium (CPIC). Available at: https://cpicpgx.org/. Accessed October 20, 2024
8. Badee P, Badali H, Boekhout T, et al. Antifungal susceptibility testing of *Candida* species isolated from immunocompromised patients admitted to ten university hospitals in Iran: comparison of colonizing and infecting isolates. *BMC Infect Dis*. 2017;17(1):727. https://doi.org/10.1186/s12879-017-2827-y
9. Karapetsa M, Tsolaki V, Arabatzis M, Petinak E, Velegraki A, Zakynthinos E. Septic shock due to *Candida famata* (Debaryomyces hansenii) candidemia in an ICU immunocompetent trauma-patient. *Med Mycol Case Rep*. 2018;22:69-72. https://doi.org/10.1016/j.mmcr.2018.11.001
10. Silva S, Negri M, Henriques M, Oliveira R, Williams D, Azeredo J. *Candida glabrata, Candida parapsilosis* and *Candida tropicalis*: biology, epidemiology, pathogenicity, and antifungal resistance. *FEMS Microbiol Rev*. 2012;36(2):288-305. https://doi.org/10.1111/j.1574-6976.2011.00278.x
11. Deorukhkar SC, Saini S, Mathew S. Non-albicans *Candida* infection: an emerging threat. *Interdiscip Perspect Infect Dis*. 2014;2014:615958. https://doi.org/10.1155/2014/615958
12. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev*. 2007;20(1):133-163. https://doi.org/10.1128/CMR.00029-06
13. García-Effron G, Lee S, Park S, Cleary JD, Perlin DS. Effect of *Candida famata* (Candida flareri) on susceptibility to amphotericin B and micafungin determined by CLSI and flow cytometric methods. *Antimicrob Agents Chemother*. 2009;53(5):1617-1622. https://doi.org/10.1128/AAC.01232-08
14. Pappas PG, Kauffman CA, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48 (5):503-535. https://doi.org/10.1086/596757
15. Caria J, Leal E, Dias A, Pinheiro H, Póvoas D, Maltez F. A case of central nervous system infection by *Candida famata* in an immunosuppressed patient with HIV-1 infection. *Med Mycol Case Rep*. 2022;38:69-72. https://doi.org/10.1016/j.mmcr.2022.09.004
16. Klasko S, et al. Voriconazole for Candida bloodstream infections. *Antimicrob Agents Chemother*. 2005;49(3):1161-1166. https://doi.org/10.1128/AAC.49.3.1161-1166.2005
17. Kullberg BJ, et al. Voriconazole versus amphotericin B for the primary therapy of invasive candidiasis. *N Engl J Med*. 2005;352 (9):889-890. https://doi.org/10.1056/NEJMe058039

Case Report

Thermal Ablation and Intralesional Cisplatin Injection as Adjunct to Systemic Chemotherapy in Managing Malignant Central Airway Obstruction: A Case Report

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ABSTRACT

Endobronchial ultrasound (EBUS)-guided intralesional chemotherapy and thermal ablation using cryotherapy and electrocautery can be used for the management of malignant central airway obstruction (CAO). This is a case of a 62-year-old male presenting with cough, hoarseness, and shortness of breath. He was diagnosed with squamous cell carcinoma stage IVA (T4N2M1a), causing malignant CAO that progressed to impending respiratory failure (ECOG performance status 4). Chest CT scan findings included a left main bronchus mass measuring 3.7 x 5.8 x 5.9 cm causing complete atelectasis, a right pleural-based mass, and osteolytic destruction of the 3rd lateral ribs. Bronchoscopy showed a fungating, friable mass in the carina extending to the orifice of the right and left mainstem bronchus with 70% and 100% occlusion, respectively. A multimodality treatment approach was taken with tumor debulking by thermal ablation with cryotherapy and electrocautery, EBUS-guided intralesional cisplatin, and systemic chemotherapy. Subsequently, there was an interval decrease in the size of the tumor in multiple areas, with left lung re-expansion. The clinical symptoms of the patient significantly improved and ECOG status increased to 1. No adverse effects were noted post procedure. Intralesional cisplatin can be an effective and safe adjunct treatment in malignant CAO, alongside thermal ablation and systemic chemotherapy.

Keywords: malignant airway obstruction, intralesional chemotherapy, cisplatin, cryotherapy, non-small cell lung cancer

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INTRODUCTION

Non-small cell lung carcinoma (NSCLC) is the most common cause of malignant central airway obstruction (CAO). In unresectable cases, systemic chemotherapy is the standard of care that offers survival benefits. This can also be given with concomitant radiation therapy. However, in cases of CAO, intravenous chemotherapy alone is often inadequate in terms of disease control, and small gains are obtained at the cost of significant toxicity.[1]

Endobronchial ultrasound (EBUS)-guided intratumoral chemotherapy can be considered a new life-saving palliative method in patients with life-threatening airway obstruction. In the study of *Mehta et al*, it was demonstrated that transbronchial injection of cisplatin can be used in improving the patency of central airways that are largely or completely occluded by endobronchial malignant tumors.[2,3]

In this case report, we summarized our experience with using EBUS-guided intralesional injection of cisplatin, thermal ablation, and systemic chemotherapy as a treatment option for patients with advanced inoperable NSCLC with life-threatening CAO.

CASE PRESENTATION

A 62-year-old male with impending respiratory failure due to malignant CAO was transferred to our center for further management.

One month prior to admission, the patient experienced non-productive cough, hoarseness, and shortness of breath, with ECOG performance status 2. He was a non-smoker with a family history of esophageal and laryngeal cancer. Computed tomography (CT) scan of the chest revealed a left main bronchus mass measuring 3.7 x 5.8 x 5.9 cm causing complete atelectasis, a right pleural-based mass in the right upper hemithorax, multiple osteolytic lesions, with subcarinal and hilar involvement. The patient underwent *ultrasound-guided transthoracic needle aspiration biopsy* of the right pleural-based mass, and was advised close monitoring pending the biopsy result. The patient was eventually diagnosed as a case of squamous cell carcinoma stage IVA (T4N2M1a), causing malignant CAO. Immunohistochemistry was as follows: P40 positive, TTF1 equivocal, no mutation on EGFR, low PDL-1 (1-49%), ALK negative, and ROS1 negative. Six days prior to transfer, the patient developed progressive dyspnea at home with severe desaturations. He was admitted to another hospital where he received five sessions of radiotherapy to alleviate the symptoms of malignant CAO. Bronchoscopy for airway evaluation was advised, however, the patient opted to transfer to our center for further management.

Upon transfer, the patient was in severe respiratory distress, ECOG status 4. He was hooked to high-flow nasal cannula with fraction of inspired oxygen of 60% which partially improved the dyspnea and addressed the desaturation. He underwent fiberoptic bronchoscopy, revealing the carina infiltrated with a fungating friable mass which extended to the orifice of the right mainstem bronchus (RMB) causing 70% occlusion, and complete occlusion of the left mainstem bronchus (LMB) (Figures 1a, 1b). The patient underwent tumor debulking by thermal ablation using cryotherapy and electrocautery, resulting in visualization of the RMB. Post-procedure, oxygen support was shifted to low-flow nasal cannula, and after 24 hours, the patient was able to tolerate room air. He was discharged and later readmitted for chemotherapy.

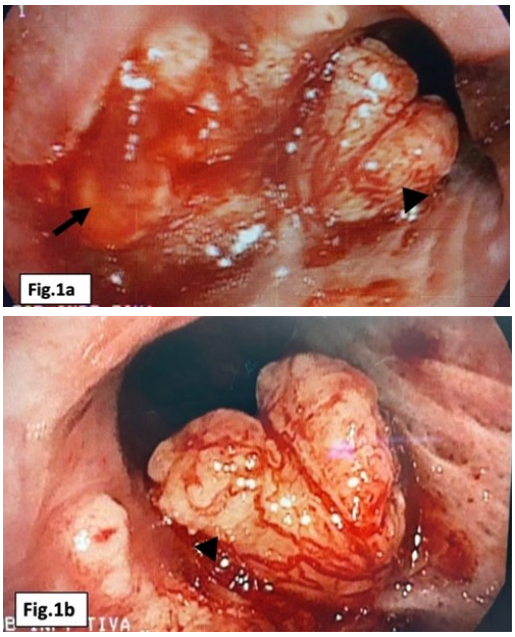

Figure 1a. Bronchoscopy showing carina infiltrated with fungating friable mass extending to the orifice of the RMB (arrow head), causing 70% occlusion. LMB (arrow) is completely occluded. **Figure 1b.** Magnified view of the mass occluding the RMB. RMB, right mainstem bronchus; LMB: left mainstem bronchus.

Table 1. Treatment timeline

Days since first biopsy confirmation of malignancy	Procedure
D30 -	Radiotherapy for 5 sessions
Transfer to our center/1st admission	
Day 36	FOB with thermal ablation using cryotherapy and electrocautery
2nd admission	
D60	Cycle 1 EBUS-guided intralesional cisplatin (10 ml: right subcarinal area, 30 ml: main mass, left)
D62	Cycle 1 gemcitabine-carboplatin
3rd admission	
D70	Cycle 2 gemcitabine
D71	Cycle 2 EBUS-guided intralesional cisplatin (10 ml: right subcarinal area, 30 ml: main mass, left)
D82	Cycle 3 EBUS-guided intralesional cisplatin (40 ml: subcarinal area)
D84	Cycle 3 gemcitabine-carboplatin
D97	Cycle 4 EBUS-guided intralesional cisplatin (40 ml: subcarinal area)
D103	Cycle 4 gemcitabine-carboplatin
5th admission	
D112	FOB surveillance with cryoablation of endobronchial mass
D114	Cycle 5 gemcitabine; subsequent chemotherapy was done as outpatient

FOB: fiberoptic bronchoscopy; EBUS: endobronchial ultrasound

Bronchoscopy was again done and EBUS-guided intralesional cisplatin was given at a dose of 40 mg (40 ml of 50 mg/50 ml cisplatin: 10 ml at right subcarinal area, 30 ml at main mass, left). Following cisplatin administration, magnesium and potassium-supplemented hydration was given. Systemic chemotherapy with gemcitabine and carboplatin was initiated three days after. The patient tolerated the procedures well and was discharged.

The patient was readmitted for subsequent cycles of chemotherapy, with delays caused by limitations in healthcare resources, among other factors. In relation to systemic chemotherapy, corresponding cycles of intralesional cisplatin were given anytime from 6 days prior to 1 day after. By the 3rd cycle, owing to prior restoration of patency of the RMB, the full dose of cisplatin was injected at the subcarinal area. The patient underwent a total of four cycles of intralesional cisplatin and five cycles of systemic chemotherapy as inpatient (gemcitabine 1200 mg/m^2 and carboplatin area under the curve 5 mg/ml min). Prior to the 5th cycle of systemic chemotherapy, the patient underwent repeat cryoablation of the bronchial mass.

Table 1 summarizes the treatment timeline. Treatment response was assessed based on ECOG, repeat chest X-ray and CT scan, and bronchoscopy (Figures 2 to 4) . The patient's performance status improved significantly from ECOG 4 to 1. Repeat chest X-ray revealed re-expansion of the atelectatic left lung (Figure 2h), and chest CT scan findings showed a decrease in the size of the left hilar/perihilar and subcarinal mass, and diminution of the endobronchial mass extension (Figure 3b). Bronchoscopy finding of more than 50% increase in the diameter of the airway lumen denoted good response to treatment (Figure 4f).

Bronchoscopic surveillance was done at three and six months post-treatment, with findings of a tumor-eroded carina with necrotic tissues; and a blunted carina, stenotic LMB, and a patent RMB, respectively. Positron emission tomography/CT scan at 10 months revealed no evidence of local tumor recurrence in the left lung, no evidence of hypermetabolic lymphadenopathies, and interval resolution of previously reported mediastinal lymph node. However, repeat chest CT scan at 12 months showed progression of bone metastases. Currently, the patient is on second-line chemotherapy with docetaxel and is alive 14 months after diagnosis. He is capable of self-care and ambulates without assistance. He has limitations in doing strenuous activities but is not dyspneic with activities of daily living and not on oxygen support.

DISCUSSION

Intralesional chemotherapy with cisplatin can improve the patency of airways occluded by endobronchial malignant tumor. It directly targets the tumor microenvironment and offers several advantages over systemic treatment for centrally -located NSCLC.[2,4,5] Cisplatin is widely used to treat lung cancer because of its ability to interfere with cell replication.[7] There are several studies on the therapeutic potential of directly injecting cisplatin (40 mg/40 mL) into lung tumors that are adjacent to the airways through an EBUS-guided intratumoral needle injection, with a survival benefit of 8 months among responders to treatment.[2,5,6,8] An effective dose of cisplatin would be possible if the drug was apportioned between five appropriately selected sites throughout the tumor rather than being delivered in its entirety at a single central site.[9] In our case, an effective dose of cisplatin was given in two sites rather than being concentrated in one site.

Based on previous publications in the field of intralesional chemotherapy, it is not merely considered an ablation technique for treatment of endobronchial tumor but also has a significant specific chemotherapeutic effect on malignant cells

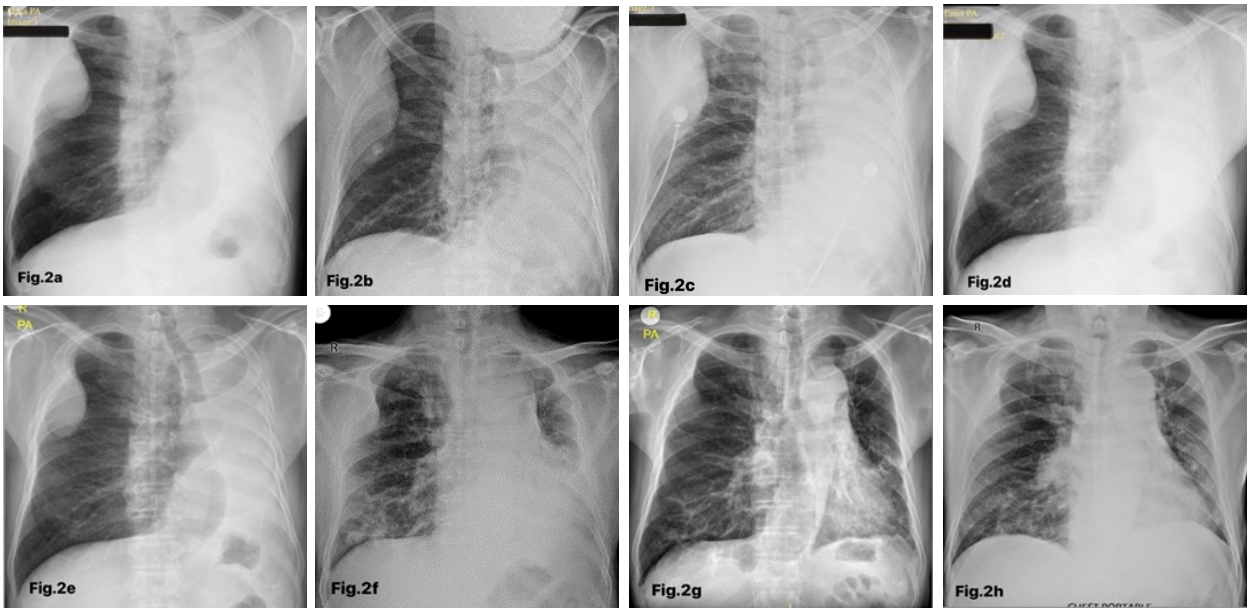

Figure 2. Serial chest X-rays during treatment course. **2a:** Baseline chest X-ray at the time of biopsy of the right upper lobe mass showing left lung atelectasis with ipsilateral mediastinal deviation, mass-like lesion in the right upper lung with lytic changes of the 3rd rib, and compensatory hyperaeration of the right lung. **2b:** Upon transfer as a case of CAO, in impending respiratory failure; no significant change noted. **2c:** Post-FOB with cryotherapy; no significant change noted. **2d to 2g:** During chemotherapy (four cycles of intralesional cisplatin as adjunct to systemic chemotherapy); with significant improvement in the opacity in the left lung with eventual re-expansion and an apparent decrease in the size of the right upper lobe pleural-based mass. **2h:** After four cycles of intralesional cisplatin with systemic chemotherapy; re-expansion of the atelectatic left lung noted. CAO, central airway obstruction; FOB, fiberoptic bronchoscopy

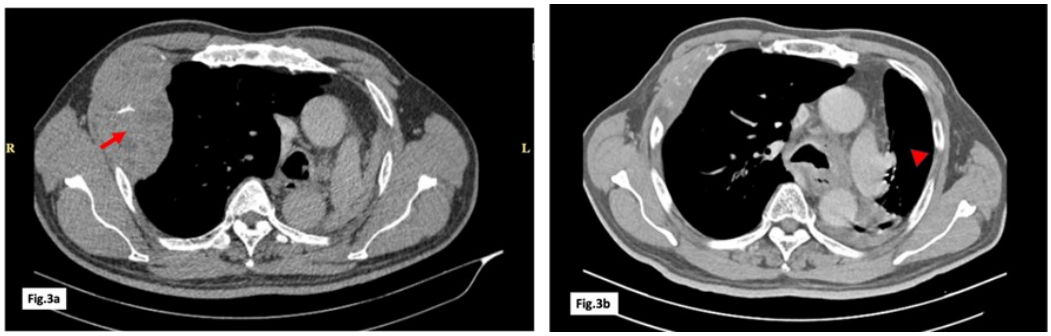

Figure 3. Chest CT scan with contrast (mediastinal view), pre- and post-treatment with thermal ablation and four cycles of intralesional cisplatin as adjunct to systemic chemotherapy. **3a:** Pre-treatment scan shows a collapsed left lung with compensatory hyperaeration of the right lung, and a solid heterogeneously-enhancing pleural-based mass (arrow) in the right upper hemithorax associated osteolytic destruction of the 3rd lateral ribs. 3b: Post-treatment scan shows an interval partial re-expansion of the left lung (arrow head) with interval decrease in the size of the pleural-based mass with lytic expansile lesion along the right 3rd rib, 6.9 x 2.8 cm in maximal axial diameter (previously 10.6 x 6.4 cm). RMB: right mainstem bronchus; LMB: left mainstem bronchus

through the localized action of cytotoxic drug.[1,3,10,11] The advantages include: precise delivery within the tumor; local concentration of drug can be 10- to 30-fold higher than could be achieved with systemic delivery to kill a greater proportion of neoplastic cells; toxic side effects which normally occur with conventional systemic chemotherapy may be avoided; and local injection of the drug can target draining lymph nodes, and disrupt the structural integrity and vascular supply of the tumor.[6,16] The procedure is contraindicated in patients with renal impairment, electrolyte imbalance, myelosuppression, and pregnancy.[12,13,14] There are reported cases of rare adverse events to intralesional chemotherapy such as mediastinitis, fistula formation, bleeding, pneumothorax, and extravasation into the airway.[15] In our case, none of these were encountered. There was also no nausea, vomiting, fever, and arrhythmia. Response to treatment is evaluated based on the patient's performance status, bronchoscopy findings, and imaging.

CONCLUSION

Intralesional injection with cisplatin can be an effective and safe therapeutic option in conjunction with tumor debulking by thermal ablation, cryotherapy, electrocautery, and systemic chemotherapy in malignant CAO. The combined local and systemic treatment improves patient's symptoms with an improvement in quality of life, especially alleviating dyspnea in end-stage lung cancer patients with malignant CAO.

Ethical Consideration

The authors declared that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

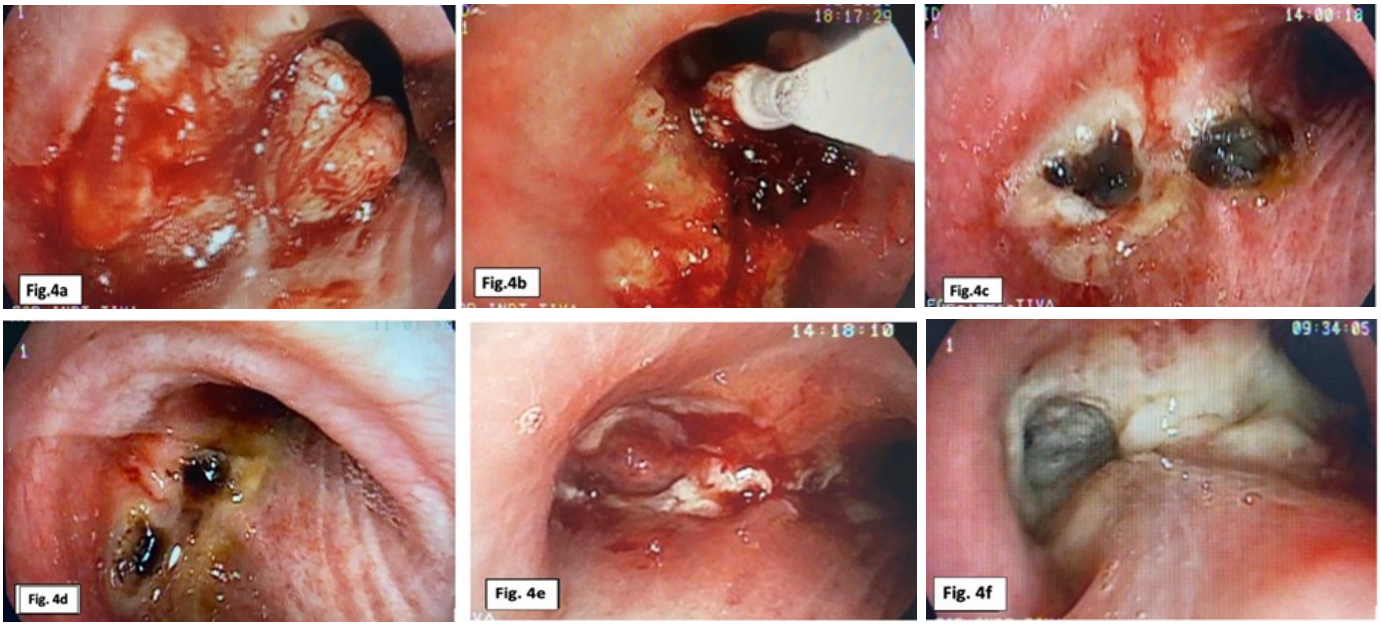

Figure 4. Bronchoscopy findings during treatment course. **4a:** Prior to FOB with thermal ablation, there was an irregularly-shaped friable mass occluding the RMB and LMB, at 70% and 100%, respectively. **4b:** Cryotherapy of the RMB and LMB. **4c:** Post-thermal ablation and cycle 1 cisplatin; irregularly-shaped necrotic mass completely obstructing the LMB extending to the opening of the RMB noted, with RMB now visualized. **4d:** For cycle 2 cisplatin; necrotic mass completely obstructing the LMB is again seen, the RMB is patent. **4e:** For cycle 3 cisplatin; no significant change in completely-occluded LMB; **4f:** For cycle 4 cisplatin; broad carina with presence of fibrin clot is noted. The LMB is now patent. FOB: fiberoptic bronchoscopy; RMB: right mainstem bronchus; LMB: left mainstem bronchus

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Authors' Disclosure
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References
1. Hohenforst-Schmidt W, Zarogoulidis P, Darwiche K, et al. Intratumoral chemotherapy for lung cancer: re-challenge current targeted therapies. *Drug Des Devel Ther*. 2013;7:571-83. https://doi.org/10.2147/DDDT.S46393
2. Mehta, HJ, Begnaud A, Penley AM, et al. Restoration of patency to central airways occluded by malignant endobronchial tumors using intratumoral injection of cisplatin. *Annals of the American Thoracic Society*. 2015;*12*(9), 1345–1350. https://doi.org/10.1513/AnnalsATS.201503-131OC
3. Celikoglu SI, Karayel T, Demirci S, Celikoglu F, Cagatay T. Direct injection of anti-cancer drugs into endobronchial tumours for palliation of major airway obstruction. *Postgrad Med J.* 1997;73 (857):159–162. https://doi.org/10.1136/pgmj.73.857.129
4. Rozman A, Grabczak EM, George V, et al. Interventional bronchoscopy in lung cancer treatment. *Breathe (Sheff)*. 2024;20 (2):230201. https://doi.org/10.1183/20734735.0201-2023
5. Khan F, Anker CJ, Garrison, G, Kinsey CM. Endobronchial ultrasound–guided transbronchial needle injection for local control of recurrent non–small cell lung cancer. *Annals of the American Thoracic Society*. 2015;12, 101–104. https://doi.org/10.1513/AnnalsATS.201408-358BC
6. DeMaio A, Sterman D. Bronchoscopic intratumoural therapies for non-small cell lung cancer. *Eur Respir Rev*. 2020;29 (156):200028. https://doi.org/10.1183/16000617.0028-2020
7. Olaussen KA, Dunant A, Fouret P, et al. DNA repair by ERCC1 in non–small-cell lung cancer and cisplatin-based adjuvant chemotherapy. *New England Journal of Medicine.* 2006;355, 983 –991. https://doi.org/10.1056/NEJMoa060570
8. Mehta HJ, Jantz MA. Endobronchial ultrasound-guided intratumoral injection of cisplatin for the treatment of isolated mediastinal recurrence of lung cancer. *J Vis Exp*. 2017; (120):54855. https://doi.org/10.3791/54855
9. Mori V, Roy GS, Bates JHT, Kinsey CM. Cisplatin pharmacodynamics following endobronchial ultrasound-guided transbronchial needle injection into lung tumors. *Sci Rep*. 2019;9 (1):6819. https://doi.org/10.1038/s41598-019-43270-y
10. Celikoglu F, Celikoglu SI, York AM, Goldberg EP. Intratumoral administration of cisplatin through a bronchoscope followed by irradiation for treatment of inoperable non-small cell obstructive lung cancer. *Lung Cancer*. 2006;51(2):225–236. https://doi.org/10.1016/j.lungcan.2005.10.012
11. Celikoglu F, Celikoglu SI, Goldberg EP. Bronchoscopic intratumoral chemotherapy of lung cancer. *Lung Cancer*. 2008;61 (1):1–12. https://doi.org/10.1016/j.lungcan.2008.03.009
12. Crona DJ, Faso A, Nishijima TF, McGraw KA, Galsky MD, Milowsky MI. A systematic review of strategies to prevent cisplatin -induced nephrotoxicity. *Oncologist*. 2017;22(5):609-619. https://doi.org/10.1634/theoncologist.2016-0319
13. Astolfi L, Ghiselli S, Guaran V, et al. Correlation of adverse effects of cisplatin administration in patients affected by solid tumours: a retrospective evaluation. *Oncol Rep*. 2013;29(4):1285-92. https://doi.org/10.3892/or.2013.2279
14. Zheng X, Zhu Y, Zhao Y, Feng S, Zheng C. Taxanes in combination with platinum derivatives for the treatment of ovarian cancer during pregnancy: A literature review. *Int J Clin Pharmacol Ther.* 2017;55(9):753-760. https://doi.org/10.5414/CP202995
15. Jang JG, Ahn JH, Lee SS. Delayed onset of mediastinitis with tracheomediastinal fistula following endobronchial ultrasound-guided transbronchial needle aspiration: A case report. *Thorac Cancer*. 2021;12(7):1134-1136. https://doi.org/10.1111/1759-7714.13888
16. Baust JG, Gage AA, Bjerklund Johansen TE, Baust JM. Mechanisms of cryoablation: clinical consequences on malignant

tumors. *Cryobiology*. 2014;68(1):1-11. https://doi.org/10.1016/j.cryobiol.2013.11.001
17. Nelson BE, Adashek JJ, Lin SH, Subbiah V. The abscopal effect in patients with cancer receiving immunotherapy. *Med.* 2023 Apr 14;4(4):233-244. https://doi.org/10.1016/j.medj.2023.02.003
18. Detterbeck FC. The eighth edition TNM stage classification for lung cancer: What does it mean on main street? *J Thorac Cardiovasc Surg.* 2018 Jan;155(1):356-359. https://doi.org/10.1016/j.jtcvs.2017.08.138

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- Guidelines and consensus statements shall not exceed 4000 words excluding figures, tables, and references.
- Unstructured abstracts of guidelines and consensus statements shall not exceed 300 words.

Feature Articles

- Invited/solicited articles from technical experts or specialists presenting up-to-date evidence-based knowledge on a particular field or topic
- Feature articles shall not exceed 1500 words excluding figures, tables, and references.
- Unstructured abstracts of feature articles shall not exceed 150 words.

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- Invited/solicited articles from technical experts or specialists expressing the author's opinion or unique viewpoint on a particular field or topic
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- Article representing opinion/s of the Editor/s on specific topics
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- Brief reports of data from original research shared by author/s to the journal
- Correspondences shall not exceed 500 words excluding references (if

any).

NOTE: Unless justified in the cover letter, manuscripts exceeding the word count may be returned to the authors for reduction before being considered for peer review.

MANUSCRIPT
Authors are strongly encouraged to use the EQUATOR Network Reporting Guidelines when writing their manuscripts.

During peer review, the same checklists will be used by external reviewers and may inform their recommendation on the manuscript.

Title
Complete title of the article shall be informative and as brief as possible (no more than 20 words

Author/s
Complete names of each author with highest academic degree(s) and complete address of a maximum of one (1) institutional affiliation per author.

Presentations in Previous Conferences/Conventions/Scientific Meetings
Listing of any meeting(s)/conference(s) where the work has been previously presented as oral report or poster, and/or any awards/distinctions. The title, venue, month, and year of the meeting/conference shall be included.

Corresponding Author
Corresponding author's name and complete contact information which includes official mailing address, telephone, and e-mail address. Personal contact information are discouraged. The corresponding author will be responsible for all questions about the manuscript. *NOTE: Only one author is to be designated as corresponding author and he/she does not need to be the first author on the manuscript.*

Appropriate footnotes for explanatory purposes or additional information may be placed with proper cross-referencing to the main text, in the following order of usage: *, **, ***

Funding Source
Information on financial support received related to the research, authorship, and/or publication of the article, if any, shall be listed, including the funding agency name and grant number. The purpose of the funding shall be described.

Abstract
Original Articles and Review Articles require a structured abstract of not more than 300 words, with the following four headings:

Background: Briefly state the problem being addressed and the purpose/s or aim/s of the study.
Methodology: State the study design (e.g., randomized clinical trial, case-control study, cross-sectional study, systematic review), setting (multi-center, institutional, etc), study population.
Results: Briefly summarize the data obtained. Results shall be accompanied by data with confidence intervals and the exact level of statistical significance.
Conclusions: Provide brief and concise conclusion(s) directly supported by the data.
NOTE: Do not place crosslinks to references in the abstract.

Case Reports/Case Series and Grand Rounds do not require a structured abstract, with a maximum of 200 words.

Keywords
At least 3 keywords (maximum of 10) should be provided. These terms are relevant to the article that readers or researchers may use to facilitate online searches in journal databases. *NOTE: Medical Subject Headings database ([MeSH] of the National Center for Biotechnology Information [NCBI] [https://www.ncbi.nlm.nih.gov/mesh/]) may be used to check if keywords provided are likely to yield search results.*

Body of the Text
For **Original Articles and Review Articles**, the manuscript shall be written following the IMRAD format (Introduction, Methodology, Results and Discussion, Conclusion).

Introduction: The Introduction shall provide a brief background for the study, to include the research question, rationale, objectives of the study, and hypothesis to be tested if any. Cite only the most pertinent past publications and shall not be an extensive review of the literature.
Methodology: Methods shall be written with sufficient detail to permit reproducibility.

- Study Design: State the study design using a phrase such as randomized or nonrandomized clinical trial, case-control study, cross-sectional study, cohort study, systematic review, meta-analysis;
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- Data and statistical analyses, to include what specific software was used for the computations.
- For Original Articles, statements regarding adherence to the Declaration of Helsinki, approval by the Institutional Review Board (IRB)/Ethics Committee, and description of the informed consent process shall be included.

Results: Results must be concise. This may include demographic data of the study population, outcomes, and measurements. Data shall be accompanied by confidence intervals (usually at the 95% interval) and exact *p-values* or other indicators of statistical significance. Negative results should also be reported.
Discussion: The discussion shall be restricted to the significant findings presented. Results should not be repeated in this section. Limitations should be stated, to include whether additional studies are required, and the implications of the results.
Conclusion/s: The conclusion(s) shall be directly supported by the results and shall state how the study addresses the objectives. Overgeneralization and speculation are discouraged.

For **Case Reports/Series and Grand Rounds**, the manuscript should contain the following general sections: Introduction, Case Presentation, Discussion, and Conclusion.

Introduction: The Introduction shall provide a brief summary of what is unique about the case and what it adds to the scientific literature.
Case Presentation: The Case Presentation shall include the patient history, physical examination, test results, differential diagnoses, diagnosis, treatment, and, when available, the course on follow-up and outcomes.
Discussion: This section should contain the discussion of the diagnosed condition, including the treatment options and managements, as in other clinical manuscripts. The strengths and limitations of the case should be stated.
Conclusion: The conclusion shall provide readers with the learning points gathered from the case report/series or grand rounds.

For **Grand Rounds**, the body of the text, including commentaries by specialty experts (discussants) should be edited from the presentation for clarity and conformity with the length guidelines described above. The names of the discussants should be reflected in the commentary, along with relevant identifiers (e.g., ***Dr. Juan Dela Cruz, Pulmonologist:*** <commentary>).

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All abbreviations shall be spelled out once (i.e., the first time they are mentioned in the text), followed by the abbreviation enclosed in parentheses.

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Measurements
All measurements and weights shall be expressed in SI units.

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Use generic names only in the text body. State the trade name of a particular drug cited in parentheses including the manufacturer's name, city, state and/or country when first mentioned in the text.

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With regard to instruments or equipment utilized in the study, enclose in parentheses the specific model, manufacturer's name, city, state and/or

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Potential conflicts of interest where existing, shall be disclosed. This includes but is not limited to: ownership, employment, research support (including provision of equipment or materials), involvement as speaker, consultant, or any other financial relationship or arrangement with manufacturers, companies or suppliers. Such disclosure will indicate whether the person and/or his/her immediate family has any financial relationship with pharmaceutical companies, medical equipment manufacturers, biomedical device manufacturers, or any companies with significant involvement in the field of health care.

Acknowledgments
Contributors to the work who do not fulfill all of the authorship criteria shall be acknowledged in this section following the Contributor Role Taxonomy.

Tables, Figures, Illustrations and Photographs
Tables
All tables shall be embedded within the body of the text at the appropriate points.

Only tables cited in the text should be included. All tables should be called out in the text and shall be numbered in ascending order depending on the sequence they were referred to in the text. A different order for tables and figures is to be used. Symbols are * † ‡ § ¶.

Table titles must be placed on top of the table.

Headings within the table must be bold-faced. Columns should be clearly labeled, including units of measure.

Explanatory notes or legends should be written at the bottom of the table or figure. All abbreviations should also be explained.

Footnotes may be placed at the bottom of the table if there is a need to make the table understandable that will not easily fit into the table title or data cells.

Figures (Graphs, Illustrations, and Photographs)
All figures shall be embedded within the body of the text at the appropriate points.

Each figure must be numbered consecutively in Arabic numerals by order of citation in the text. Each shall have a brief explanatory legend as necessary. Legends must identify all symbols or letters that appear on the prints. Any figure that has been published elsewhere or adapted shall have an acknowledgement to the original source. A copy of the release to publish the figure signed by the copyright holder must also be submitted.

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Modifications, such as cropping, changes in color, orientation, or placement of arrows or shapes, should be disclosed.

Arrows or other indicators used to identify key structures in illustrations and photographs should be part of the picture and not pasted as a separate object.

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Graphs may be submitted in "PowerPoint" or "Excel" format. Raw data may be requested by the Editorial Board for verification of computations.

Illustrations
Illustrations must be professionally rendered with appropriate labels.

Photographs
Photographs (clinical photographs, fluorescein angiograms, computed tomography [CT] scans, magnetic resonance imaging [MRI], X-ray, photomicrographs, transmission/scanning electron micrographs [TEM/SEM], graphs, etc.) shall have a resolution of at least 600 dpi. Photographs may be in black and white, or submitted in full color.

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Supplementary Material
Supporting material that cannot be included in the publication of the manuscript for reasons of space but is complementary and directly relevant to the manuscript content, can be made available online as supplementary material. These may include additional figures or tables, data sets, or detailed methods.

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Authors are responsible for the accuracy and completeness of their references and for correct text citations. All references should be identified at the appropriate parts of the text using Arabic numerals as superscript, cross-referenced in consecutive order in the list of references.

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On behalf of all the authors, I shall act as the corresponding author with the journal from hereon.

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Philippine Journal of CHEST DISEASES

The official publication of the Philippine College of Chest Physicians

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Philippine Journal of CHEST DISEASES
The official publication of the Philippine College of Chest Physicians

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It is the commitment of the **Philippine Journal of Chest Diseases** to ensure that patient rights to confidentiality and privacy are observed as part of its ethical publication practices. For case reports, case series, and grand rounds to be accepted by the **Philippine Journal of Chest Diseases**, the author/s must document that patients or patients' legal guardian/relative have provided informed consent to publish information about them in the journal. The completely accomplished Informed Consent Form shall be scanned and submitted along with the manuscript. **No manuscript shall be received without the form.**

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Further, we appreciate the thoughtful comments and efforts of the following reviewers of 2024:

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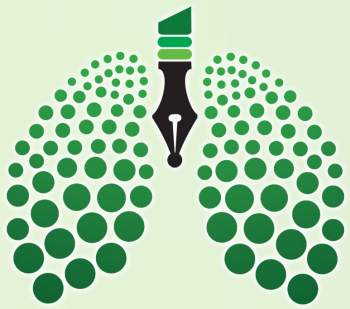

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