CONSENSUS PERSPECTIVE

A Perspective Summary of the ISHLT Consensus Statement on Acute Lung Allograft Dysfunction (ALAD)

Stephen Juvet,[a] Gregory I. Snell,[b] Saskia Bos,[c] Marie M. Budev,[d] John R. Greenland,[e] Kieran Halloran,[f] Sandra Lindstedt,[g] Laurie D. Snyder,[h] Rayid Abdulqawi,[i] Atefeh Abedini,[j] Selim M. Arcasoy,[k] Meghan Aversa,[a] Alberto Benazzo,[l] Daniel R. Calabrese,[m] Fiorella Calabrese,[n] Marlene Cano,[o] Kevin Chan,[p] Satish Chandrashekaran,[q] David Darley,[r] Amir Emtiazjoo,[s] Tara Fallah,[t] Laurent Godinas,[u] Rene Hage,[v] Don Hayes, Jr.,[w] Howard J. Huang,[x] Jana Kleinerova,[y] Sakhee Kotecha,[b] Akshay Kumar,[z] Francesca Lunardi,[n] Jorge Mallea,[aa] Tereza Martinu,[a] Federica Meloni,[n] Anoop Mohandas,[ab] Eric D. Morrell,[ac] Arun Nair,[ad] Rene Novysedlak,[ae] Michael Perch,[af] Federica Pezzuto,[n] Clement Picard,[ag] Peter Riddell,[y] Anja C. Roden,[ah] Justin P. Rosenheck,[ai] Julie Semenchuk,[a] Unmil Shah,[aj] Heather Strah,[ak] Laneshia K. Tague,[o] Rade Tomic,[al] Anil J. Trindade,[am] Katherine Vandervest,[an] Geert M. Verleden,[ao] Glen Westall,[b] and Ciara M. Shaver,[am]

[a]Toronto Lung Transplant Program, Ajmera Transplant Centre, University Health Network, and Department of Medicine, University of Toronto, Toronto, Canada; [b]Lung Transplant Service, Alfred Hospital, Melbourne, Australia; [c]Department of Respiratory Diseases, University Hospitals Leuven, Leuven, Belgium, and Laboratory of Respiratory Diseases and Thoracic Surgery (BREATHE), Department of CHROMETA, KU Leuven, Leuven, Belgium; [d]Department of Pulmonary, Integrated Hospital Care Institute, Lerner College of Medicine, Cleveland Clinic, Cleveland, OH; [e]Department of Medicine, University of California, San Francisco, CA; [f]Department of Medicine, University of Alberta, Edmonton, Canada; [g]Department of Cardiothoracic Surgery and Transplantation, Lund University Hospital, Lund, Sweden; [h]Department of Medicine, Duke University, Durham, NC; [i]Lung Health Centre Department, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia and College of Medicine, Alfaisal University, Riyadh, Saudi Arabia; [j]Masih Daneshvari Hospital, Tehran, Iran; [k]Columbia University Lung Transplant Program, Department of Medicine, New York-Presbyterian Hospital, New York, NY; [l]Department of Thoracic Surgery, Medical University of Vienna, Vienna, Austria; [m]Department of Medicine, University of California, San Francisco, CA, USA and Medical Service, San Francisco VA Medical Center, San Francisco, CA; [n]Department of Molecular Medicine, University of Pavia, Pavia, Italy; [o]Department of Medicine, Washington University in St. Louis, Saint Louis, MO; [p]Department of Internal Medicine, University of Michigan, Ann Arbor, MI; [q]Department of Medicine, University of South Florida, Tampa General Hospital, Tampa, FL; [r]St Vincent's Healthcare Campus, University of New South Wales, Sydney, Australia; [s]Department of Medicine, University of Florida, Gainesville, FL; [t]Department of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, OH; [u]University Hospitals Leuven, Leuven, Belgium; [v]Division of Pulmonology, University Hospital Zurich, Zurich, Switzerland; [w]Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH; [x]Department of Medicine, Houston Methodist Hospital, Houston, TX; [y]Mater Misericordiae University Hospital, Dublin, Ireland; [z]Department of Cardiothoracic Surgery, New York University Langone Health, New York, NY; [aa]Department of Critical Care and Department of Transplantation, Mayo Clinic Florida, Jacksonville, FL; [ab]KIMS Hospital Secunderabad, Secunderabad, India; [ac]Department of Medicine, University of Washington, Seattle, WA; [ad]Institute of Transplantation, Freeman Hospital, Newcastle upon Tyne, United Kingdom; [ae]3rd Department of Surgery, First Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czech Republic; [af]Department of Cardiology and Department of Clinical Medicine, Rigshospitalet, Copenhagen, Denmark; [ag]Respiratory and Lung Transplantation Unit, Foch Hospital, Suresnes, France; [ah]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN; [ai]Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, OH; [aj]Heart & Lung Transplant Department, KIMS, Secunderabad, Telangana, India, and Sir HN Reliance Hospital, Mumbai, India; [ak]Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE; [al]Department of Medicine, University of Chicago, Chicago, IL; [am]Department of Medicine, Vanderbilt University Medical Center, Nashville, TN; [an]Lung Transplant Program, Baylor University Medical Center, Dallas, TX; [ao]Department of Lung Transplantation, Antwerp University Hospital, Edegem, Belgium.

DOI of original article: https://doi.org/10.1016/j.healun.2026.02.1677

Abbreviations: ALAD, Acute Lung Allograft Dysfunction; CLAD, Chronic Lung Allograft Dysfunction; FEV_1, Forced expiratory volume in one second

https://doi.org/10.1016/j.healun.2026.02.1676

1. INTRODUCTION

Chronic Lung Allograft Dysfunction (CLAD) is the major barrier to long-term survival post-lung transplantation and is defined primarily by spirometric assessment. However, because substantial and potentially irreversible pathology may develop before the diagnostic criteria for CLAD are met, it is critical to identify lung transplant recipients at high risk for lung function decline that might benefit from early therapeutic interventions to reverse ongoing injury. Equally, CLAD progression may result from similar acute insults after the diagnosis of CLAD is established. To this end, to evaluate these acute events, the syndrome of Acute Lung Allograft Dysfunction (ALAD) was proposed.

ALAD has increasingly become a recognized but inconsistently defined clinical entity within the field of lung transplantation. The recently published ISHLT Consensus Statement on ALAD aims to address the clinical and research implications of this condition by providing a structured framework for its definition, diagnostic approach, treatment considerations, and research priorities.[1] This Perspective Piece draws attention to the critical summary points of this peer-reviewed Delphi Consensus process.[2] The Consensus was formed through a comprehensive process involving international multidisciplinary experts, including transplant physicians, immunologists, pathologists, pharmacists, and scientists. The group were challenged to create a novel definition of ALAD with very limited pre-existing literature or prior concordance. Clinicians and researchers are encouraged to consult the full consensus document for a comprehensive overview of ALAD, including the methodology employed and areas of both consensus and uncertainty.[1]

2. TOP ALAD FEATURES AND MESSAGES

1. ALAD is now proposed as a distinct clinical syndrome separate from primary graft dysfunction (PGD) and CLAD.[3,4]
2. The document outlines a tiered definition of ALAD based on spirometric decline and clinical symptoms, recognizing the limitations of spirometry alone. While a ≥ 10% decline in FEV_1 remains the primary spirometric criterion, the statement acknowledges situations where spirometry may be impractical or simply unavailable, advocating for the use of supplemental oxygen needs, symptoms, and imaging findings to support the diagnosis.
3. ALAD can have many potential causes.[5] The etiologies of ALAD are classified into alloimmune, non-alloimmune, and idiopathic categories, with practical recognition of the possibility of overlapping or multiple concurrent mechanisms.
4. A flexible diagnostic approach is suggested, focusing on history, spirometry, blood work, imaging and bronchoscopy where appropriate, but not uniformly mandating exhaustive testing for all cases.
5. Management strategies are stratified by ALAD severity, emphasizing expedited diagnostics and therapy in select cases. Rapidly progressive ALAD is notably associated with increased mortality and warrants urgent, often empiric antibiotics or immunosuppressive therapies.
6. One of the most critical implications of ALAD is its potential to initiate, or at least signal, the early stages of CLAD. Potentially, even reversible ALAD episodes warrant close follow-up and may justify preemptive therapeutic therapy to prevent long-term damage.
7. Research gaps are acknowledged, particularly regarding validation of the proposed ALAD definition and its utility as a clinical trial endpoint. Spirometric cutoffs, the relevance of the ALAD timeline, and clinical trajectory after ALAD diagnosis, are all appropriate clinically relevant variables to explore further. Further discussion is required regarding the validity of including each contributing etiology in the definition.
8. The consensus highlights the importance of defining phenotypes and pathophysiological underpinnings to guide future biomarker and therapeutic approaches.
9. A call is made for international collaboration and prospective cohort studies to refine the diagnostic, phenotypic and management strategies for ALAD. Prognostic studies and trials of novel therapies now have a starting point.

3. CONCLUSION

The ISHLT Consensus Statement on ALAD represents an important step in standardizing our understanding of acute graft dysfunction in lung transplant recipients. By proposing a clear, yet adaptable framework, this document sets the stage for benchmarking, road testing and coordinated research efforts across the lung

transplant community. The consensus document underscores the importance of recognizing ALAD early and creating management strategies to mitigate long-term graft damage, potentially in the form of CLAD. As with any novel clinical definition, ongoing validation and refinement of the recommendations will be necessary. We encourage clinicians and investigators to engage with the full document and consider how its principles can be integrated into both routine practice and future study design.

FUNDING SOURCES

The authors received no funding support for this document.

DISCLOSURES

Listed in Appendix 1 of (1).

References

1. Juvet S, Snell G, Bos S, et al. ISHLT Consensus Statement on Acute Lung Allograft Dysfunction (ALAD): definition, etiology, diagnostic and therapeutic approaches, and research priorities. J Heart Lung Transpl 2025. (N/A).

2. Diamond IR, Grant RC, Feldman BM, et al. Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. J Clin Epidemiol 2014;67:401-9.

3. Todd JL, Weigt SS, Neely ML, et al. Prognosis and risks for probable chronic lung allograft dysfunction: a prospective multicenter study. Am J Respir Crit care Med 2025;211:239-47.

4. Keller MB, Tian X, Jang MK, et al. Higher molecular injury at diagnosis of acute cellular rejection increases the risk of lung allograft failure: a clinical trial. Am J Respir Crit care Med 2024;209:1238-45.

5. Mazo C, Pont T, Ballesteros MA, et al. Pneumonia versus graft dysfunction as the cause of acute respiratory failure after lung transplant: a 4-year multicentre prospective study in 153 adults requiring intensive care admission. Eur Respir J: J Eur Soc Clin Respir Physiol 2019;54:1801512.